About the Calibration and PET Performance of a preclinical PET/MRI insert equipped with digital Silicon Photomultipliers

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1. Abstract

Positron Emission Tomography (PET) is a functional imaging modality that offers a high sensitivity to image metabolic processes with a wide range of application from oncology, cardiology to neurology and more. As it is a tracer-based imaging modality it only gives limited anatomical information. Therefore, PET is often combined with another imaging modality, e.g. X-ray computed tomography or magnetic resonance imaging (MRI). A combined PET/MRI device can be used for true simultaneous image acquisition with both modalities. The integration is a technical challenge as the PET must be operable inside the strong magnetic field used by the MRI and tolerate time-varying magnetic fields as well. This poses some requirements on the light detectors employed in the scintillation gamma detector for PET. Commonly, solid-state photosensors are being used in PET/MRI applications which can be operated in the MRI environment. Furthermore, all readout electronics must be designed with special consideration in order to keep the interference between the two modalities at a minimum.

Our group developed a PET insert aimed at being operated inside a 3-T clinical MRI providing a preclinical PET/MRI device with a bore size fitting small rodents. The photosensor employed is a digital silicon photo-multipliers (dSiPMs), the latest evolutionary step in silicon-based photo detectors. The readout architecture allows to store the raw sensor data of the dSiPMs and to use an offline and software-based calibration and processing approach.

In this thesis, the calibration procedure and the employed algorithms in order to process the dSiPM raw data to PET relevant events are presented. This process includes the energy calibration, timer calibration and time alignment of the whole system. Furthermore, the influence of operating parameters as well as dSiPM configuration parameters on the stand-alone PET performance was evaluated.

A second, clinically motivated scintillator geometry was used to investigate the PET performance during MRI operation. This readout scheme allows to achieve a better energy and timing resolution and is more sensitive to any induced degradations. Especially, for gradient-intense MRI sequence a vulnerability could be shown. While this degradation is only of minor importance for normal MRI imaging sequence, a further integration of the PET system with the MRI might show stronger interference. Therefore, a hardware component was improved and compared to the old version where the vulnerability to gradient switching could be reduced to a non-measurable level.

The employed system and used algorithms proved to deliver a PET performance which is on level or even better than the commercially available systems today outside and inside a simultaneously operated MRI.
2. Zusammenfassung


Unserer Gruppe hat ein PET-Detektor entwickelt, welcher in einem klinischen 3 T MRT betrieben werden kann und damit ein präklinisches PET/MRT System bereitstellt mit welchem kleine Nagetiere untersucht werden können. Als Photodetektor wird ein digitaler Siliziumphotomultiplier (dSiPM) eingesetzt, die neueste Generation von siliziumbasierten Photosensoren. Die Ausleseplattform erlaubt das Speichern der dSiPM-Rohdaten und damit das Anwenden einer offline und softwarebasierten Kalibrations- und Verarbeitungssoftware.


Das eingesetzte System und die verwendeten Algorithmen zeigen eine PET-Performance die auf einem Niveau oder sogar besser ist als die von heute kommerziell erhältlichen Systemen sowohl außerhalb als auch in einem MRT.
3. Introduction

Positron emission tomography (PET) is a functional imaging modality that offers a high sensitivity to image metabolic processes. The positron emitter is coupled to a chemical compound which is introduced to the metabolic system of the specimen (Bailey 2005). This labeled compound is called tracer and PET tries to image the distribution as a function of position and time. Applications range from oncology (Rohren et al. 2004) to cardiology (Keng 2004) to neurology (Nordberg et al. 2010; Bohnen et al. 2012) and more. As a tracer-based imaging modality, PET images contain only limited anatomic information. This complementary information is commonly added by combining PET with a second imaging modality that provides anatomical information (D. W. Townsend et al. 2004; Bar-Shalom et al. 2003).

An introduction to the combination of PET with other imaging modalities is given in section 4.3 with focus on the combination with magnetic resonance imaging (MRI). Until recently, conventional PET-only detectors were based on photomultiplier tubes (Humm et al. 2003; Surti et al. 2007) which cannot be operated inside strong magnetic fields required by MRI. Therefore, silicon-based photo detectors are commonly used for PET/MRI applications. An overview of designs that combine PET with MRI can be found in Pichler et al. (2008), Zaidi and Del Guerra (2011), Disselhorst et al. (2014), and Vandenberghe and Marsden (2015).

Our group developed a PET insert for preclinical imaging based on digital silicon photo-multipliers (dSiPMs), the latest evolutionary step in silicon-based photo detectors, which is designed to be operable in an MRI system (The system is presented in chapter 5). The underlying platform employing analogue SiPMs, Hyperion-I, has been evaluated in Weissler et al. (2014). The successor of the platform, Hyperion-II D, which is used in this thesis, was first presented in Weissler et al. (2012b). The system is aimed at imaging animals up to the size of rabbits. Details of the integration and the comparison of the analogue and digital version of the Hyperion platform are presented in Weissler (2016).

This thesis focuses primarily on the PET side of the Hyperion-II D insert. A fundamental introduction to the physics and phenomena involved in PET and a very brief discussion of MRI and the challenges in combining the two modalities is given in chapter 4. The system is presented in detail chapter 5. chapter 6 presents the calibration and data processing techniques used with the Hyperion-II D scanner employing a preclinical detector configuration (detector configurations are discussed in section 5.1.1). Using these techniques the PET stand-alone performance of this configuration is evaluated in chapter 7. In chapter 9 and chapter 10 a PET/MRI interference investigation
is presented with focus on the PET performance degradation during gradient-intense MRI operation. For these studies a clinical scintillator configuration is used which provides a superior PET performance in terms of energy and timing resolution and therefore is more sensitive to any degradations caused by the simultaneous MRI acquisition. The later study (presented in chapter 10) evaluates an upgraded hardware platform and shows that any previously found PET performance degradations could be completely eliminated even for the most extreme MRI conditions. The presented studies cover only a selection of the possible PET/MRI interference investigations. A more detailed and much broader study of the interference between the two modalities, covering several further phenomena, is presented in Wehner (2016).

3.1. Previous Publications

The work presented in this thesis has already been published in great parts in the following peer-reviewed journal articles.


D. Schug et al. (2015c). “PET performance and MRI compatibility evaluation of a digital, ToF-capable PET/MRI insert equipped with clinical scintillators”.
In: Physics in Medicine and Biology 60.18, p. 7045. DOI: 10.1088/0031-9155/60/18/7045


Content of these articles, of which I am the main author, has been copied, rearranged, reformulated and sections and details have been added to write this thesis. As it is not feasible to mark each text passage or fraction that has been published before, explicit citations are not given. No text has been copied from other papers as the ones listed above. At the beginning of each chapter it is again stated on which articles the particular chapter is based on. The sources for previously published figures and tables is clearly indicated and citations are given.

The following publications of which I am the main author are not discussed in this thesis. They present smaller topics related to the light-detection technology presented
3.1. Previous Publications

in this thesis and a proposition of a calibration method that can be applied to a large variety of geometries of scintillating gamma detectors.

D. Schug et al. (2013). “Fast and unbiased 3D calibration method of arbitrary scintillator based PET detectors”. In: Nuclear Science Symposium and Medical Imaging Conference (NSS/MIC), 2013 IEEE, pp. 1–4. DOI: 10.1109/NSSMIC.2013.6829084

D. Schug et al. (2012). “First Evaluations of the Neighbor Logic of the digital SiPM tile”. In: Nuclear Science Symposium and Medical Imaging Conference (NSS/MIC), 2012 IEEE, p. 2817. DOI: 10.1109/NSSMIC.2012.6551642

In the supplementary section A.1 all co-authored publications are listed which I contributed to during my PhD.
4. Fundamentals

This chapter gives an overview over the basic principles and the physical phenomena involved in the image acquisition process in PET. MRI is briefly introduced and the integration of PET with MRI is discussed shortly.

The PET basics are based on the following books:


4.1. Positron Emission Tomography

4.1.1. Basic Principle

A positron emitter is coupled to a chemical compound which is introduced to the metabolic system of a patient or specimen. This labeled compound is called tracer and PET tries to visualize and quantify its distribution as a function of position and time.

The tracer constantly decays and emits positrons which annihilate in the surrounding material causing two high energetic gamma rays to be emitted in opposite directions. If these two gammas are detected by a detector arrangement surrounding the specimen a line-of-response (LOR) connecting the two points of detection defines the line in space on which the annihilation took place. If a precise time difference between the two gamma detections can be measured the annihilation can even be placed, with a given uncertainty, along the LOR. One needs to measure multiple annihilations, respectively LORs, in order to perform a tomographic reconstruction and derive the underlying spatial distribution of the tracer.

In the following, a brief introduction into the fundamentals of the physics and technologies involved in a PET is given.
4. Fundamentals

4.1.2. Tracer

Atoms are built up by nucleons, the neutrons and protons. The number of positively charged protons defines the element and is called atomic number (Z). The total number of nucleons in an atom is called mass number (A). All the atomic configurations with the same Z are called isotopes of an element. The unstable isotopes of an element which undergo a radioactive decay and thereby change their configuration of protons and neutrons are called radioisotopes. One depicts an isotope of an element with the symbol X as $^{A}_{Z}X$ to describe it with its atomic number and mass number.

In PET positron-emitting isotopes are coupled to molecules which are then called tracers. These radioisotopes have an abundance of protons which may lead to the emission of a positron ($e^+$) and a neutrino ($\nu$) in a $\beta^+$-decay (Equation 4.1). The neutrino is not very important for PET as it can not be measured easily. It is only important as it leads to a non-monoenergetic emission of the positron.

$$^{A}_{Z}X \rightarrow ^{A-1}_{Z-1}Y + e^+ + \nu \quad (4.1)$$

The emitted positron is the antiparticle of the electron with a positive charge and the same rest mass of approximately 511 keV.

There might be a competing decay mode, the electron capture (EC), in which an electron is incorporated into the nucleus of the atom reducing its atomic number.

$$^{A}_{Z}X \rightarrow ^{A}_{Z-1}Y + \nu \quad (4.2)$$

A large variety of PET tracers is available today (Schwaiger and Wester 2011). The two radioisotopes used in this work are $^{18}_{9}F$ and $^{22}_{11}Na$.

4.1.2.1. $^{18}_{9}F$

$^{18}_{9}F$ is the standard radioisotope used in clinical PET studies. The most common tracer is the fludeoxyglucose labeled with $^{18}_{9}F$ ($^{18}_{9}F$-FDG or in the context of this work just FDG). The uptake of FDG marks the uptake of glucose and thus indicates areas of a high glucose metabolism which can be used to visualize tumors or to image brain activity (Kelloff et al. 2005). The decay modes of $^{18}_{9}F$ are listed in Fig. 4.1. It decays with an half life of 109.77 min via a $\beta^+$-decay in 96.7% of the cases. The mean kinetic energy of the emitted positron is $E_{\text{mean}} = 250$ keV and the maximum kinetic energy is $E_{\text{max}} = 635$ keV. The other decays are by EC without the emission of a positron.

4.1.2.2. $^{22}_{11}Na$

$^{22}_{11}Na$ is often used as a test source for calibration or test sources used in the laboratory. It can be packaged into closed sources and its relatively long half-life of 2.6 yr allows for several years of storage and usage. It decays in only 0.06% of the cases directly to the ground state of $^{22}_{11}Ne$ via a $\beta^+$-decay with a mean kinetic energy of $E_{\text{mean}} = 835$ keV.
4.1. Positron Emission Tomography

Figure 4.1.: Decay modes of $^{18}$F. 96.7% decay via $\beta^+$-decay and 3.3% decay without the emission of any radiation via EC. (reprinted from S. Cherry et al. (2012), Copyright (2012), with permission from Elsevier)
and an end-point kinetic energy of $E_{\text{max}} = 1830$ keV. The other two decay modes include an excited $^{22}\text{Ne}$ state which de-excites via emission of a gamma ray with an energy of 1274.5 keV. About 90% of the decays of $^{22}\text{Na}$ are via the excited state by a $\beta^+\gamma$-decay with a mean kinetic energy of 215 keV and an an maximum kinetic positron energy of 542 keV. The other 10% of the decays is by EC via the excited state. To conclude, in almost 100% of the $^{22}\text{Na}$ decays a 1274.5 keV gamma ray is emitted and in 90% of the decays an additional positron is emitted. This has to be accounted for, if a $^{22}\text{Na}$ probe is used to measure the sensitivity of a PET for coincident gammas.

Figure 4.2.: Decay modes of $^{22}\text{Na}$. (reprinted from S. Cherry et al. (2012), Copyright (2012), with permission from Elsevier)
4.1.2.3. Positron Emission and Annihilation

As described at the beginning of this section, the positron is emitted with a kinetic energy following the beta spectrum of the three-body $\beta^+$-decay (Fig. 4.3).

Figure 4.3.: Theoretical positron kinetic energy spectra for $^{18}$F, $^{11}$C, $^{13}$N and $^{15}$O (normalized to have equal area under the curves). (reprinted from Levin and E. J. Hoffman (1999), © Institute of Physics and Engineering in Medicine. Reproduced by permission of IOP Publishing. All rights reserved.)

4.1.2.3.1. Positron Range The positron thermalizes in the surrounding material before it annihilates with an electron (Fig. 4.4). The path length that it travels during this process is called the positron range and depends on the tracer, receptively the kinetic energy of the positron (Fig. 4.5 shows the distribution for $^{18}$F and Fig. 4.6 shows the root mean square of the positron range for different tracers). It is also influenced by the properties of the surrounding material and the presence of electro-magnetic fields. The positron range causes a fundamental blurring of the PET resolution ($R_{\text{range}}$) that can not be circumvented.

4.1.2.3.2. Acollinearity The positron either annihilates directly with an electron or an intermediate bound state is formed which is called positronium. In the annihilation process the rest mass of the positron and electron is converted to energy which is $2 \times 511 \text{ keV} = 1022 \text{ keV}$ (Fig. 4.4). As the energy and momentum has to be conserved in the annihilation, the predominant channel is the emission of two gammas in opposing directions each with an energy of 511 keV. This is only exactly true in the center-of-mass frame of the positron and electron, neglecting a possible kinetic center-of-mass energy. The center-of-mass has a small rest momentum with respect to the laboratory frame and therefore a boost of the two gammas can be observed which leads to a small
Figure 4.4.: Blurring caused by positron range effects. The perpendicular distance from the decaying atom to the line defined by the two 511-keV annihilation photons is referred to as the effective positron range. (reprinted from S. Cherry et al. (2012), Copyright (2012), with permission from Elsevier)

Figure 4.5.: Results of Monte Carlo simulations showing the distribution of annihilation sites for positron-emitting point sources in water for $^{18}$F ($E_{\text{max}} = 635$ keV). (reprinted from S. Cherry et al. (2012), Copyright (2012), with permission from Elsevier, originally from Levin and E. J. Hoffman (1999))
deviation from the 180° angle between the two gammas and also a small deviation in their energy from 511 keV (Fig. 4.7). This so called acollinearity leads to a deviation from the back-to-back emission that can be described with a distribution of the angle between the two gammas around 0.25° with a full width at half maximum (FWHM) of approximately 0.5°. The distribution of the angle and the energy is shown in Fig. 4.8 for one dimension (for details and definition of the angle of that plot see Shibuya et al. (2007)).

For a ring geometry of a PET the FWHM of the system resolution caused by the acollinearity $R_{acol}$ can be approximated as a function of the ring diameter $D$ by Equation 4.3 (Shibuya et al. 2007).

$$R_{acol} = (0.00243 \pm 0.00014) \times D$$  \hspace{1cm} (4.3)

There are higher order channels with emissions of more than two gammas, but these are highly suppressed and occur only in about 0.003% of the cases.

Both effects, the positron range and the acollinearity, pose fundamental physical limits to the maximum spatial resolution a PET can achieve.

**4.1.3. Gamma Interaction in Matter**

The 511 keV gammas produced in the annihilation are of a higher energy compared to the energy of photons used for radiography (X-ray imaging and computed tomography)
Figure 4.7.: Acollinearity of annihilation photons resulting from residual momentum of the electron and positron at annihilation. Acollinearity leads to positioning errors. Angles are exaggerated in this example for purposes of illustration. Actual range of angles is about \( \pm 0.25^\circ \), centered at \( 0.25^\circ \). (reprinted from S. Cherry et al. (2012), Copyright (2012), with permission from Elsevier)
Figure 4.8.: Distribution of energy deviation and angular deviation of the annihilation radiation from FDG in a phantom (solid line) plotted against energy (upper x-axis) and angle (lower x-axis). The curve is compared with data of Colombino et al. (1965) directly measured for pure water at 4 °C (crosses) and 22 °C (filled circles) plotted against the angle. The number of counts are normalized to compare the shapes. (reprinted from Shibuya et al. (2007). © Institute of Physics and Engineering in Medicine. Reproduced by permission of IOP Publishing. All rights reserved.)
by almost a factor of 10. Therefore, the probability for the 511 keV gammas to traverse the specimen is higher but on the other hand they are also harder to stop and measure in the surrounding detector.

The two relevant effects of the interaction of the gammas with matter are the photoelectric effect and Compton scattering. In both interactions, the gamma transfers its energy to an electron which looses its energy via ionization in a very confined volume in the surrounding material.

4.1.3.1. Photoelectric Effect

In a photoelectric absorption (pe) the complete gamma energy is transferred to an electron of the material (Fig. 4.9). This photoelectron is ejected from the bound state in an atom resulting in a kinetic energy that is equal to the gamma energy minus the binding energy of the photoelectron. The binding energy is consumed for the process of ejection from the bound state in the atom. If the vacant electron position is filled by a free electron the binding energy is again emitted as a gamma with the energy equal to the binding energy, which is typically in the order of a few tens of keV and depends on the atom and the exact position of the vacant electron position. This gamma is absorbed again in the surrounding material as the mean free path length is much shorter for this lower energy. Therefore, the total initial gamma energy is deposited in the material in a very confined region. The probability of a photoelectric absorption is dependent on the gamma’s energy and on the atomic number $Z$ of the material. The cross-section at 511 keV can be approximated by

$$\sigma_{\text{pe}}(E_{\gamma} = 511 \text{ keV}) \propto Z^{3.4}.$$ 

For a given material the probability for photoelectric absorption declines towards higher energies ($\sigma_{\text{pe}} \propto E_{\gamma}^{-3.5}$), but it increases stepwise if the gamma energy suffices to ionize a further electron of a shell with a higher binding energy (see e.g. Fig. 4.13).

![Figure 4.9.](image.png)

Figure 4.9.: Schematic representation of the photoelectric effect. The incident photon transfers its energy to a photoelectron and disappears. (reprinted from S. Cherry et al. (2012), Copyright (2012), with permission from Elsevier)
4.1. Compton Scattering

In a Compton scattering (sc) only a part of the gamma’s energy is transferred to an electron (Fig. 4.10). The gamma changes its direction (scatter angle $\theta$) which is only dependent on its energy after the scattering process ($E_{\text{sc}}$) if free or loosely bound electrons are assumed.

$$E_{\text{sc}} = \frac{m_e}{E_{\gamma}} + 1 - \cos \theta$$  \hspace{1cm} (4.4)

Using Equation 4.4 one can define for the ratio of the gamma energy before and after the Compton scattering:

$$P(E_{\gamma}, \theta) := \frac{E_{\text{sc}}}{E_{\gamma}} = \frac{1}{1 + (E_{\gamma}/m_e)(1 - \cos \theta)}$$  \hspace{1cm} (4.5)

The differential cross-section $\frac{d\sigma}{d\Omega}$, describing the probability of a specific angle to occur in a Compton scattering, can be computed using quantum electrodynamics. The first order solution is given by the Klein–Nishina formula:

$$\frac{d\sigma}{d\Omega} = \alpha^2 r_c^2 P(E_{\gamma}, \theta)^2 [P(E_{\gamma}, \theta) + P(E_{\gamma}, \theta)^{-1}] - 1 + \cos^2(\theta)]/2$$  \hspace{1cm} (4.6)

$\alpha$ is the fine structure constant ($\sim 1/137.04$) and $r_c = \hbar/m_e$ is the reduced Compton wavelength of the electron ($\sim 0.38616 \text{ pm}$). Fig. 4.11 shows the energy of the gamma after the Compton scattering and the differential cross-section as a function of the scattering angle for 511 keV gammas. The forward direction is clearly preferred at
these energies, meaning that the direction of the gamma after the Compton scattering is still strongly correlated to the original direction.

The difference of the incident gamma energy and the energy after the scattering is transferred to the recoil electron (re).

\[ E_{re} = E_\gamma - E_{sc} \] (4.7)

The maximum energy is transferred for an angle of 180°, a so called back-scatter. For this case the remaining gamma energy for a 511 keV-gamma (Equation 4.4) is

\[ E_{sc}(E_\gamma = 511 \text{ keV}, \theta = 180^\circ) = 170 \text{ keV} \] (4.8)

A further process for gammas interacting with matter is Rayleigh scattering, which is the coherent scattering of a gamma of a larger wavelength, or lower energy, with an atom as a whole. In this process almost no energy is transferred to the atom and only the direction of the incident gamma is changed. For PET it only plays a minor role and is not discussed any further.

### 4.1.3.3. Attenuation of Gammas in Matter

The probability that a gamma interacts with matter is a statistical process therefore the probability for an interaction is increased for a longer path of the gamma through
the material. The intensity $I$ of a beam of gammas traversing matter is attenuated depending on the path length $x$ in the material and follows an exponential distribution that can be expressed using the linear attenuation coefficient $\mu_l$.

$$I(x) = I(0)e^{-\mu_l x} \quad (4.9)$$

The attenuation coefficient is often normalized to the density of the material for comparison reasons and is then called mass attenuation coefficient.

The tissue of a human or rodent can be approximated as water in which the predominant interaction process for 511 keV gammas is Compton scattering (Fig. 4.12). If the specimen is large, meaning several tens of centimeters in diameter, a large fraction of gammas detected outside the specimen have already undergone a scattering process. These gammas can be identified if their energy can be measured with sufficient precision.

![Figure 4.12: Mass attenuation coefficient of water as a function of gamma energy. (data from Berger et al. (2010))](image)

Dense and scintillating materials with a high effective atomic number are commonly used as a detector material (more information on scintillators is given in the following section). In Fig. 4.13 the mass attenuation coefficient for LYSO, a typical PET scintillator (more information in the next section) is given. The probability for photoelectric absorption is higher compared to water but at 511 keV Compton scattering is still the predominant process. If the gamma is scattered in the detector material, this process is called detector scatter in order to distinguish it from the object scatter occurring inside the object.
4. Fundamentals

Figure 4.13.: Mass attenuation coefficient of Lu$_{1.8}$Y$_{0.2}$SiO$_5$ as a function of gamma energy. (data from Berger et al. (2010))

The large fraction of gammas which are either scattered in the object or in the detector material pose some requirements on the PET detectors performance as well as limitations on the maximum performance the scanner is able to achieve. A good energy resolution is needed in order to reject object scatter. The detector material must be able to stop the gammas to achieve a sufficient sensitivity and it should be thick enough to prevent detector-scattered gammas from exiting the detector material. Escaped detector-scattered gammas may lead to missing energy and make it harder to distinguish these kind of events from object-scattered gammas.

4.1.4. Gamma Detectors

The optimal gamma detector would be able to identify and distinguish each single interaction in the detector material with a precise spatial resolution, the amount of deposited energy and a timing information. This is very hard to accomplish as normally the number of readout channels as to be kept at a reasonable level. But there are detectors that can identify multiple gamma interactions up to a certain degree.

Already mentioned in the last section, a PET employs a number of gamma detector surrounding the object which shall be imaged. These gamma detectors are traditionally built from a high-density scintillator to stop the high energetic gammas and transform the gamma’s energy to optical photons. Then, these optical photons can be measured by a photo detector.
4.1.4.1. Scintillators

The molecules of scintillators are excited by the energy which is deposited by high energetic photons or ionizing particles. This excitation energy is emitted as optical photons. A good PET scintillator has a high stopping power for gammas, a high light output with only a small variation in the number of produced photons for a given amount of deposited energy and the photons should be emitted very fast after the energy deposition in order to allow for a precise measurement of the interaction time.

The scintillation mechanism of inorganic scintillators (crystals) can be explained by the electron band structure of the scintillator (Fig. 4.14). Deposited energy is used to excite electrons from the valence band to the conduction band. The energy needed for that process is equal to the energy gap ($E_g$) and is for the common scintillators in the order of a few electronvolts. This energy is emitted as an optical photon when the electron de-excites back to the valence band. The optical photons are emitted isotropically and do not carry any directional information of the primary particle. These photons would be trapped inside the scintillator material as they are reabsorbed again, the crystal is not transparent for photons with the energy of $E_g$. Therefore, impurities are introduced (this process is called doping) to the crystal in order to modify the band structure of the scintillator. These so called activator states introduce ground states slightly above the valence band and excited states slightly below the conduction band. Excited electrons can de-excite via the activator states and produce optical photons with a slightly smaller energy than $E_g$. As the number of activator states is relatively low, the scintillator is transparent for these photons to a certain degree and they can exit the material and can be measured externally. This process is also referred to as luminescence. Electrons might de-excite via a radiation-less transition, which is called quenching. Quenching and inhomogeneities in the crystal structure itself and in the light yield over the scintillator volume are one of the factors influencing the intrinsic energy resolution of a scintillator worsening it beyond the Poissonian uncertainty.

The scintillators most commonly used in PET today are bismuth germanium oxide (Bi$_4$Ge$_3$O$_{12}$, BGO), Ce doped lutetium orthosilicate (Lu$_2$SiO$_5$(Ce), LSO) or lutetium yttrium orthosilicate (Lu$_{2(1-x)}$Y$_{2x}$SiO$_5$(Ce), LYSO). LYSO can be produced with different fractions of Lu to Y. Throughout this thesis Lu$_{1.8}$Y$_{0.2}$SiO$_5$(Ce) scintillators were used.

Important properties of a scintillator are the density or effective stopping power for gammas, the ratio of the cross-section for the specific attenuation process (pe or cs), the light yield (number of optical photons produced per absorbed energy), the variation of the light output (intrinsic energy resolution), the emission spectrum, the decay time (at which point in time after the energy absorption the optical photons are emitted).

The attenuation is important as a cheap material with low cost per volume can not just be upscaled in terms of the amount of used material to deliver the same
4. Fundamentals

Figure 4.14.: Schematic diagram of the energy levels in a scintillation crystal and the mechanism of light production after energy is absorbed. The photon energy is sufficient to move a valence band electron to the conduction band. In returning to the ground state, light photons are emitted. (reprinted from Bailey (2005), with kind permission from Springer Science and Business Media)

Table 4.1.: Scintillator properties, if not stated otherwise for a gamma energy of 511 keV. The properties largely depend on the exact doping and production of the scintillators and are not to be taken as exact values. (data taken from S. R. Cherry and Dahlbom (2006), Kimble et al. (2002), and Bailey (2005))

<table>
<thead>
<tr>
<th>Parameter</th>
<th>NaI</th>
<th>BGO</th>
<th>LSO</th>
<th>Lu$<em>{1.8}$Y$</em>{0.2}$SiO$_5$</th>
<th>Lu$<em>{0.6}$Y$</em>{1.4}$SiO$_5$</th>
</tr>
</thead>
<tbody>
<tr>
<td>effective $Z$</td>
<td>50.6</td>
<td>73</td>
<td>66</td>
<td>65</td>
<td>54</td>
</tr>
<tr>
<td>Density / g/cm$^3$</td>
<td>3.67</td>
<td>7.13</td>
<td>7.4</td>
<td>7.1</td>
<td>5.4</td>
</tr>
<tr>
<td>peak emission / nm</td>
<td>410</td>
<td>480</td>
<td>420</td>
<td>420</td>
<td>420</td>
</tr>
<tr>
<td>Light output / ph.</td>
<td>19400</td>
<td>4200</td>
<td>~13000</td>
<td>~16000</td>
<td>~12000</td>
</tr>
<tr>
<td>Intrinsic $\Delta E/E$(%)</td>
<td>5.8</td>
<td>3.1</td>
<td>9.1</td>
<td>~9</td>
<td>~9</td>
</tr>
<tr>
<td>$\Delta E/E$(%)</td>
<td>6.6</td>
<td>10</td>
<td>10</td>
<td>~10</td>
<td>~10</td>
</tr>
<tr>
<td>Decay time / ns</td>
<td>230</td>
<td>300</td>
<td>~47</td>
<td>~40</td>
<td>~39</td>
</tr>
<tr>
<td>Index of refraction</td>
<td>1.85</td>
<td>2.15</td>
<td>1.82</td>
<td>1.8</td>
<td>1.8</td>
</tr>
<tr>
<td>Attenuation / cm$^{-1}$</td>
<td>0.34</td>
<td>0.96</td>
<td>0.88</td>
<td>0.82</td>
<td>0.53</td>
</tr>
</tbody>
</table>
stopping power as a denser material without problems. A larger scintillator volume leads to readout problems, reconstruction problems (discussed later) and mechanical limitations. A high fraction of pe events is preferable as detector-scattered events deteriorate the spatial resolution of the gamma detector. A high light yield is a indicator for a good energy resolution and timing resolution that can be achieved with that scintillator. The emission spectrum should be narrow and match the employed photo sensor’s sensitivity. A fast scintillator with a small decay time is needed in order to measure precise time stamps for the gamma interaction and to reduce the intrinsic dead time due to pile up of events in the scintillator.

LSO and LYSO with a low fraction of yttrium have a very favorable set of parameters for PET and are therefore often used in state-of-the-art detectors.

4.1.4.2. Photo Detectors

Photodetectors are used to detect the optical photons produced in the scintillation process. There are two main categories of photodetectors used today: Photo-multiplier tubes (PMTs) and semiconductor-based photosensors.

4.1.4.2.1. Photomultiplier

PMTs are the classical photodetectors used to detect low levels of light. The sensitive entrance window is made from a thin photocathode layer. In this layer the optical photons are absorbed and a photoelectron is released. This photoelectron exits the backside of the photocathode layer if its energy is high enough to surpass the surface potential. Behind the photocathode is a vacuum enclosed dynode system used to amplify the photoelectron to a measurable level. Each dynode is connected to a high voltage supply in such a way that a cascaded electrical field is produced that accelerates electrons towards the next dynode. Upon impact on one of the dynodes, multiple secondary electrons are produced per incident electron and are again accelerated towards the next dynode. Due to this multiplication process, several million electrons hit the last dynode, called anode, which is used to read out the signal (Fig. 4.15).

The amplification process itself is very stable and gives very good signal-to-noise (SNR) ratios. But the quantum efficiency (QE), the ratio of incident optical photons and the number of photo-electrons escaping the photocathode towards the dynode system, is rather low with typical values of about 25%.

Advanced implementations of PMTs use multi-anode readout schemes to decode the position of the incident photon on the photocathode of a single PMT device.

4.1.4.2.2. Semiconductor-Based Photo Detectors

Semiconductor-based photo detectors are based on p-n-junctions which are boundaries between doped semiconductor materials (doping: positively (p) or negatively (n)). At the boundary, electrons and holes are attracted to the material with a scarcity of the respective charge carrier. This diffusion process is stopped by the electrical field that is induced by the diffusion
process over the boundary region called space charge region. Effectively, an intrinsic voltage is created over the p-n-junction. In the space charge region, no free charge carriers are present which prevents a current flow through the p-n-junction if no external voltage is applied. Therefore the space charge region is also called depletion region.

If an external voltage is applied to the p-n-junction (also called diode), its behavior is very dependent on the polarity of the voltage. The resistance characteristics is in both direction highly non-linear. An external voltage with a polarity counter-acting the intrinsic voltage is called forward bias. If the intrinsic voltage is counter-acted the electron-hole pairs recombine again, allowing a current to flow through the diode. This voltage is called knee-voltage and is for silicon diodes in the order of 0.7 V. After the knee-voltage is surpassed the current flow increases exponentially with rising bias voltage.

If a reverse bias voltage is applied, the depletion zone is increased and only a small leakage current is flowing until the the breakdown voltage is reached. The small leakage current is caused by defects in the depletion zone leading to the creation of charge carriers (called dark current). This process is especially dependent on temperature, high temperatures lead to a higher number of thermally induced charge carrier pairs in the depletion zone. If the voltage is increased even higher, the breakdown voltage is reached. At this voltage charge carriers gain enough momentum in the electrical field to create additional charge carriers leading to an avalanche condition. This effect can be used to build up photosensitive semiconductor devices.

Figure 4.15.: Basic principles of a photomultiplier tube. (reprinted from S. Cherry et al. (2012), Copyright (2012), with permission from Elsevier)
4.1.4.2.2.1. Photodiode

The sensitivity of a diode for incident photons can be improved by increasing the depletion zone which is commonly done by introducing an additional, low-doped material between the p- and n-region called the intrinsic region (this kind of diode is called a PIN-diode) (Figure 4.17a).

If operated below the breakdown voltage, the measured current is proportional to the number of incident photons which create free charge carriers in the depletion zone (Figure 4.17b). The current is not very dependent on the applied voltage and the proportionality is given over a very large range of photon intensities until saturation effects start to play a role. The downside is, that the current is very small as each photon only produces a single electron-hole pair.

4.1.4.2.2.2. Avalanche Photodiode

Avalanche photodiodes (APDs) are PIN-photodiodes with an additional high-field region (Figure 4.18a) in which the charge carriers (namely the electrons) are amplified by the occurring avalanche effect (Figure 4.18b). This internal amplification or gain is in the order of 100 – 1000 and is dependent on the applied reverse bias voltage. This makes APDs prone to voltage and temperature fluctuations opposed to simple PIN-photodiodes without an internal amplification process. The current signal on the other hand is much higher.

4.1.4.2.2.3. SiPM

If a PIN-diode is operated above the breakdown voltage on purpose, it is called a single-photon avalanche diode (SPAD). The operation mode is also known as Geiger-mode. Each free charge carrier in the depletion zone leads to a self-sustaining avalanche which must be stopped by reducing the bias voltage. This quenching process can either be implemented passively or actively. To implement a
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Figure 4.17.: (a) Pin-diode with space charge distribution under reverse voltage (top), and corresponding electric field distribution (bottom).
(b) PIN-photodiode with space charge distribution under reverse voltage. Absorption of photons with $E=\hbar \nu$ and creation of charge carrier pairs. The material gets transparent for photons with $E < E_g$ (energy of the band gap).

(© User:Kirnehkrib/Wikimedia Commons/©@3.0)
Figure 4.18.: (a) Si-Avalanche-Photo-Diode (APD) with space charge distribution under reverse voltage (top), and corresponding electric field distribution (bottom).
(b) Charge carrier multiplication in a Si-Avalanche-Photo-Diode (APD) under reverse voltage. Colors indicate doping of the corresponding layer. (© User:Kirnehkrib/Wikimedia Commons/3.0)
passive quenching circuit, a high-ohmic resistor is used in series with the SPAD. Due to the current induced voltage drop over the resistor, the bias voltage over the SPAD is reduced and the avalanche is stopped. After that the bias voltage recovers to the previous level, the SPAD is sensitive again and can detect the next free charge carrier that is induced. This recovery process takes some time (depending on the SPAD implementation a few nano seconds) in which the SPAD is insensitive to newly induced charge carriers. The signal of a SPAD is very fast (few pico seconds rise time) and the internal gain is much higher compared to APDs and more or less the same for each avalanche event. Therefore, SPADs are considered trigger devices detecting photons in a binary manner.

Active quenching circuits detect the voltage drop caused by the avalanche and actively reduce the bias voltage below the breakdown voltage. The SPAD has to be actively reset again in order to detect the next photon.

PIN photodiodes and APDs detect multiple photons incident on their sensitive area, whereas a SPAD gives a more or less binary signal for a single photon. Therefore, multiple small-area SPADs are needed to count the number of photons that illuminate a certain detection area. Thermally induced charge carriers result in the same avalanche process as charge carriers induced by incident photons. Consequently, SPADs are commonly separated into very small area devices to reduce the rate of noise events per SPAD. An array of SPADs is used to generate a sensitive array which can be used to measure a signal proportional to the photon intensity. Such an array connects all SPADs parallely resulting in a current signal which is proportional to the number of SPADs that encountered an avalanche (breakdown). This is only true if the analog SPAD breakdown signals are all equal in height and if the integration window is large enough to account for all the signals (Fig. 4.19).

Problems of an SIPM are optical crosstalk and afterpulsing which both have a negative influence on the signal. During an avalanche optical photons with a long wavelength are generated which might trigger an avalanche in an neighboring SPAD. This optical crosstalk probability is in the order of a few tens of percent but strongly depends on the SPAD design. It leads to a higher number of triggered SPADs and might lead to saturation effects and might destroy the linearity of the SiPM signal. Afterpulsing occurs if a trapped charge carrier is released after the original avalanche has already finished and triggers another avalanche only a short time after the original one. This increases the number of detected SPAD breakdowns.

The sum of the analog signals of all SPADs needs to be digitized using an application specific integrated circuit (ASIC) delivering a timestamp and via the pulse height or shape a measure of the number of SPADs that contributed to the signal (Fig. 4.20). This analog-signal-summation process is prone to temperature-induced gain changes which need to be accounted or compensated for.
4.1. Positron Emission Tomography

Figure 4.19.: Left: schematic of the equivalent electrical circuit of a SiPM. Only 6 micro-cells, each represented by a diode symbol, are shown. Right: illustration of the signal formation in a SiPM. The pile-up of the individual micro-cell pulses is achieved by means of summing via a common readout line. (reprinted from Spanoudaki and Levin (2010), ©3.0).

Figure 4.20.: Scintillation light detector systems based on an analog silicon photomultiplier. (reprinted from Frach et al. (2009), © 2009 IEEE).
Digital SiPMs consequently employ SPADs as single photon trigger devices by binary digitizing the breakdown of each SPAD individually. No analog signal summation is required anymore. This binary detection of a single SPAD breakdown is much more robust to analog-signal-height changes due to gain variations. The SPAD signals could be connected to time-to-digital converters (TDCs) individually, which is often not feasible due to power and space constraints. Therefore, for a fast trigger generation a logical network can be used to connect the individual SPAD trigger signals to a single TDC for a larger area containing several SPADs, e.g. a readout-channel. The dSiPM would theoretically allow to read the status of each individual SPAD. Again, for reasons of readout speed and simple data-rate reduction, a summation can be implemented returning the number of SPAD breakdowns for a readout channel. The active quenching circuitry of individual SPADs can be implemented in a way that allows to program and keep the SPAD in the quenched state. With this mechanism a dark count rate (DCR) for each SPAD can be recorded and based on it a certain fraction of SPADs of a readout channel can be disabled. This can reduce the overall DCR of a readout channel significantly by sacrificing only a small fraction of its sensitive area.

In chapter 5 a more detailed description of the dSiPM employed in this work is given.

4.1.4.3. Detector Stack

The segmented scintillator is coupled to a photosensor and both make up a gamma detector which is the basic building block (Detector stack) of a PET system. Depending on the application, there are several commonly used coupling or readout schemes. The simplest one employs a coupling of a single scintillator element to a single readout channel of the photosensor array. This so called one-to-one coupling is normally only feasible to implement on human whole-body PET systems with a crystal and readout
channel pitch in the order of 3 mm – 4 mm (Figure 4.22a). The scintillator elements are wrapped in reflective foil except for the readout face which is covered by the sensitive area of the photosensor.

Figure 4.22.: Different crystal configurations and readout schemes. (a) A one-to-one coupling of scintillator elements and readout channels. This is the simplest readout scheme. Due to the limited dynamic range and the power consumption per readout channel this scheme is often only feasible for a minimum scintillator element size (a few millimeters). (b) High-resolution scintillator arrangement coupled via a light guide to read out channels of a pitch which is much bigger than the scintillator element pitch. This scheme requires the combination of multiple readout channels and an identification algorithm. (c) A monolithic scintillator element which is read out by a number of readout channels. This detector stack requires a knowledge of the correlation of the scintillation position and the measured signals in the readout channels in order to reconstruct the three-dimensional interaction position.

If large photosensors, e.g. PMTs, are used or if a high-resolution crystal pitch (∼1 mm, e.g. preclinical imaging of rodents) is required, the one-to-one coupling is not feasible anymore. A high number of channels often leads to a higher power consumption and complicates the readout architectures. Most photosensors are furthermore limited in the minimum size of a readout channel in order to provide the needed dynamic range. Therefore, preclinical systems and PMT-based clinical systems typically employ scintillator elements read out by a much lower number of readout channels. In order to allow an identification of the scintillating crystal, light sharing is employed by e.g. employing a light guide (Figure 4.22b). This light guide spreads the scintillation light exiting a single crystal over a larger area of a photosensor array (Fig. 4.23). Crystal identification algorithms, one of the simplest being a center-of-gravity algorithm, can then be used to identify the scintillating crystal.

A single-sided readout scheme for small crystals normally does not allow to reconstruct the depth-of-interaction (DOI). One solution is to design a height-dependent optical cross-talk between crystals and use the width of the light distribution as a measure for the DOI. Or different scintillator materials can be stacked which can then be distinguished by their pulse-shape, which requires waveform sampling to a certain degree. A further solution is to use several layers of scintillator arrays that are arranged with defined offsets with respect to each other so that a layer can be identified
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![Diagram of gamma and optical photons](image)

Figure 4.23: A sketch of the high-resolution scintillator arrangement (Figure 4.22b) showing a gamma interaction with a single scintillator element. The scintillation light exits the crystal at the bottom and is spread by the light guide over a larger area of the photosensor array.

by slightly different COG positions. If the scintillator array is read out from two sides the DOI can be reconstructed using the light ratio of the two photosensor arrays.

A further readout scheme employs a continuous crystal volume read out by a number of photosensors (Figure 4.22c). These monolithic detector blocks require elaborate calibration procedures and position reconstruction algorithms. But, they allow decoding of the DOI from the characteristic light distribution pattern which changes as a function of all three spatial dimensions in the volume.

All multiplexing readout techniques share the disadvantage that a single gamma interaction occupies more than one readout channel rendering a certain area insensitive to consecutive gamma interactions. Multiple scintillation positions (due to Compton scattering this can occur for a single gamma) that fall within the same time window are much harder to separate in a multiplexing readout scheme.

4.1.5. Coincidence PET Detector

To capture both annihilation gammas and all tomographic projections that are needed for a good reconstruction of the tracer distribution, a ring geometry is normally used that surrounds the imaging volume. The ring diameter is designed to fit the maximum object or specimen size. The extent of the ring in axial direction is limited by the costs for the gamma detectors. Especially for human whole-body clinical PETs the complete tracer distribution is therefore not contained in the FOV. The typical axial extent of these PETs is in the order of a few tens of centimeters. If scattering is neglected, a single out-of-field annihilation can not produce coincident signals in the PET detector ring (further problems caused by out-of-field activity are discussed in section 4.1.8).
4.1.5.1. Coincident Gamma Detection

The two gammas produced in the annihilation should be detected on opposite sides of the imaging volume. The individual gamma event is also referred to as single. Assuming a single interaction of the gamma with the scintillator material no directional information can be measured for a single.

The two gamma interactions are detected individually and have to be checked for coincidence to identify them as belonging to the same annihilation event. This can be realized either by using the analog signals of the gamma detectors and checking them with the help of analog circuitry for coincidence. A benefit of this method is that no synchronization has to be performed but the downside is that the coincidence circuitry can be very complex as each possible coincidence has to be connected by wires. A different approach is to provide a reference clock signal for each gamma detector. This allows to assign a globally valid timestamp to each single. Singles can then be checked for coincidence at a later point in time. To provide ToF, either of the methods have to implement a very precise time measurement to deduce the time difference between the detection of the two singles with high precision (at least in the order of several 100 ps). Coincidence checking involves a coincidence window (CW, \( \tau \)). The CW has to be chosen to account for the available temporal resolution of the gamma detectors and the intended FOV as an annihilation location with different distances to the two detectors will also lead to a time difference between the two signals. More of this effect is covered in the chapter about ToF (section 4.1.5.2).

The line connecting the two detectors is the LOR and one has to assume that the annihilation took place on that line. Defining all singles within the CW to be in coincidence can lead to misidentification of coincidences. The following types of coincidences can occur (see Fig. 4.24).

A so called true coincidence is the intended case when the two gammas are not scattered inside the object and are correctly assigned to the same annihilation event. It is possible that one or both of the gammas are not completely absorbed and does only deposit a part of its energy in the scintillator. These singles are then measured with a lower energy but if the measured interaction position is still on the LOR (e.g. the first Compton scatter location; the remaining gamma energy leaves the detector) these events still allow a precise LOR reconstruction. The only problem is to distinguish them from unwanted classes of coincidences which may also result in a lower measured energy.

If one or both of the gammas is Compton scattered in the object, its direction is altered which leads to a wrongly assumed LOR. These so called scattered coincidences can be identified to a certain degree by lower energy values of at least one of the two gammas. For a gamma with a measured energy smaller than 511 keV it can not be deduced if the energy was lost due to a scattering process in the object or in the detector material.
The third class of coincidences is a random coincidence. They occur if two gammas from two different annihilations are falsely correlated and are assumed to originate from a single annihilation. There is a number of reasons for one of the gammas of one annihilation to not be measured by the detector. It can be absorbed in the object, its path might simply not intersect the sensitive scintillator volume (this is often the case for the second gamma from an out-of-field annihilation) or it is not absorbed in the scintillator (depending on the thickness of the scintillator and its stopping power this can be very probable). If the CW is large enough it might happen that the detector measures two singles, correlates them but that they originated from two completely unrelated annihilations. The number of falsely correlated singles increases in the first order linearly with the length of the CW. The random rate of a detector pair can be approximated from the singles rate of the detectors if the fraction of singles belonging to true coincidences is negligible by Equation 4.10.

\[ R_{AB} = 2\tau S_A S_B \]  \hspace{1cm} (4.10)

It is also possible that more than two detectors are detected to be in coincidence. One can either discard these multiples or try to find the most likely LOR(s) which might lead to misidentifications of the correct coincidence.
4.1. Positron Emission Tomography

Figure 4.25.: A, A pair of annihilation photons are emitted from a source (red dot) and detected in coincidence by opposing detectors. B, In the absence of time-of-flight information, there is no information about the location of the source along the line joining the two detectors. During reconstruction, the event is backprojected with equal probability of having occurred in all pixels along that line. C, With time-of-flight information, some limited localization of the event is possible and events are backprojected with probabilities that follow a Gaussian distribution, centered on pixel $\Delta d$ (Equation 4.11) from the center of the scanner and with a full width at half maximum equal to the timing resolution of the detector pair. (reprinted from S. Cherry et al. (2012), Copyright (2012), with permission from Elsevier)
4.1.5.2. Time of Flight

With a very precise measurement of the time difference between the two gamma detections, the position along the LOR can be reconstructed with a certain precision. This is called ToF-PET (Fig. 4.25).

The ability of a PET system to measure the time difference of the two gamma interactions is expressed by the coincidence resolution time (CRT). This is the width of the time difference distribution for a point-like source. As the two gammas fly in opposite directions with the speed of light in vacuum, Equation 4.11 gives the relation between the measured time difference $\Delta t$ and the position offset $\Delta d$ from the center of the LOR and the uncertainty $\sigma_d$ implicated by the system’s CRT.

$$\Delta d = \Delta t \frac{c_0}{2} \Rightarrow \sigma_{\Delta d} = \text{CRT} \frac{c_0}{2}$$ (4.11)

In a non-ToF reconstruction, the annihilation point can only be assumed to have an equal probability for all locations along the LOR. If ToF information is used, the annihilation position can be narrowed down and the probability distribution follows the ToF kernel which should be known for the system (Fig. 4.25). More details on the influence of ToF information during reconstruction is covered in the following section about reconstruction methods.

4.1.6. Tomography and Coincidence Storage

PET normally defines a right-handed coordinate system with the $z$-axis along the axial axis of the scanner and the $x$-axis in horizontal direction (Fig. 4.26).

The measured and qualified coincident gammas are either stored in a histogram, counting the occurrence of an LOR, or in a listmode format which stores each individual measured LOR and may contain a timestamp, and eventually ToF information, as well.

The histogram method was historically used for 2D acquisitions. The simplest two dimensional histogram format is the sinogram which uses an azimuthal angle in the transaxial plane ($x$-$y$) and the offset to the isocenter as axis for a single plane (also called slice) ($\theta = 0^\circ$). These sinograms represent the activity distribution in the image space forward projected into the tomographic scanner space (Fig. 4.27 and Fig. 4.28). The histogram storage method is very complex if a three dimensional acquisition is used and time information should be included as well. The advantage is that the sinogram representation is independent of the PET system’s geometry and a common reconstruction can be used.

Listmode data is used for most modern scanners which is also much easier to use with the advanced reconstruction methods discussed in the next section. Each detected LOR is represented in the data stream with identifiers for the two scintillation crystals in coincidence. Very often further data fields, e.g. a timestamp for the coincidence, energy for each single, a time difference between the two singles and more, are included.
in the data stream. To reconstruct a listmode datastream, the geometry of the scanner has to be provided.

Figure 4.26.: A diagram of a full-ring camera is shown with the coordinate system that describes the orientation of the camera. The azimuthal angle ($\phi$) is measured around the ring, while the polar angle ($\theta$) measures the angle between rings. (reprinted from Bailey (2005), with kind permission from Springer Science and Business Media)

### 4.1.7. Image Reconstruction

Traditional PET image reconstruction techniques are based on sinograms. The easiest method is to use a simple back projection of the sinogram into the image space. This results in very blurred images as the activity of an entry in the sinogram space is equally distributed along the LOR in image space. To counteract this effect, the filtered backprojection (FBP) uses a filter of the fourier transformed sinogram data. With FBP quite a lot of details can be resolved in a reconstructed image. For a long time it was the standard method used for image reconstruction.

These simple backprojection algorithms assume a fully sampled 2D slice and missing tomographic directions, gaps in the scanner’s ring geometry, have to be specially corrected or accounted for. Backprojection algorithms can be applied to 3D acquired data which either involves a rebinning of 3D data to 2D slices in order to apply a
Figure 4.27.: The \((r,s)\) coordinate system is rotated by projection angle \(\phi\) with respect to the \((x,y)\) coordinate system of the object and is fixed with respect to the gamma camera. (reprinted from S. Cherry et al. (2012), Copyright (2012), with permission from Elsevier)
Figure 4.28.: Two-dimensional (2-D) intensity display of a set of projection profiles, known as a sinogram. Each row in the display corresponds to an individual projection profile, sequentially displayed from top to bottom. A point source of radioactivity traces out a sinusoidal path in the sinogram. (reprinted from S. Cherry et al. (2012), Copyright (2012), with permission from Elsevier)
4. Fundamentals

The 2D formulation of the algorithm or the backprojection can be formulated in three dimensions which requires very complex corrections.

The state of the art tomographic image reconstruction algorithms are iterative methods and are now commonly used for PET. The image space is segmented into voxels and the activity distribution is forward projected into the tomographic space with the help of a system matrix, which models how the PET would measure activity as a function of image space. The obtained tomographic data is compared to the actual measurement. Using the difference between the estimate and the actual measurement a correction can be applied and backprojected to the image space.

The expectation-maximization (EM) reconstruction method employs a system model \( M_{ij} \) which denotes the sensitivity of projection \( j \), which is a single LOR measured by the scanner, for the image voxel \( f_i \). The forward projection for a specific LOR is then given by Equation 4.12.

\[
p_j = \sum_i M_{ij} f_i \quad (4.12)
\]

These LOR intensities calculated from the assumed activity distribution and the system matrix are compared to the actual measurement. Based on this comparison, the initial image \( f_i^k \) is updated resulting in the next image estimate \( f_i^{(k+1)} \) following Equation 4.13 with \( k \) denoting the iteration.

\[
f_i^{(k+1)} = \frac{f_i^k}{\sum_j M_{ij}} \sum_j M_{ij} \frac{p_j}{\sum_l M_{lj}} f_l^k \quad (4.13)
\]

The ordered subset EM (OSEM) runs per iteration only on a subset of measured projections. This leads to a higher frequency of image updates and leads to a faster convergence of the algorithm. The EM and OSEM algorithm can be constrained e.g. to prefer smooth image solutions. This can simply be implemented by employing an averaging filter (e.g. Gaussian blur) after each update of the image that suppresses high frequency noise at the cost of image spatial resolution.

If the iterative algorithms are used for a fully three dimensional reconstruction, the system matrix \( M_{ij} \) can be very large for PET systems with a large number of crystals. It might not be feasible to store it in memory of a modern computer and one has to reduce its size by exploiting symmetries in the scanner’s geometry or it has to be calculated on the fly.

4.1.8. Performance Parameters of a PET

4.1.8.1. Energy Resolution

One of the basic performance parameters of a PET is the energy resolution. It is obtained from an energy spectrum which contains all singles for a certain part of the PET, e.g. a single module, or for the system as a whole. An energy spectrum can
be generated for singles without checking for coincidence or just for singles which pass all required criteria for a coincidence. Not all systems have the ability to output the energy of a single. For these systems one has to indirectly measure the energy spectrum by evaluating the count rate as a function of the selected energy window. The generation of a coincident spectrum using this method is complicated as on many systems only one single global energy window can be set which might biases the spectrum in coincidence detection mode.

Typically, the energy spectrum is reported for the response of the detector to incident gammas with an energy of 511 keV. The spectrum will change if a significant part of the gammas is attenuated or scattered before reaching the detector. If the tracer used for the investigations is not a pure $\beta^+$ emitter, the recorded spectrum might contain singles produced from gammas of different energies (e.g. $^{22}$Na). The energy resolution stated as the performance measure of a PET is typically evaluated around the photopeak corresponding to a gamma energy of 511 keV as the FWHM. Therefore it is required to state if a background modeling or a specific function is fitted to the spectrum in order to obtain the FWHM.

4.1.8.2. Coincidence Resolution Time

The CRT is a further fundamental performance parameter of a PET. It is obtained by generating a spectrum of the measured time differences between coincident gammas. The source position has to be known and the measured time stamps have to be corrected for the path length from the source to the respective detector element if they are not equally far away from the source’s location. Again, the FWHM of the time difference spectrum is typically reported but due to differences in the time resolution of individual detector elements, randoms and scattered events, the time difference spectrum might contain a constant background and non-Gaussian tails. One should state if a background modeling or a specific fit to the spectrum is performed to obtain the FWHM.

4.1.8.3. Image Spatial Resolution

The image spatial resolution of PET can be evaluated by measuring very small point sources and evaluating the scanners response. As discussed in the previous sections there are fundamental limits to the spatial resolution that can be achieved with a PET. The system’s resolution $R_{\text{sys}}$ can be approximated by adding up the effects of the positron range $R_{\text{range}}$ (Fig. 4.6), the acollinearity $R_{\text{acol}}$ (Equation 4.3) and the detector (PET system LOR) resolution $R_{\text{det}}$ by Equation 4.14.

$$R_{\text{sys}} = \sqrt{R_{\text{range}}^2 + R_{\text{acol}}^2 + R_{\text{det}}^2}$$ (4.14)

It has to be noted that $R_{\text{det}}$ is for most PETs dependent on the position in the FOV. If the intrinsic spatial $R_{\text{int}}$ resolution of a detector stack is known (and can be
modeled by a Gaussian), it can be used to estimate the PET system resolution in the isocenter \( R_{\text{det}} \approx \sqrt{2} R_{\text{int}} \).

The effective achievable spatial image resolution is of course also influenced by the employed reconstruction algorithm. For comparison one defines to use a FBP algorithm to report the point source resolution. An iterative reconstruction (maybe even with modeling the point spread function during reconstruction) might deliver far superior point source resolutions. These point source resolutions might not be achievable for more complex activity distributions. Therefore, larger structured phantoms are often used to demonstrate the image spatial resolution of a PET. These phantoms often use rods filled with a PET tracer aligned with the axial coordinate of the PET of a specific diameter and spacing. If the phantom contains rods of various sizes the reconstructed image gives a good impression of the size of structures which can still be resolved by the scanner in larger volumetric activity distributions. Again, these phantoms are artificial and the contrast and symmetry of the activity distribution do not represent structures found in biological specimens.

4.1.8.4. Count Rate Performance

To evaluate the count rate performance of a scanner one tries to separate the measured coincident events into trues, randoms and scattered events. For this purpose an artificial phantom is used with an narrow line source aligned with the axial axis of the scanner inside a scattering cylinder of the size close to the size of the target specimen.

First, the randoms have to be estimated. This can e.g. be done by using the singles rate per detector element. The simplest model assumes that the fraction of coincident events is negligible (Equation 4.10). To account for the coincident rate that is measured by each detector element one can further enhance this model and account for the known trues rate per detector element. These enhanced models are quite independent of the activity distribution used for the random estimation measurement (Oliver and Rafecas 2012). Some detectors use delayed signals to estimate the random rate, this is often used in hard wired system where the individual singles data is not available.

The sinogram data of the scatter phantom is used to distinguish scatter from true events and is evaluated in slices for individual projection angles. Each slice is centered around the peak representing the line source. The trues are located in a narrow corridor around this peak whereas the scattered events form a larger background beneath this peak.

With these evaluations the trues \( T \), randoms \( R \) and scattered events \( S \) can be separated and a noise equivalent count rate (NECR) is defined.

\[
\text{NECR} = \frac{T^2}{T + S + 2fR}
\]
The focus of this thesis is on the PET performance degradation during MRI operation. The MRI performance is not evaluated, therefore MRI will only be introduced briefly. For a comprehensive introduction to MRI see Wehner (2016).

MRI employs a strong homogeneous static magnetic $B_0$ field to polarize spins of atomic nuclei. The $B_0$ field is typically in the order of 1.0 T – 9.0 T.

The thermal equilibrium state of the magnetization can be perturbed by using radio frequency (RF) pulses that match the Larmor frequency of the spins which shall be used for the image acquisition. The Larmor frequency $f_{\text{Larmor}}$ depends on the nuclei (namely its mass $m$, charge $q$ and Landé $g$-factor) and the strength of the $B_0$ field.

$$f_{\text{Larmor}} = g \frac{q}{4\pi m} \cdot B_0$$

For protons in a 3 T field it is $\sim 127.7$ MHz.

For the spatial encoding MRI uses gradient coils which produce linear timely variant magnetic fields in three spatial dimensions. The magnetic gradient fields (for a human whole body system) have a strength (gradient strength, GS) in the order of a few 100 mT and can be switched with a speed (slew rate, SR) of several 100 mT/(m ms). One defines a duty cycle of the gradient system (switching duty cycle, SDC) that gives
the fraction of measurement time of the whole MRI sequence in which the gradient system is in a switching state and produces a time-varying magnetic field.

The amount of RF pulses and the parameters of the gradient system (GS, SR and SDC) strongly depend on the employed MRI imaging sequence. Especially the gradient system is often not running with the highest possible activity during normal imaging sequences, this is of importance if one wants to study PET/MRI interferences which are briefly discussed in the next section.

### 4.3. PET/MRI

As mentioned in the introduction PET is a powerful tool in nuclear medicine enabling e.g. the visualization of metabolic processes but as a tracer-based imaging modality, PET images contain only limited anatomic information. This complementary information is commonly added by combining PET with CT. After having introduced the first combined PET/CT systems in the late 1990s, fully integrated solutions are nowadays prevailing in clinical practice (Beyer and D. Townsend 2006).

In spite of this development, a combination of PET with MRI was first discussed in the 1990s and gained interest over the years. In contrast to CT, MRI provides a decent soft-tissue contrast and avoids the administration of an additional radiation dose as MRI makes use of static and time-varying magnetic fields to acquire image information (Buchbender et al. 2012a; Buchbender et al. 2012b; Schulthess and Schlemmer 2009; Jadvar and Colletti 2014; Drzezga et al. 2012). Furthermore, MRI offers a wide range of different contrast mechanisms emphasizing a potential benefit of PET/MRI over PET/CT. However, in contrast to PET/CT, the integration of a PET and MRI system is a complex task as the extensively used magnetic fields require a higher level of compatibility. The associated induction effects or occurrences of Lorentz forces might either lead to degradation effects on the PET side or on the MRI side (Vandenberghe and Marsden 2015). Whereas for the latter, typical problems range from $B_0$ distortions over signal-to-noise ratio (SNR) losses to spatial encoding disturbances, the PET system and its sub-components might show a sensitivity for magnetic fields resulting in either a malfunction or a performance degradation. Several groups reported such kind of performance degradation when e.g. RF or gradient pulses are applied during PET operation (Schlyer et al. 2006; Weirich et al. 2012): for instance, (Weirich et al. 2012) reported count-rate losses associated with the application of gradient-intense MRI sequences.

Despite these potential risks, a couple of different research systems were developed in recent years whereby the integration topology changed over time: starting from a "separate system approach", in which the scintillation crystals are separated by exploiting optical fibers from the photomultiplier tubes operated outside the magnetic field because of their strong magnetic field sensitivity, a higher level of integration was achieved with the utilization of solid-state photon detectors. Devices of such kind
allow an operation inside the strong magnetic field of the MRI scanner and thus enable a higher level of integration Avalanche photodiodes (APD) as utilized in Schlyer et al. (2007), Pichler et al. (2006), and Delso et al. (2011) and more recently Silicon Photomultipliers (SiPM) (see e.g. (Schulz et al. 2009; Hong et al. 2013; Weissler et al. 2014; Weissler et al. 2015)) are mainly chosen in this regard. Apart of the choice of photon detection technology, the downstream readout platforms differ from its topology and integration level. In contrast to more conservative approaches in which most of the electronics are installed outside the MRI system, our group presented a more aggressive approach (Weissler et al. 2014; Weissler et al. 2015): here, the digitization takes place directly inside the MRI bore and thus reduces the need for analogue signal transmission over long routing and hence minimizes the risk of signal quality degradation related to RF pulses or switching gradients. Furthermore, in a second generation, the utilized analogue SiPMs of the Hyperion-I scanner were replaced by a digital version, presented in 2009 by Philips Digital Photon Counting (PDPC). These dSiPM devices digitize the signal directly on sensor level by counting the number of micro-cell (SPAD) breakdowns, meaning that no analogue signal has to be transferred to separate digitization-performing electronics such as an ASIC. A potential downside of the highly integrated approach is the presence of most of the electronics inside the MRI system’s field-of-view (FoV), thus intensifying MR compatibility issues.

In Wehner (2016) a very detailed PET/MRI interference study is presented and the fundamentals are explained. As this work focuses on the PET, the PET/MRI interference investigations cover a sub-part of the whole PET/MRI interferences, namely the PET performance degradation due to MRI operation with special focus on gradient-intense sequences as it has been shown that these have the strongest influence on the PET performance. In this work a special scintillator geometry (section 5.1.1) is used to investigate the PET performance degradation. Furthermore, an upgraded version of the underlying readout platform is investigated. The PET/MRI interference studies are presented in chapter 8, chapter 9 and chapter 10.
5. Hyperion-II\textsuperscript{D} PET/MRI insert

The content of this chapter is partly based on the description of the Hyperion-II\textsuperscript{D} platform previously published in the following articles:


D. Schug et al. (2015c). “PET performance and MRI compatibility evaluation of a digital, ToF-capable PET/MRI insert equipped with clinical scintillators”. In: *Physics in Medicine and Biology* 60.18, p. 7045. DOI: 10.1088/0031-9155/60/18/7045

Content has been copied, rearranged, reformulated and details have been added. Furthermore, a lot of figures are reprinted from articles published by our group describing the hardware components of the scanner in more detail. They are cited in this paragraph and are referenced as the origin of the specific figure used.

The Hyperion-II\textsuperscript{D} platform (Weissler et al. 2015) is made up by individual singles detection modules (SDM) (Weissler et al. 2012a) each housing up to six detector stacks (Dueppenbecker et al. 2012b; Düppenbecker et al. 2016). The SDMs are mounted on a gantry and form the PET detector ring. They are read out by a data acquisition system capturing the complete raw DPC sensor data and which is able to process the raw data to listmode data in software in realtime (Gebhardt et al. 2012; Goldschmidt et al. 2013; Goldschmidt et al. 2016) The individual components will be described in the following.
5. Hyperion-IID PET/MRI insert

5.1. Detector Stack

The detector stack is the basic PET detector unit which is used to build up the whole scanner. In this thesis two different detector stack configurations are investigated. The preclinical configuration of the detector stack consists of a scintillation crystal array, a light guide, a sensor tile which is used to read out the scintillation light and an control and readout interface (IF) board based on an field-programmable gate array (FPGA) (Dueppenbecker et al. 2012b; Düppenbecker et al. 2016) (Fig. 5.1). The clinical configuration does not employ a light guide and uses a different scintillator geometry. Both configurations are explained in the following.

![Figure 5.1.: Exploded photo of the arrangement of a preclinical detector stack. The reflective film on top of the crystal array has been removed to show the individual crystals. In the final scanner, after the components have been glued together, the detector stack is wrapped with Teflon tape to close up the optically transparent light guide. (adapted and reprinted from Schug et al. (2015b), 3.0)](image)

5.1.1. Scintillator and Light Guide

The scintillator is the key element to stop the high energy gammas and convert them to light. LYSO crystals (Agile, Knoxville, USA) are used with a lutetium fraction of 20%.

An optional light guide is needed to spread the scintillation light from a single scintillator element over a multitude of readout channels. On the hardware side, the only difference between the preclinical and clinical detector stack is the scintillator geometry and the light guide.
5.1. Detector Stack

Figure 5.2.: Sketches of the detector stack configurations. (a) The preclinical detector configuration employs a lightguide between the LYSO scintillator and the sensor tile. (b) The clinical detector configuration used in this work uses a one-to-one coupling of crystals to readout channels. (reprinted from Schug et al. (2015c), ②③.0)

5.1.1.1. Preclinical Configuration

30 × 30 LYSO crystals with a height of 12 mm and a pitch of 1 mm are mounted on a trenched 2 mm glass plate used for light spreading (Figure 5.3b and Figure 5.2a). The crystals are wrapped in 67 μm Vikuity™ ESR film (3M, St. Paul, USA).

5.1.1.2. Clinical Configuration

The detector stacks of the clinical configuration (Figure 5.2b) employ a pixelated LYSO crystal scintillator array with 8 × 8 crystals, 10 mm height and a pitch of 4 mm. This leads to a one-to-one coupling of each crystal to a single readout channel.
5.1.2. Sensor Tile and PDPC DPC3200 sensor

The sensor tile is 32.6 × 32.6 mm$^2$ in size and is made up of 16 DPCs (Philips Digital Photon Counting DPC3200) (Frach et al. 2009; Frach et al. 2010; Degenhardt et al. 2012) (Figure 5.3a). It is similar in terms of geometrical layout of the readout channels to the sensor tile presented by PDPC which is also used on their Technology Evaluation Kit (TEK) platforms (Degenhardt et al. 2010; Frach et al. 2010). Otherwise, the sensor tile was redesigned for MR compatibility and to allow a stable cooling. On the backside it is equipped with two 80-pin connectors, non-magnetic decoupling capacitors, a digital temperature sensor, a 16 Mbit flash memory and two large cooling surfaces. Dedicated钟ling, synconization and data lines per DPC are routed via the connectors. The sensor tile is split into two galvanically isolated halves in order to prevent any conductive loops through the connectors, the sensor tile and the IF board (Fig. 5.4).

![Sensor Tile Sketch](image)

Figure 5.3.: (a) Sketch of the sensor tile. (b) Sketch of the preclinical LYSO array coupled via a slitted lightguide onto the sensor tile of the preclinical configuration. (both reprinted from Schug et al. (2015b), ΘΩ3.0)

5.1.2.1. DPC3200

DPCs provide a digital photon count per readout channel and, after calibration, a single DPC wide time stamp. A DPC comprises 2 × 2 pixels consisting of 3200 SPADs each. When an avalanche is induced in a SPAD, the voltage drop is detected and stored as binary information. An active quenching circuit stops the avalanche. When a readout is requested, all SPAD breakdowns are summed up. This means that a single SPAD can only detect one breakdown per acquisition cycle. SPADs can be inhibited individually, this is used to disable a certain fraction of SPADs per pixel that show a significantly high DCR.
Figure 5.4.: Implementation details of sensor tile (top row) and IF board (bottom row). (reprinted from Düppenbecker et al. (2016) Ω3.0)
Table 5.1.: Geometrical properties of the DPC3200

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>Die size (layout)</td>
<td>$7834.8 \times 7107.8 \mu m^2$</td>
<td>Layout size based on outermost visible layer (METAL4)</td>
</tr>
<tr>
<td>Pixel size</td>
<td>$3860.86 \times 3276.78 \mu m^2$</td>
<td>Includes pixel peripheral logic</td>
</tr>
<tr>
<td>Active Pixel Area</td>
<td>$3.8016 \times 3.2 \text{mm}^2$</td>
<td></td>
</tr>
<tr>
<td>Cells per Pixel</td>
<td>3200</td>
<td></td>
</tr>
<tr>
<td>Cells per Sub-Pixel</td>
<td>800</td>
<td></td>
</tr>
<tr>
<td>Cell Size</td>
<td>$59.4 \times 64 \mu m^2$</td>
<td>Includes half of the cell electronics block</td>
</tr>
<tr>
<td>Sensitive area</td>
<td>$2953.5 \mu m^2$</td>
<td>Sensitive area of a core diode</td>
</tr>
<tr>
<td>Diode fill factor</td>
<td>82.9%</td>
<td>Fill factor of a core diode</td>
</tr>
<tr>
<td>Cell fill factor</td>
<td>77.7%</td>
<td>Includes cell electronics</td>
</tr>
<tr>
<td>Pixel fill factor</td>
<td>71.5%</td>
<td>Includes pixel electronics</td>
</tr>
<tr>
<td>Overall die fill factor</td>
<td>65.0%</td>
<td>Include entire die and guard ring diodes</td>
</tr>
</tbody>
</table>

5.1.2.1.1. Supply and I/O Interfaces The most important I/O pads of the DPC3200 chip are briefly and in a simplified form described here. Three voltage lines are used to power and operate a DPC3200: the core voltage $V_{DD}$ is used to power the digital chip itself, the constant bias voltage $V_{bias}$ is applied directly to the SPADs and the voltage $V_{DDA}$ is used to quench the SPADs by reducing the $V_{bias}$ above the SPADs below their breakdown voltage $V_{bd}$ (Fig. 5.5).

A JTAG interface is used to configure the DPC and allows to set individual SPADs to a permanent quenched state (also referred to as inhibition of SPADs). At the main clock input should be driven with a low jitter 200 MHz signal. A sync input/output line can be used for an external trigger or to transmit internal trigger information to the outside. The DPC outputs hit data via two data lines.

The interfacing of the DPCs is explained in more detail in the section about the IF board (Fig. 5.10 and section 5.1.3).

5.1.2.1.2. Trigger and Validation Hardware Implementation A pixel is further divided into four sub-pixels (Figure 5.7a). The 800 SPADs per sub-pixel are grouped together for the generation of a trigger signal. 32 SPADs form a row trigger line (RTL) which leads to 25 RTLs per sub-pixel. The trigger signals of the RTLs are used for a fast and low-threshold trigger generation and for the validation network which is used as a higher readout threshold to discard noise triggers. While for the fast trigger mechanism all RTLs of a sub-pixel are combined with OR gates, the validation network can be programmed for different logical combinations of the RTLs of a sub-pixel. The
5.1. Detector Stack

5.1.1. Detector Stack Overview

Figure 5.5.: Overview of the cell electronics. Each cell contains an active quenching and resetting circuitry. The break-down of a cell is sensed by an inverter that pulls down the trigger line. From this point on, the whole detector works on a digital basis. (courtesy of PDPC)

state of a trigger signal will persist until the respective SPADs have been reset. The readout state machine of the DPC is shown in Fig. 5.6. The involved steps will be explained in the following and further information can be found in Tabacchini et al. (2014) and Philips Digital Photon Counting (2015).

Figure 5.6.: Sketch of the DPC trigger, validation and readout state machine. (reprinted from Philips Digital Photon Counting (2015), courtesy of PDPC)

5.1.2.1.3. Trigger and Timestamp

A trigger scheme, which defines how the trigger lines of the four sub-pixel are connected, can be set between 1-4 (Figure 5.7b). The trigger scheme 1 generates a trigger on the first measured breakdown of a SPAD in any of the four sub-pixels. The higher schemes 2, 3 and 4 are logical operations of the four sub-pixel trigger lines (Table 5.2) requiring $2.33 \pm 0.67$, $3.0 \pm 1.4$ and $8.33 \pm 3.80$ mean number of SPAD breakdowns, respectively, in order to reach the trigger condition and

55
5. Hyperion-IID PET/MRI insert

Figure 5.7.: DPC3200 trigger generation. (both reprinted from Philips Digital Photon Counting (2015), courtesy of PDPC)

Table 5.2.: DPC3200 trigger settings

<table>
<thead>
<tr>
<th>Trigger Scheme</th>
<th>Sub-Pixel Configuration</th>
<th>Average Threshold</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>sp1 ∨ sp2 ∨ sp3 ∨ sp4</td>
<td>1.00 ± 0.00</td>
</tr>
<tr>
<td></td>
<td>[(sp1 ∨ sp2) ∧ (sp3 ∨ sp4)]</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>2.33 ± 0.67</td>
</tr>
<tr>
<td></td>
<td>[(sp1 ∨ sp4) ∧ (sp2 ∨ sp3)]</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>(sp1 ∨ sp2) ∧ (sp3 ∨ sp4)</td>
<td>3.00 ± 0.14</td>
</tr>
<tr>
<td>4</td>
<td>sp1 ∧ sp2 ∧ sp3 ∧ sp4</td>
<td>8.33 ± 3.80</td>
</tr>
</tbody>
</table>
5.1. Detector Stack

![Graph showing trigger probability after n photons for the DPC3200 sensor.](image)

Figure 5.8.: Trigger probabilities for the DPC3200. (reprinted from Philips Digital Photon Counting (2015), courtesy of PDPC)

assuming a homogeneous distribution of SPAD breakdowns over the area of a pixel (Tabacchini et al. 2014) (Fig. 5.8). The trigger lines of the four pixels of a DPC are connected by an OR gate meaning that each pixel can generate the DPC wide trigger independently. Low trigger schemes result in a better timing performance but are more prone to thermally induced SPAD breakdowns which may result in a higher dead time and lower sensitivity.

If trigger schemes higher than 1 are used, RTL noise triggers will accumulate over time and can generate a noise trigger. To overcome this limitation, the optional RTL refresh feature recharges single RTLS that generated a trigger after 10 ns–15 ns of its occurrence if subsequently the global DPC trigger is not reached (Frach et al. 2009).

When the trigger condition is reached, the time stamp is generated. Two TDCs are running at half the DPC’s clock speed (the design frequency of 200 MHz is used throughout this work), resulting in 100 MHz, with a phase shift of half a TDC clock cycle with respect to each other. The coarse counter is 15 bit wide and defines the length of a frame (Details of the TDC design are discussed in Frach et al. (2010)). Each uses a tapped delay line (TDL) with 512 bins and a bin width of approximately 20 ps–25 ps. The TDLs are used to measure the time to the next rising flank of the respective TDC coarse counter and are used to generate a high resolution time stamp with sub-coarse-counter resolution. Due to the phase shift between the two TDCs, the coarse counter values are either the same or one of the coarse counters has a value which is one tick higher than the other.

As the data package a DPC sends out does not contain the complete 15 bit of the DPC coarse counter the FPGA capturing the DPC data runs a coarse counter as well. Furthermore, an additional frame counter is needed to provide a time stamp that is spanning multiple frames. To generate a timestamp in pico seconds the frame counter
of the FPGA, the FPGA coarse counter and the two DPC coarse counters and the two TDL values have to be combined. Details about the counter information in the final data stream are explained in the following (paragraph 5.1.2.1.6 and section 5.1.3.1).

5.1.2.1.4. Validation  A trigger causes the DPC to enter a validation phase of programmable length (VL). The logic condition set in the configurable validation network (val) has to be fulfilled during the validation phase in order to validate a trigger (Fig. 5.6). The validation network uses 7 bits to connect trigger groups of 3–4 RTLs of a sub-pixel using logical operations (Fig. 5.9). A further bit defines the logical operation of the four sub-pixels. The validation lines of the pixels on a DPC are connected using an OR gate to allow a validation of individual pixels, as for the trigger generation. Assuming a uniform photon distribution, thresholds for the required number of registered photons for different validation network settings used in this work are listed in Table 5.3.

Figure 5.9.: Validation network of DPC3200. The 7 bit of the validation network (val) can be set to configure a logical OR or AND for the combination of groups of 3–4 RTLs on a sub-pixel. A further bit sets the logical operation of the four sub-pixels. The configurations used in this thesis are listed in different notations in Table 5.3. (reprinted from Philips Digital Photon Counting (2015), courtesy of PDPC)

5.1.2.1.5. Integration and SPAD Readout  For a validated event an integration phase is started. This phase is used to accumulate SPAD breakdowns caused by the incoming photon pulse. The integration length should be chosen long enough to
capture the relevant part of the scintillation pulse. After integration, the readout is started and the binary information of each SPAD register is summed up resulting in the photon count per pixel. This readout is performed line by line and the lines which have not been read out yet are still sensitive to optical photons. Therefore, half of the readout time of 680 ns can be considered to contribute to the integration time.

After the consecutive recharge phase, all SPADs are sensitive again and the DPC is set back into the ready state waiting for the next trigger Frach et al. (2009) (Fig. 5.6).

5.1.2.1.6. Data Transmission  After the readout phase and the summation of all broken down SPADs, the DPC transmits the hit information via the two datalines with half the system’s clock frequency at a rate of 100 MHz (Table 5.4). Only the 8 least significant bits (LSB) of the two coarse counters are contained in the DPC hit data package. This explains why the firmware in the FPGA needs to run a coarse counter as well. The 8 bit are sufficient to unambiguously expand the DPC coarse counter again to the full 15 bit (more about the timestamp information that is finally contained in the data stream is explained in section 5.1.3.1).

If the DPC is configured to send out framing packets, a full acquisition cycle with a forced validation is started at the event of the coarse-counter overflow. The DPC will postpone the framing packet generation if it is processing a normal hit at the moment of the coarse-counter overflow. Framing packets are very helpful to test and monitor the integrity of the data stream as at least one framing packet per DPC is generated during each frame and send through the complete data acquisition pipeline. Depending on the exact nature of a potential fault, one may be able to deduce if the DPC’s logic is running correctly, a data line is damaged or the bias voltage is not correctly applied.

Table 5.3.: DPC-3200-22 validation schemes in the notation used throughout the text given in SPAD triggers or measured photons (ph), hexadecimal notation and in the notation used by PDPC and the resulting validation threshold per pixel. (data taken from Thon 2012, partly published in Philips Digital Photon Counting 2015 and Tabacchini et al. 2014)

<table>
<thead>
<tr>
<th>val(text)</th>
<th>val(hex)</th>
<th>val(PDPC)</th>
<th>avg. SPADs</th>
<th>min. SPADs</th>
</tr>
</thead>
<tbody>
<tr>
<td>17 ph</td>
<td>0x55:0R</td>
<td>4-OR</td>
<td>16.9 ± 6.2</td>
<td>4</td>
</tr>
<tr>
<td>28 ph</td>
<td>0x54:0R</td>
<td>n.a.</td>
<td>27.5 ± 10.3</td>
<td>4</td>
</tr>
<tr>
<td>37 ph</td>
<td>0x50:0R</td>
<td>n.a.</td>
<td>37.1 ± 12.8</td>
<td>6</td>
</tr>
<tr>
<td>52 ph</td>
<td>0x00:0R</td>
<td>8-OR</td>
<td>52.2 ± 15.0</td>
<td>8</td>
</tr>
</tbody>
</table>
Table 5.4.: DPC3200 data output

<table>
<thead>
<tr>
<th>Bit</th>
<th>data_1</th>
<th>data_2</th>
</tr>
</thead>
<tbody>
<tr>
<td>0:12</td>
<td>Photon count pixel 2 (LSB first)</td>
<td>Photon count pixel 3 (LSB first)</td>
</tr>
<tr>
<td>13:20</td>
<td>TDC 1 coarse counter (LSB first)</td>
<td>TDC 2 coarse counter (LSB first)</td>
</tr>
<tr>
<td>21:29</td>
<td>TDC 1 fine counter (LSB first)</td>
<td>TDC 2 fine counter (LSB first)</td>
</tr>
<tr>
<td>30</td>
<td>Coarse counter status</td>
<td>&quot;0&quot;</td>
</tr>
<tr>
<td>31</td>
<td>Coarse counter overflow</td>
<td>&quot;0&quot;</td>
</tr>
<tr>
<td>32:44</td>
<td>Total hit counter (LSB first)</td>
<td>&quot;00000000000000&quot;</td>
</tr>
<tr>
<td>45</td>
<td>&quot;0&quot;</td>
<td>&quot;0&quot;</td>
</tr>
<tr>
<td>46</td>
<td>&quot;1&quot;</td>
<td>&quot;1&quot;</td>
</tr>
<tr>
<td>47:59</td>
<td>Photon count pixel 1 (LSB first)</td>
<td>Photon count pixel 4 (LSB first)</td>
</tr>
</tbody>
</table>

Figure 5.10.: Functional overview of the detector stack. The sensor tile contains the digital SiPMs, a digital temperature sensor and a Flash memory. Data acquisition, configuration and power supply is controlled by the interface board. Acquired measurement and control data is bundled into one communication stream and forwarded to the singles processing unit. The low-drop voltage regulator (LDO) for the 1.2V supply was added during optimization of the detector stack. (reprinted from Düppenbecker et al. (2016) 3.0)
5.1.3. Interface Board

The IF board houses an FPGA (Xilinx SPARTAN-6 XC6SLX45) which is used to control voltages and to configure the DPCs of the sensor tile and capture their hit data. It is connected on the top via two 80-pin connectors to the sensor tile via which it interfaces the DPCs, the temperature sensor and the flash memory (Fig. 5.4).

On the backside it is equipped with a single 80-pin connector which allows mounting on and connecting to the singles-processing unit. Power is routed from the SPU to the IF board and distributed further to the sensor tile (Fig. 5.10). The 1.8 V is stabilized by an LDO and is used to power the FPGA as well as the DPCs ($V_{DD}$) located on the sensor tile. The 1.2 V line powering the FPGA was only stabilized by employing an LDO during optimization of the IF board. The optimized IF board with the LDO on the 1.2 V line is referred to as "IF board v2" (the difference is investigated in chapter 10). DPC voltage lines controlled by the IF board are the $V_{DDA} = 3 V - 4 V$ and $V_{bias} = 15 V - 35 V$ lines. They are parallely distributed to all DPCs on a sensor tile. $V_{bias}$ sets the operating voltage of the SPADs. The SPADs should be operated at an excess voltage (overvoltage) in the range of about $V_{ov} = 2 V - 3.3 V$ above the measured breakdown voltage ($V_{bd}$). $V_{DDA}$ is used to actively quench and recharge SPADs. It has to be larger than $V_{ov}$ to ensure stable quenching of SPADs and an additional safety margin of at least 0.2 V should be taken into account (Philips Digital Photon Counting 2015).

There is a design-related 100 mA current limitation on the $I_{DDA}$ current line which is meant to prevent damage to the DPCs. This limits the maximum power consumption of the DPCs and may prevent the use of very aggressive and power consuming parameters. Especially the trigger scheme 1 causes a high load on the $I_{DDA}$ line due to many dark noise induced triggers, especially at high temperatures, and may be influenced by the current limitation.

5.1.3.1. Firmware and DPC Readout

The firmware module responsible for the DPC data collection was adopted from the firmware module running on the PDPC TEK FPGAs. It is capsuled into the Hyperion-II$^D$ firmware architecture as a submodule.

The hit information of the 16 DPCs of the sensor tile is collected. As mentioned before, the firmware has a coarse counter running in sync with the DPC’s coarse counters. The FPGA coarse counter is read out at the moment the firmware is notified that a DPC measured a hit which is at the moment the data transmission starts. The delay between the trigger generation in the DPC and the detection in firmware depends on the configuration of the length of the validation phase and the length of the programmed integration time. Therefore the FPGA coarse counter is always read out later than the DPC coarse counter. As the DPC only transmits the eight LSB of its framecounter, the upper bits of the FPGA coarse counter are needed to reconstruct
the full 15 bit of the DPC coarse counter. The firmware ensures, that the 8 bit suffice to cover any possible delay that might occur between the DPC timestamp generation and the FPGA hit detection. One peculiarity is, that only the 14 most significant bits of the FPGA coarse counter are included in the data package used to store the DPC hit information. But again, this is not a problem, as only the upper seven bits are needed.

14 bytes are used to store the information of a single DPC hit. The PDPC firmware packs all hits of the DPCs of a frame, which spans 327.68 µs, into one single data packet with some general information in a header. For example the framecounter of the PDPC firmware module is included in this header. As mentioned before, the PDPC frame counter is only 8 bit wide and needs an expansion in software if a continuous time line is desired. The timespan of this frame counter only covers 83.89 ms which can lead to problems if larger amounts of data is lost.

The Hyperion-IID firmware runs a 32 bit wide frame counter in sync with the PDPC frame counter. This frame counter is added to the packet that wraps the PDPC frame packet ensuring an unambiguous time stamp for each captured hit data package (wrap around after more than 16 days). Therefore, each DPC hit has a globally valid time stamp generated in firmware. In software the calibration of the TDLs has to be performed and all counters have to be combined to calculate a time stamp with a physical unit with an intrinsic resolution of about 20 ps – 25 ps.

Finally, the stack FPGA sends the hit data packages to the FPGA on the SDM which has to concentrate the detector stack data streams into a single data stream.

5.2. Singles Detection Module

Up to $2 \times 3$ detector stacks are mounted on a singles-processing unit (SPU) to form a SDM (Fig. 5.11).

The SPU is designed to be MR-compatible and to be very flexible as it targets a research platform (Weissler et al. 2012a). For example, besides the digital detector stacks used in this thesis, analog detector stacks (analog SIPM with an ASIC-based digitization) can be mounted as well (Weissler et al. 2014). The FPGA used on the SPU is a Xilinx Virtex-5. It handles the communication with the detector stacks and controls the components on the SPU itself. Furthermore, it sends data downstream to a data acquisition and processing server (DAPS) via an transceiver for Plastic Optical Fibers (POF) able to provide a gigabit Ethernet (GbE) interface. The POF transceiver was especially designed in corporation with the manufacturer in a non-magnetic version.

A liquid cooling circuit, made from interrupted brass pipes, runs between the IF and the sensor tile board (Figure 5.11c). The difference of the programmed cooling temperature and the temperature measured on the back of the sensor tiles is approx-
imatively 5°C–10°C under operation. The SPU’s FPGA and its power supply are connected to the cooling pipes as well.

The SDMs are shielded with a light- and RF-tight housing made from a 0.8-mm-thick carbon fiber composite (Dueppenbecker et al. 2012a) (Figure 5.11b). Dry air is routed through the SDMs and through the complete insert to prevent condensation.

5.3. Synchronization Unit

A central synchronization unit (also called backbone) is used to distribute reference clocking (RefCLK) and trigger signals to all SDMs. The main PCB is an SPU equipped with special expansion PCBs to provide the capabilities needed in the backbone. The backbone translates the POF data lines of each SPU to a laser-via-glass-fiber-based communication line. All the data lines, including the data line to address the backbone, are concentrated into a single non-conductive cable which is used to connect the insert to the DAPS located outside the MRI room. The backbone also houses a board with the POF synchronization lines running to each SPU. The synchronization line is used to transmit the 100 MHz RefCLK signal and, modulated on the same line, trigger pulse capabilities that can be used to synchronously perform an action on all SPUs or detector stacks of the system (e.g. start the clocking signal for all DPCs and ensure reproducible global timing information).

Furthermore, the backbone offers multiple connectors that offer trigger capabilities for external components as well as the input connectors for external signals. These recorded signals can be incorporated into the PET data stream with the timing information of the PET system and thus allows a very precise data alignment with external components (e.g. the MRI’s status signals or of an animal monitoring systems).

The backbone is placed into a copper housing to shield any RF transmission.

5.4. Power Supply

The switch-mode power supply is placed in a copper housing taking special consideration to only introduce a single ground star point to the whole system. This prevents the power supply cables to form any loops that might be sensitive to RF-signal coupling. On the one hand, this might lead to ripples on the power lines and might harm the PET electronics, and on the other hand, the loops might transport RF signals of the power supply into the MRI’s sensitive volume and lead to MRI imaging artifacts. Three power lines run from the power supply to each SDM and the backbone. Coaxial, partly semi-rigid cables have been used as they promise the best MR-compatibility with the least RF emission. All outputs of the power supply have been filtered with a combination of differential- and common-mode filters.
5. Hyperion-IID PET/MRI insert

(a) 3D model of the open Singles Detection Module. The dimensions given describe the size of the preclinical crystal arrays – the active detection area. It is difficult to differentiate the corner and side crystals on an array using the Anger method. Therefore, the outer rows of crystals are skipped to ensure that the second row is detected properly. The sensor boards (visible in blue underneath the crystal arrays) are therefore slightly larger than the active detection area.

(b) An SDM contains up to six detector stacks. The carbon fiber shield is pushed over the module and the RF screen is closed on both sides by shielding plates.

(c) Liquid cooling system inside the SDMs: four brass cooling pipes are thermally, but not electrically, coupled to all the sensor- and IF boards, to the SPU, and to a power supply conversion board.

Figure 5.11.: The SDM. (all reprinted from Weissler et al. (2015), Θ3.0)
5.4. Power Supply

Figure 5.12.: The synchronization unit generates and distributes RefCLK/Sync signals for the SDMs. It furthermore provides synchronization to external devices and a user control interface. Communication to the SDMs is translated from POF to glass fiber. (reprinted from Weissler et al. (2015), §3.0)

Figure 5.13.: Power supply: The power supply is placed in an RF screened housing (left). (reprinted from Weissler et al. (2015), §3.0)
5. Hyperion-IID PET/MRI insert

5.5. Gantry

The gantry can be equipped with up to ten SDMs (Fig. 5.14). The liquid cooling system as well as the dry air is distributed through the gantry to the SDMs. The gantry is able to house PET-transparent radio-frequency transmit and receive (RF Tx/Rx) coils with different inner bore sizes which are described in the next section.

The inner diameter is constrained first by the bore-size of the RF coils and secondly by the RF screen, but the PET crystal-to-crystal spacing is 209.6 mm for the preclinical configuration and 217.6 mm for the clinical configuration.

The axial field of view (FOV) of the PET also depends on the crystal configuration and the number of populated rings. For a fully populated preclinical configuration the axial FOV is 96.6 mm (Figure 5.11a) whereas for a single-ring-clinical configuration the extend is 32 mm.

![Figure 5.14.: Side view of the PET gantry. The SDMs are mounted on the cooling distribution rings. There is no further material between the SDMs and the RF coil to keep the attenuation for the gamma photons low. The infrastructure is connected to the SDMs at the gantry. (reprinted from Weissler et al. (2015), @3.0)](image)

5.5.1. RF Coils

Several MRI RF Transmit/Receive (Tx/Rx) coils have been manufactured. As they are placed between the object to be scanned and the PET detector stacks they have been designed to be gamma transparent (Details can be found in Weissler et al. (2015)). The three coils that have been built so far are shown in Fig. 5.15.
For this work, the small RF Tx/Rx coil with an inner diameter of 46 mm was mainly used. To measure a large rabbit-sized phantom, the large RF Tx/Rx coil with an inner diameter of 160 mm was installed. The multi-nuclei coil was not used.

Figure 5.15.: Three gamma-transparent Tx/Rx RF coils, built for the insert: CT scans (transverse slice and coronal X-ray image) indicate the gamma transparency in the FOV. (reprinted from Weissler et al. (2015), ©3.0)

5.6. Insert

The gantry, the synchronization unit and a power supply are mounted on an MRI patient table which allows easy installation in a Philips Achieva 3 T MRI system (Fig. 5.16). Only two hoses for the cooling liquid, one hose for the dry air, a single power plug and the data link have to be connected. The data link is meant to go through a wave guide to the technical room, where the DAPS is located.

5.7. Data Acquisition and Processing

All SDMs are linked via the GbE interface to a DAPS which is connected to a control computer running a monitoring and controlling software. The DAPS can be used to store the DPC hit data for offline analysis or it can process the DPC data to coincident listmode data in real time (Goldschmidt et al. 2013; Goldschmidt et al. 2016). Control and status data are routed from the control PC to the system and vice versa. The
5. Hyperion-IID PET/MRI insert

Figure 5.16.: The gantry of the PET insert holds ten SDMs. The gantry is mounted on a trolley which allows easy insertion into an MR scanner. A backbone and a power supply are also mounted onto the trolley. Only a single data cable, a power cable and the cooling tubes have to be connected allowing for an easy installation and mobile setup. (reprinted from Wehner et al. (2015), ©3.0)
5.7. Data Acquisition and Processing

The physical connection layout is shown in Fig. 5.17. The FPGA on the SPU handles the communication with the detector stacks (Gebhardt et al. 2012). Each SDM is connected via POF to a DAPS (Goldschmidt et al. 2013). An additional POF per SDM is connected to the synchronization unit. The DAPS either processes hit data in real time or stores it for offline analysis on hard disks. It is controlled via a control PC and routes the status and command communication between the PC and the SDMs.

Figure 5.17.: The communication architecture of the Hyperion-II\textsuperscript{D} detector. The 10 SDMs and the backbone are connected via separate GbE links to the DAPS. Each SDM houses six PET detector stacks and is connected to the backbone for synchronization. The DAPS acquires detector raw-data from the SDMs and also routes status and control information between the detector and the control PC. (reprinted from Goldschmidt et al. (2016), © 2015 IEEE)

For this work the raw data stream captured by the DAPS is used. The realtime capabilities of the DAPS to process the DPC data on the fly to listmode data have not been used. The DAPS is capable of capturing a total of 1 GB/s of raw data. This includes the overhead for the Hyperion-II\textsuperscript{D} message protocol as well as the embedded PDPC hit message protocol.

The next chapter will cover the data processing that has been developed as a part of this thesis to transform the DPC raw data to PET relevant singles information and how to check them for coincidence. A detailed explanation of all calibration steps needed is given as well.
6. Processing and Calibration for the Preclinical Configuration

The content of this chapter is subject of the following paper, of which I am the main author. Content has been copied, rearranged, reformulated and details have been added.


6.1. Introduction

This chapter describes the techniques used to process raw DPC hit data to PET singles information on the Hyperion-II scanner presented in the last chapter. The techniques presented here can be translated to a wide range of other systems using segmented scintillators coupled to sensor arrays with digitization and self-triggering per channel employing a light sharing element. This is especially the case for systems based on the TEK using the same DPC technology as the presented system. The next chapter will evaluate the PET performance that can be achieved when applying the presented calibration and processing methods.

The center-of-gravity (COG) or Anger algorithm has been widely used as a crystal identification algorithm for detectors using a light sharing element. For analog detectors, it can be implemented using a resistive network for signal summation (Anger 1958). If the light pulse is distributed only over a small fraction of the total number of channels of a readout sensor array, the noise of sensors located far away from the position of the scintillation event deteriorates the calculated COG. Therefore, advanced COG algorithms try to give the channels closest to the event a higher weight compared to channels capturing none or only a small fraction of the scintillation pulse or they define a region-of-interest (ROI) around the readout channels with the highest signal. In a purely analogue implementation of a COG this can be realized by an offset subtraction in each channel. It has been shown that the crystal identification can be improved by such a subtraction (Wojcik et al. 2001; Qi et al. 2007).
6. Processing and Calibration for the Preclinical Configuration

If the channel values are digitized and processed individually, more advanced algorithms can be implemented. One method to reduce the noise channel contribution is an intensity-weighted COG (Pani et al. 2009). Another possibility is to use a ROI to restrict the channels used for the COG calculation (Netter et al. 2009). These algorithms can benefit from an iterative formulation (Liu and Goertzen 2013) at the expense of increased computation time.

Nevertheless, an unrestricted COG is commonly used on systems with digital information available per readout channel (Georgiou et al. 2014). Using the PDPC TEK and its capability to trigger all readout channels, one can restrict to calculate the COG only if all channels are present, which leads to a stable number of input values. As it mimics the simple analogue COG, it is still very prone to noise and reduces the sensitivity of the gamma detector due to requiring all channels to have been read out. A subtraction algorithm implemented for digitized data acquired with the TEK shows improvements of the COG stability (Georgiou et al. 2014). Using no light guide but transparent coupling between crystals on a \(2 \times 2\) channels DPC sensor, the COG calculation can be restricted to the four channels of this DPC (Marcinkowski et al. 2014).

Our group presented a stable ROI filter, which was used for the energy calculation, in 2011 (Dueppenbecker et al. 2011). In this chapter a further improved version of a COG algorithm with a stable ROI selection is presented. In order to improve the sensitivity, an enhancement of the algorithm to accept up to two ROIs or sets of channels for each crystal is shown.

Besides a COG approach, there are more advanced algorithms which can be used for crystal identification, like for example a maximum-likelihood identifier (C. Lerche et al. 2011). These algorithms can handle changing sets of input channels for the same crystal very robustly but are computationally more complex and require a more elaborate calibration scheme than a COG approach. They are not in the scope of this chapter.

6.2. Methods

The full DPC raw data stored by the DAPS is used. An offline analysis is performed using a multi-threaded calibration and processing framework written in C++.

Data processing consists of the following steps which are described in detail in this section. The data of each SDM is split into separate streams for each detector stack which can be processed in parallel. Raw hit data of a DPC is used to generate a time stamp and a corrected photon count (paragraph 5.1.2.1.6). The hits are sorted, correlated and clustered according to their timestamps. Detector scatter between two stacks is not accounted for.

The resulting clustered data is used to identify the crystal that scintillated. The photon count of a subset of channels is used to calculate the energy deposited in the
6.2. Methods

The photon count measured by the DPC is corrected for saturation with the help of a simple exponential saturation model taking the inhibited fraction of SPADs into account.

Differences of the effective PDE between pixels on the same sensor tile may occur. This is caused by slight variations in the break down voltage of DPCs or by coupling defects (e.g. glueing problems) between the light guide and the DPCs. Differences in the effective PDE can lead to an ambiguous relation of a crystal and the readout pixel capturing most of its scintillation light. As described later, this relation is essential for the COG ROI selection. If the effective PDE is not accounted for it can lead to distortions of the floodmap or even multiple COG positions for a single crystal due to an ambiguous ROI selection. The effective PDE of a pixel is estimated using the individual saturation-corrected photon data per pixel for non-clustered DPC hit data (method described in C. W. Lerche et al. (2015) and mentioned in C. W. Lerche et al. (2013)). The estimation was performed with $^{22}$Na data as well as FDG measurements and yields similar results.

The spectrum $H(i)$ lists the frequency of the photon value $i$. For each photon value $i$ of the spectrum, the integral of photon value frequencies with at least $i$ photons is calculated. These integral values are logarithmized and then normalized to the logarithmized integral of the whole spectrum ($i = 0$). These monotonically descending functions $I_{\text{sum'}}$, are used to define a stable high photon value per pixel via threshold $t$ as a measure for the effective PDE: $I_{\text{sum'}}(t) = t$.

The threshold $t$ was empirically chosen to be 0.5 because values $\lesssim 0.3$ have proven to be prone to low statistic and therefore noisy high photon values. All effective PDE values of pixels are normalized to the system wide median. The linear effective PDE factor is applied after the saturation correction resulting in a corrected photon count.

6.2.2. Clustering and Singles Processing

It takes up to several nano seconds to fulfill the trigger condition on DPCs capturing only a small fraction of the scintillation light. Therefore, a fixed cluster window of 40 ns is chosen to find timely correlated hits on a sensor tile and combine them into singles. The timestamp of a single is defined as the timestamp of the the earliest
hit. This is in most cases the DPC located directly beneath a crystal and therefore captures the largest fraction of light.

### 6.2.2.1. Classification of Singles

The pixel with the highest corrected photon count in a single is defined as the main pixel. Pixels adjacent to the main pixel are called neighbor pixels. One distinguishes between direct neighbors which are horizontally and vertically directly adjacent to the main pixel and the diagonal neighbors.

Singles are classified into two classes according to the presence of the neighboring pixels (Fig. 6.1).
The set of singles with all neighbor pixels present is depicted as FN and the set of singles with all direct neighbors present as DN. A further set, depicted as DNe, only includes the singles belonging to DN but not to FN, these singles miss a diagonal neighbor pixel. Due to the $2 \times 2$ pixel layout of the DPCs there is a maximum of one DPC housing a diagonal neighbor pixel which is allowed to miss for a single to be an element of DN (Figure 6.1b). The relations between the sets are given in equation (6.1).

\[ FN \subseteq DN, \quad FN \cap DNe = \emptyset, \quad DN = FN \cup DNe \]  

To be a member of FN, singles need to contain the hit data of a varying number of DPCs depending on the position of the main pixel: one DPC for a corner pixel, two DPCs for an edge pixel and four DPCs for one of the central pixels.

If the main pixel of a single is located at the corner or at the edge of the sensor tile, all its neighbors are either located on the same DPC as the main pixel or on a second DPC that includes at least one direct neighbor. Therefore, these singles are always a member of FN and cannot be a member of DNe (Fig. 6.1).

### 6.2.2.2. COG Calculation

The proposed COG algorithms operate on the main pixel and neighbor pixels with filtering for different classes of singles.

The COG algorithm which handles singles that are a member of FN, but not DNe, and which uses the main and all neighbor pixels is called COG with full neighborhood (COG-FN) (Figure 6.1a). This strict quality criterion leads to a loss of sensitivity, especially for high validation thresholds and for crystals located close to the center of a DPC as shown in the results.

A second algorithm recovers this sensitivity loss by accepting singles which are a member of DN, which includes singles that are a member of DNe. For central main pixels this means a single diagonal neighbor pixel can be missing or is omitted. The algorithm is called COG-DN and the resulting positions for crystals (see result Fig. 6.2 COG-DN) are different from the positions obtained with the COG-FN algorithm (see result Fig. 6.2 COG-FN).

The difference of positions between the two algorithms can be handled either by using a lookup table (LUT) for each algorithm, which might be a disadvantage on platforms with restricted memory, or by correcting the positions of the COG-DN to match those of the COG-FN algorithm.

Possible implementations of a correction algorithm could be a purely geometrical calculation rule or an algorithm which uses the measured channel information to calculate the missing pixel information.

For the presented processing used throughout this work, a transformation method based on the measured photon information available is used which allows to use a single 2D LUT for both algorithms. This reduces the calibration complexity and reduces the amount of calibration data. The COG-DN positions are transformed by
Figure 6.2.: COG positions for $8 \times 8$ crystals located over a central DPC calculated using the COG-FN (left), the COG-DN (middle) and the COG-DN-Ex (right) algorithm for a measurement using trigger scheme 4 and val = 17 ph. (reprinted from Schug et al. (2015b), @03.0)

linearly extrapolating the missing pixel’s photon count (COG-DN-Ex). If the situation in Figure 6.1b is assumed the calculation, using the corrected photon values of each channel, is given in (6.2).

$$C = 0.5 \left( 0.5 \left( \frac{c}{a} + \frac{D}{A} \right) B + 0.5 \left( \frac{b}{d} + \frac{B}{A} \right) D \right)$$

(6.2)

This estimates the positions of crystals similar to the positions obtained with the COG-FN method (see result Fig. 6.2 COG-DN-Ex) and allows us to use a single LUT for the COG-FN and COG-DN-Ex.

The sensitivity gain evaluated in this chapter is independent of how the DNe events are handled. A performance evaluation of the chosen correction algorithm and possible further distortion correction algorithms is beyond the scope of this thesis.

To get the best results, the COG-FN is applied for singles which are a member of FN and the COG-DN-Ex algorithm only for singles that are a member of DNe. This method is called COG with adaptive corner extrapolation (COG-ACE).

To extract the COG crystal position LUT, the COG-ACE positions for singles are filled into a 2D flood histogram per detector stack. Besides requiring that singles are a member of DN, only a photon count filter of at least 400 corrected photons is applied. The crystal positions of all $30 \times 30$ crystals are then being extracted from this flood histogram as described in the following.

As there is a fixed mapping between a crystal and its main pixel, the floodmap is divided into 64 areas containing only COG positions above a single pixel. Using a background removal and deconvolution algorithm (Mariscotti 1967; M. Morhăe et al. 2000; Silagadze 1996) the 9–16 peaks are identified (see result Fig. 6.3). These positions are used to map the calculated COG of a single to a crystal using a nearest position search. This can either be done by calculating the distance of a single’s COG to all crystal positions or by using a precalculated 2D LUT. Using a 2 byte crystal ID
the LUT on a 25 µm pitched grid is approximately 2.4 MB in size. The resolution of the LUT can be reduced further if the algorithm is implemented on a platform with restricted memory. The calculation of the COG and the lookup using a precalculated 2D LUT is computationally inexpensive compared to complex statistical classification algorithms.

### 6.2.2.3. Energy Calibration and Calculation

For a single that is a member of FN, the energy can be calculated using all DPCs housing the main pixel and all neighbor pixels (E-FN) (Figure 6.1a). If the single is a member of DN, a second energy calculation can be performed with only the requested DPCs (E-DN) (Figure 6.1b). The latter method is the only one that can be applied for singles that are a member of DNe. To obtain the best possible energy resolution, the energy can be calculated using the E-FN method for singles which are a member of FN, and using the E-DN method if the single is a member of DNe. This adaptive energy calculation method is depicted as E-FD.
For each crystal a corrected photon spectrum is generated separately for E-FN and for E-DN. In the range of 500–3000 corrected photons the background is calculated and removed from the spectrum (Ryan et al. 1988; M. Morháč et al. 1997; Burgess and Tervo 1983). A peak search is performed using a Markov chain algorithm (M. Morháč et al. 2000). All found peaks are fitted with a Gaussian function. If more than one peak is found and successfully fitted, the highest peak is selected. For the energy calculation, the photo peak is set to an energy value of 511 keV. No baseline offset is considered. Thus, two different energy calibration factors are obtained and stored for each crystal, one for E-FN and one for E-DN.

6.2.2.4. Singles Filtering

The software framework allows singles filtering at all stages of the processing (e.g. prior or after coincidence processing). As the full raw hit data is used, a wide range of filters can be defined, e.g. filtering for energy, photon counts, presence of channels and more. A singles filter is used before the coincidence processing in order to reduce the amount of data which is forwarded to the coincidence search. Using the described COG algorithms, all channels needed for the COG calculation are required to be present discarding all other singles. Two different energy windows are used: the narrow energy window (NE) selects singles around the photo peak and ranges from 411 keV–561 keV, whereas the wide energy window (WE), commonly used in preclinical studies, ranges from 250 keV–625 keV.

6.2.3. Coincidence Processing

Singles of all sensor tiles are timely ordered and synchronized into a single processing pipeline for the whole scanner. During calibration, a sliding CW of 12.5 ns is used to account for time offsets of SDMs, detector stacks and individual DPCs. This setting covers ±5 ns, which accounts for one clock cycle delay per element at 200 MHz, and includes a safety margin. Only coincidences of exactly two singles are accepted. A minimum distance of 5 sensor tiles in tangential direction between the two singles is requested.

Due to cable lengths, the individual SDMs, Stacks and DPCs in the system can have a systematic time offset with respect to each other. This constant offset needs to be calibrated and accounted for in order to measure the time difference of two singles as accurate as possible. Time alignment is performed with either point sources distributed along the z-axis of the scanner or a line source. For the time alignment of the sensors, only the 4 crystals located closest to the center of a pixel are taken into account. Crystals above bond gaps and between two pixels are expected to have a larger time delay and worse timing resolution and thus will be discarded for the calibration of the DPC offsets. The timing difference for each measured pair of DPCs in the system is corrected for the known source position and filled into a histogram. In
order for the minimization problem to be over-determined and thus get absolute delay values for the whole system, it is beneficial to vary the $x$ and $y$ position (coordinates on the transversal plane) of point sources or place the line source slightly off center. This allows to measure coincidences to different stacks for a single stack. The source position is determined using a straight LOR and selecting the closest point source or the closest point on the line source. The mean value and its error is extracted from each histogram. A single delay value per DPC is fitted to all measured difference values using a least squares fit.

The same algorithm can be applied to fit delay values for individual crystals as an additional time offset correction. Fitting delay values of all 54,000 crystals of the system poses challenges to the minimizer. A simplification is to only correct for a mean delay for each of the 900 crystal positions assuming that the mean delay value of a specific crystal position is a reasonable approximation for all detector stacks.

After time offset calibration the coincidence window is narrowed. This depends on the object size and the trigger scheme which influences the timing performance.

### 6.2.4. Experiments

Five $^{22}$Na point sources with $\sim 1.3$ MBq each and an FDG filled line source were used for the measurements shown in this chapter. An overvoltage of 2.5 V was employed, 20% of the SPADS per DPC which showed the highest DCR are inhibited, a validation length of 40 ns was used, the RTL refresh feature was enabled and an integration length of 165 ns was used.

Energy resolutions for the system are given as FWHM of a Gaussian function fitted iteratively in the range of $-0.5$ FWHM to 1 FWHM around the photo peak of the coincident energy spectrum without background modeling.

### 6.3. Results and Discussion

Fig. 6.2 demonstrates that the COG-DN-Ex was able to correct the COG-DN positions reasonably well to match those of the COG-FN allowing to use a single LUT for both algorithms. The calculated COG positions for all crystals using the COG-ACE algorithm demonstrates that the COG-ACE algorithm was able to retain the separability of all crystal positions (Fig. 6.3).

The readout probability of the DPCs for a selected crystal located centrally on a sensor tile using the COG-ACE algorithm is shown in Figure 6.4a. Only singles that are a member of DN were accepted, the readout probability for DPCs housing a direct neighbor pixel was 100%. For the measurement taken with the WE, trigger scheme 3 and val = 28 ph the readout probability of the DPC needed for the single to be a member of FN was 35%. This high fraction of singles being a member of DNe is typical for crystals located close to the center of a single DPC. In Figure 6.4b the
6. Processing and Calibration for the Preclinical Configuration

(a) Readout probability as a function of the pixel position. The DPCs needed to be present in order for the single to be a member of DN are outlined in black, the additional DPC needed for the single to be a member of FN is outlined in blue.

(b) Mean corrected photon value for readout events for each pixel. The mean corrected photon values of pixels far away from the crystal position, which have a low readout probability, are dominated by pile up and noise values. The pixels used for a stable COG-DN and COG-DN-Ex calculation are outlined in black. The additional pixel needed for the COG-FN calculation is outlined in green.

Figure 6.4.: The selected crystal, which is located centrally on the tile, is depicted in light blue. The measurement was taken using trigger scheme 3 and val = 28 ph. The data shown is plotted for coincident singles in a energy range of 250 keV – 625 keV using the COG-ACE algorithm. (reprinted from Schug et al. (2015b), DOI:03.0)
6.3. Results and Discussion

Figure 6.5.: Ratio of the cardinalities $|\text{FN}| / |\text{DN}|$ per crystal. The measurements were conducted at a cooling temperature of 5 °C and trigger scheme 2 applying the wide energy window. Values are plotted for each crystal using the position in the crystal array. One can clearly see the location of the centers of DPCs, where the light has to propagate a longer path to reach the diagonal pixels. The fraction of events missing the corner DPC at high validation thresholds (b) is higher compared to a low validation threshold (a). (reprinted from Schug et al. (2015b), ©3.0)

mean corrected photon value for the same crystal is shown individually for each pixel. The mean corrected photon value was strongly biased by the energy window employed which is in this case the WE ranging from $250 \text{ keV} - 625 \text{ keV}$. It can be seen, that for a centrally located crystal the neighbor DPCs carry only a small fraction of the total light of a single. This is the motivation to limit the COG calculation to the main pixel and its neighbors and the energy calculation to the DPCs housing these neighbors. DPCs which are further away, which do not house a neighboring pixel, would not help to improve the energy resolution or the position. On the contrary, one can see that the mean values of DPCs which are far away start to show noisy behavior due to their very low readout probability and their.

Plotting the ratio of singles being a member of FN to those being a member of DN, one can observe the dependence of the readout probability of the corner pixel on the crystal’s position (Figure 6.5a). For higher validation thresholds this effect intensified (Figure 6.5b). This ratio can be interpreted as a sensitivity loss when filtering for singles being a member of FN compared to a filter requiring singles to be a member of DN. Crystals located above the region where four DPCs adjoin showed no sensitivity loss even for the highest validation threshold used. In contrast, crystals located close to the center of a single DPC showed a sensitivity loss of about 30% - 40% for val = 17 ph which increases to almost 100% for val = 52 ph using the WE.

This translated into a relative loss of the system’s sensitivity using the wide energy window for val = 17 ph and depending on the temperature of about 10% - 15%. The
Figure 6.6.: Ratio of the crystal sensitivity of the single filter asking for all neighbors to be present to the filter allowing a missing corner pixel for the insert. The measurements were conducted at a cooling temperature of $-5\,^\circ\text{C}$ and $15\,^\circ\text{C}$ and trigger scheme 2 as a function of validation threshold. Lines are plotted to guide the eye. (reprinted from Schug et al. (2015b), 3.0)

relative sensitivity loss increased to $\sim 55\%$ for $\text{val} = 52\,\text{ph}$ (Fig. 6.6). Higher temperatures introduce more thermal noise to the system and thus lead to more dead time resulting in the corner DPC to be missing more often.

Depending on the geometrical position of the crystal – towards the edge of the sensor tile, above the center of a DPC or above a bond gap – the 511 keV peak can be found at different corrected photon count values (Figure 6.7a). Edge crystals and crystals located over bond gaps show a smaller corrected photon count of about 700–1200 corrected photons and a slightly worse energy resolution of 13%–14.5% compared to more than 1600 corrected photons and an energy resolution of 11%–14% for crystals centrally located over DPCs (Figure 6.7b). Corner crystals show the lowest corrected photon count and the worst energy resolution of $\sim 15\%$.

The calibrated energy spectrum for all crystals of a detector stack is shown in Figure 6.8a. The linearity can be checked by the second peak of the $^{22}\text{Na}$ with a gamma energy of 1275 keV which is only $\sim 5\%$ below the expected value. For PET the linearity is important if energy resolutions are determined by fitting the 511 keV peak.

The coincident energy spectrum of the whole scanner from a measurement with an FDG filled line source with an activity of 8.3 MBq is shown in Figure 6.8b. The COG-ACE and E-FD algorithms are used with a selection of singles which are a member of DN with a minimum photon value of 100 corrected photons.

The scanner’s energy resolution for coincident singles calculated using the different energy calculation algorithms is shown as a function of validation threshold in Fig. 6.9. All methods for energy calculation are close to each other and only differ by about 1.6%
6.3. Results and Discussion

Figure 6.7.: The plots show the median value of the 60 detector stacks. Crystals located above the center of a DPC have a higher corrected photon value of the photo peak and a better energy resolutions compared to those above bond gaps. Values are plotted for each crystal using the position in the crystal array. The calibration was performed with a measurement conducted at a cooling temperature of 5 °C, trigger scheme 2 and val = 28 ph. (reprinted from Schug et al. (2015b), §3.0)

Figure 6.8.: (a) Singles energy spectrum for a calibrated detector stack. The $^{22}$Na 1275 keV peak can be seen at a slightly too low energy value. (b) Energy spectrum of coincident singles using only the neighbor filter and a minimum 100 corrected photons from a measurement with the FDG filled line source with an activity of 8.3 MBq. The photopeak at 511 keV and the compton spectrum can be seen. (reprinted from Schug et al. (2015b), §3.0)
6. Processing and Calibration for the Preclinical Configuration

Figure 6.9.: Energy resolution as a function of the validation threshold for different energy calculation methods. The measurements were conducted at a cooling temperature of 15°C and trigger scheme 3 as a function of validation threshold. Lines are plotted to guide the eye. (reprinted from Schug et al. (2015b), 3.0)

(relative difference). For E-DN the energy resolution stays stable for all validation thresholds at about 12.6%. The energy resolution for E-FN starts at about 12.4% at low validation thresholds and degrades to the level of E-DN at high validation thresholds. This behavior can be explained by the bias of the filter requiring singles to be a member of FN. This filter has a higher efficiency for crystals located over bond gaps which have a worse energy resolution and thus increases their statistical weight (see Figure 6.5a, Figure 6.5b and Figure 6.7b). The E-FD method is able to maintain the energy resolution constantly at about 12.4%. Thus, even allowing for data to be missing using the E-FD algorithm the overall systems energy resolution is not deteriorated. It even improves for higher validation thresholds and delivers the best system wide performance for the energy resolution of the three methods.

Timing offsets for the DPCs with respect to each other can be determined with an uncertainty of only a few pico seconds.

The delay between SDMs is caused by different signal run times in the synchronization lines and are in the order of a few hundreds of ps. The detector stacks on a SDM show a delay pattern with values in the order of ±200 ps with respect to each other. This pattern is similar for all SDMs as the firmware and signal paths are the same on all SDMs. For DPCs a similar pattern on all detector stacks can be observed with
DPC delays in the order of ±100 ps. The order of magnitude of these values shows the need to perform a time alignment down to the level of individual DPCs.

Even crystal delay values can be determined with a high accuracy but their absolute value is small compared to the timing performance of the scanner and is in the order of a few tens of ps and does not influence the overall timing performance (Fig. 6.10). The timing performance of the system, which is evaluated and discussed in detail in the next chapter, is roughly in the order of 260 ps, 430 ps, 540 ps and 1250 ps for trigger settings 1-4, respectively using 5 $^{22}$Na sources, a cooling temperature of −5 °C and the NE. The timing performance of the system is not expected to change, if a corner DPC is allowed to be missing, as it only captures a small fraction of the scintillation light and therefore has a long delay until the trigger is generated and does not influence the timestamp of a single.

6.4. Conclusion/Outlook

For most crystals, the corner DPC captures the least scintillation light especially for crystals located close to the center of a DPC. Depending on the validation threshold, this leads to the corner DPC not being validated and missing in clustered singles data. Accepting singles with this DPC missing helps to improve the sensitivity of the scanner compared to only accepting singles with all neighbors present of up to a factor of two, depending on the validation threshold.

The presented extrapolation method COG-DN-Ex is able to correct the distorted COG position of the COG-DN method. Using a purely geometrical distortion corrections or a second 2D LUT are further possibilities to handle singles being a member of DNe for the crystal identification. If correctly accounted for, allowing the corner DPC
6. Processing and Calibration for the Preclinical Configuration

to be missing improves the overall system energy resolution compared to filtering for singles with all neighbors present.

The presented time alignment procedure is able to accurately determine the systematic time offsets that can occur in the system and even allows to calibrate individual crystal offsets the timing resolution will be evaluated in the following chapter.

A robust DPC-raw-data-to-single algorithm has been presented which allows to obtain stable results regarding COG position and energy while maintaining a good sensitivity. This has been realized by accepting and correctly accounting for up to two sets of input channels per crystal. Especially high resolution applications, using a light sharing element, pose challenges due to low signal to noise levels of some channels. The proposed method is only slightly more complex than a simple COG method but still less computational expensive than more advanced crystal identification methods like a maximum likelihood algorithm. The model could be further enhanced to handle further sets of input channels.

In the following chapter the PET performance of the Hyperion-II\textsuperscript{D} PET/MRI insert will be evaluated employing the presented calibration and processing techniques.
7. PET Performance Evaluation of the Preclinical Configuration

The content of this chapter is subject of the following paper, of which I am the main author. Content has been copied, rearranged, reformulated and details have been added.


7.1. Introduction

The PET performance evaluation presented in this chapter employs the calibration and processing techniques explained in the previous chapter and to my knowledge evaluates for the first time a DPC based high-resolution, preclinical PET system in this detail for a bigger, imaging capable scanner.

So far, investigations of the DPC for PET applications were mainly conducted using small demonstrators based on the TEK provided by PDPC with a maximum of 4 detector stacks (very few evaluation were conducted with the Tile TEK allowing to connect up to 8 detector stacks). For example, the influence of DPC configuration parameters on the readout probability (Tabacchini et al. 2014) and on the number of counted photons (Dam et al. 2012) was investigated. The timing performance of TEK-based gamma detectors was evaluated (Dam et al. 2013). Scintillator arrangements ranging from pixelated (Yeom et al. 2013; Schug et al. 2013; Georgiou et al. 2014; Marcinkowski et al. 2014) to monolithic scintillators (Seifert et al. 2013) were implemented on the TEK. Only a few imaging-capable demonstrators using DPCs on the TEK were presented (España et al. 2014; Schneider et al. 2015). Apart from a single demonstrator built up by PDPC (Degenhardt et al. 2012) and results presented for a clinical PET/CT (Miller et al. 2014), DPCs have not been investigated on the larger system level, yet. Hyperion-II\(^D\) (chapter 5) was used to perform the first extensive performance study of a DPC-based preclinical PET.

Hyperion-II\(^D\) employs sensor tiles which are specially optimized for MR compatibility, but similar in terms of the geometrical layout to the sensor tiles distributed by PDPC. The scanner houses 60 sensor tiles, while the TEK platform can be used to
read out a maximum of 4 tiles with the Tile TEK and 8 tiles with the Module TEK and thus offers only a limited maximum sensitivity, bore size and limits PET performance evaluations to small system designs. In this chapter, the influence of the DPC operating parameters on the PET performance of the insert equipped with a preclinical scintillator configuration outside an MRI system was investigated. The used data processing and calibration techniques were presented in chapter 6 and can be used on a wide range of system designs based on DPCs utilizing a similar scintillator geometry. The influence of operating parameters, such as temperature and the applied voltage, as well as DPC configuration parameters on the energy resolution, the timing performance, the sensitivity and the spatial image resolution of the insert was evaluated. The findings shall allow system architects, aiming at a similar detector design using DPCs, to make predictions on the design requirements and the performance that can be expected.

7.2. Materials

The Hyperion-II\textsuperscript{D} scanner was used equipped with 10 SDMs fully populated with six detector stacks in the preclinical configuration (chapter 5).

7.2.1. Test sources and Phantoms

Figure 7.1.: (a) slice through the mouse-sized scatter phantom. The scatter phantom has an axial extent of 70 mm. (b) hot-rod phantom used to investigate the spatial resolution. The structured region has an diameter of 28 mm. The evaluated profiles are marked in orange. (c) rabbit-sized phantom used to investigate the benefit of ToF information for image reconstruction. The structured part of the phantoms (b) and (c), for which the slices are shown, have an axial extent of 20 mm. The FDG-filled areas are marked in red. (reprinted from Schug et al. (2016), @2016)
7.3. Methods

Five point-like $^{22}$Na sources with an active diameter of 0.25 mm and an activity of 1.1 MBq - 1.5 MBq enclosed in a cast acrylic cube with an edge length of 10 mm (NEMA cubes) were used for performance studies under a large variety of different operating parameters at a constant activity.

A mouse-sized scatter phantom (NEMA NU 4 standard) was used for investigations of activity-dependent performance parameters including the count rate performance of the scanner (Figure 7.1a). The phantom has an axial extent of 70 mm and a diameter of 25 mm with a hole to hold a tube with a radioactive tracer solution. The hole is placed 10 mm off center and is 3.2 mm in diameter. The tube fits the hole and has a wall thickness of 0.5 mm. The activity was distributed over the full 70 mm of the phantom opposed to the distribution defined in the NEMA NU 4-2008 standard (60 mm).

For image-spatial-resolution studies, a mouse-sized hot-rod phantom with six regions with rods of 0.8 mm, 0.9 mm, 1.0 mm, 1.2 mm, 1.5 mm and 2.0 mm in diameter, a center-to-center spacing of two times the diameter and an axial extent of 20 mm (Figure 7.1b) was used.

To investigate the benefits of ToF image reconstruction, a rabbit-sized phantom with a diameter of 114 mm (Figure 7.1c) was used. The phantom is structured with rods with a diameter of 3 mm and an axial extent of 20 mm distributed on a Cartesian grid with a pitch of 6 mm. All phantoms were filled with an FDG solution.

7.3. Methods

The unprocessed raw DPC sensor data was evaluated using the processing techniques described in the previous chapter (chapter 6). The COG with automatic corner extrapolation (COG-ACE) was used for all performance evaluations in this chapter. A correction of time stamps as a function of the light output of the scintillator (walk correction) was not applied.

7.3.1. Temperature Measurements

The cooling temperature $T_C$ was set and controlled by the process thermostat. The operating temperature $T_{op}$ was measured with the temperature sensor on the backside of the sensor tiles. A system $T_{op}$ is reported as the mean and standard deviation of all sensor tile $T_{op}$ readings.

7.3.2. Measurement of the Breakdown Voltage and Bias Voltage Regulation

By connecting the SPADs to ground and measuring the current-voltage characteristic, $V_{bd}$ was determined for each sensor tile individually. This measurement was performed
7. PET Performance Evaluation of the Preclinical Configuration

for different \( T_C \) resulting in \( T_{op} \approx 0^\circ C - 27^\circ C \). To determine the dependence of the DPC’s \( V_{bd} \) on \( T_{op} \), a linear regression on the measured data was performed.

For the following experiments, \( V_{bias} \) was set to a constant value prior to and not dynamically adjusted during a measurement. For one set of measurements with different \( T_C \), \( V_{bias} \) was kept constant using the \( V_{bd} \) value obtained at \( T_C = 15^\circ C \), which means that a change in \( T_C \) lead to an effective change of \( V_{ov} \). For the other set of measurements, \( V_{bias} \) was adjusted before the start of a measurement for the selected \( T_C \), meaning that the effective \( V_{ov} \) was kept constant as a function of \( T_C \).

7.3.3. Basic PET Performance Measurements

The influence of the \( V_{ov} \), \( T_C \), trig, val, activity and energy window on the basic PET performance parameters: energy resolution (\( \Delta E/E \)), CRT and sensitivity was investigated. It is not feasible to scan all parameter combinations of the multi-dimensional space. Therefore, several testing scenarios around conservatively chosen benchmark points were chosen and parameters were varied along some axes of the parameter space. For all measurements 20% of the noisiest SPADs per pixel were inhibited. A validation length of 40 ns, an integration length of 165 ns and a fixed cluster window of 40 ns were used. Two different energy windows were used: the narrow energy window (NE) ranges from 411 keV – 561 keV to reject scattered gammas and discard high-light-output and pile-up events. The wide energy window (WE) was set to 250 keV – 625 keV to increase the sensitivity compared to the NE. Singles were filtered before performing a coincidence search with a sliding CW. If not mentioned otherwise, \( CW = 400 \) ps, 550 ps, 650 ps and 1500 ps was used for trig 1-4, respectively, which corresponds to approximately \( \pm 3 \sigma \) CRT.

Coincidences with more than two singles were discarded. A minimal distance of 4 detector stacks between the two singles in tangential direction was required. For the rabbit-sized phantom, this was reduced to 3 detector stacks to increase the FOV.

7.3.3.1. \( ^{22} \text{Na} \) Point Sources:

The five NEMA cubes were distributed in the FOV along the z-axis (axial). The positions and activities of the point sources are listed in Table 7.1. This allows a very precise determination of the CRT as each LOR can be unambiguously assigned to one of the point sources.

For the measurement series with constant \( V_{bias} \), the default benchmark point was chosen as \( V_{ov} = 2.5 \) V, \( T_C = 15^\circ C \), trig 2 and val 17 ph. Starting from this benchmark point, \( V_{ov} = 2.5 \) V, 2.8 V, 2.9 V and 3.0 V and \( T_C = -5^\circ C, 5^\circ C, 15^\circ C \) and 20\(^\circ C \), trig 1-4 and val 17 ph, 28 ph and 52 ph were investigated. Additionally, at \( T_C = -5^\circ C \) the influence of the overvoltage was investigated with \( V_{ov} = 2.5 \) V, 2.8 V and 2.9 V. The data was processed with the NE and WE. All performed measurements and their settings are listed in supplementary Table A.1.
7.3. Methods

Table 7.1.: Source positions for the measurements with the five NEMA cubes. (reprinted from Schug et al. (2016), ①3.0)

<table>
<thead>
<tr>
<th>NEMA cube</th>
<th>constant $V_{\text{bias}}$</th>
<th>constant $V_{\text{ov}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$x$/mm $y$/mm $z$/mm activity/MBq</td>
<td>$x$/mm $y$/mm $z$/mm activity/MBq</td>
</tr>
<tr>
<td>1</td>
<td>-0.6 -1.8 -0.5 1.48</td>
<td>-2.7 -11.8 -37.9 1.35</td>
</tr>
<tr>
<td>2</td>
<td>-1.3 -1.7 30.2 1.37</td>
<td>-1.9 -9.8 -18.7 1.26</td>
</tr>
<tr>
<td>3</td>
<td>-0.6 -1.8 -15.5 1.28</td>
<td>-1.6 -9.9 -1.4 1.17</td>
</tr>
<tr>
<td>4</td>
<td>-1.5 -1.7 14.4 1.25</td>
<td>-2.4 -10.9 12.9 1.15</td>
</tr>
<tr>
<td>5</td>
<td>-0.2 -1.8 -32.1 1.20</td>
<td>-2.3 -11.8 29.7 1.10</td>
</tr>
</tbody>
</table>

The benchmark point for the measurement with constant $V_{\text{ov}} = 2.5$ V was chosen as val 17 ph. The cooling temperatures $T_C = -5$°C, 5°C, 10°C, 15°C and 20°C were investigated for trig 1, 3 and 4. Trig 2 was omitted as it yields similar results to trig 3, as learned from the first measurement series. All measurements and their settings are listed in supplementary Table A.2.

7.3.3.2. FDG Mouse-Sized Scatter Phantom:

The mouse-sized scatter phantom was filled with FDG (Figure 7.1a) and measurements started at an activity of $\sim 110$ MBq and were performed down to $\sim 0.5$ kBq. $T_C = 0$°C, $V_{\text{ov}} = 2.5$ V were used and the DPCs were programmed with combinations of trig 1, 2 and 3 and val 17 ph, 28 ph, 37 ph and 52 ph during the decay of the FDG. All measurements and their settings are listed in supplementary Table A.3.

7.3.3.3. Result Extraction and Computation

$\Delta E/E$ was determined using the energy spectrum of coincident singles. A Gaussian was iteratively fitted to match a fit range of $-0.5$ FWHM to 1.0 FWHM from the mean. No background removal or modeling was performed (see result plot Fig. 7.3).

To show the energy spectrum of the scanner over a larger range for one exemplary measurement of the mouse-sized scatter phantom only a very small lower threshold of only 100 measured photons on the channels used for energy calculation on coincident singles (see previous chapter) were applied.

The CRT was calculated by evaluating the FWHM of the spectrum of the measured timing differences between coincident singles corrected for known source positions either of the point sources or the line source. A Gaussian was iteratively fitted to match a fit range of $-0.5$ FWHM to 0.5 FWHM from the mean. No background removal or modeling was performed.

For measurements using the $^{22}$Na point sources, the sensitivity was evaluated using the prompts rate without correcting for randoms and scatter. The branching ratio of the $^{22}$Na $\beta^+$ decay of 0.906 was accounted for. The sensitivity as a function of
activity was measured with the mouse-sized scatter phantom corrected for scatter and randoms. The randoms rate was estimated based on the singles rate per crystal and was corrected for prompts and pile-up (Oliver and Rafecas 2012). Scatter estimation was performed based on the *NEMA NU 4-2008* standard using a single sinogram (projection of all LORS on a single transaxial plane) for the whole scanner. The prompts rate, randoms rate, scatter rate and NECR were evaluated in the corridor defined in the *NEMA NU 4-2008* standard.

**7.3.4. Imaging Experiments**

All imaging experiments were conducted using the NE to suppress object scatter and trig 1 and trig 3 were employed. If not stated otherwise, the same parameters as for the basic PET performance measurements were used. Reconstructions were performed for the whole datasets of the two measurements and, for comparison, they were trimmed once for the same number of tracer decays and once for the same number of recorded coincidences. This allowed comparisons taking the respective sensitivity into account as well as neglecting it and using the same statistics.

Image reconstructions were performed using an OSEM (Hudson and Larkin 1994) 3D reconstruction (Salomon et al. 2011; Salomon et al. 2012). After each subset of an iteration, a 3D Gaussian smoothing was performed. A self-normalization was used but no corrections for scatter or attenuation were applied. The reconstructed activity distributions were linearly normalized using the same region of interest per phantom. The 3D data was projected on a transaxial plane using a defined extent in axial direction (slice thickness) in order to reduce the required measurement time to acquire enough coincidences for image reconstruction showing the 2D resolution of the scanner in the transaxial plane. Specific parameters for the reconstructions are stated for the respective phantom measurement.

All of the above mentioned datasets were reconstructed with and without ToF information, and the absolute difference between the two reconstructions was calculated for each dataset. The absolute-difference images were multiplied with a factor of 5 in order to better visualize the difference using the same grayscale as used for the reconstructed data sets.

**7.3.4.1. FDG Mouse-Sized Hot-Rod Phantom:**

For the mouse-sized hot-rod phantom (Figure 7.1b), the measurement parameters were chosen as $T_C = -5\, ^\circ\text{C}$, $V_\text{ov} = 2.5\, \text{V}$ and val 28 ph. The trig 3 measurement was started with an activity of 9.0 MBq for a measurement time of 762 s. Approximately 8 min later, the phantom was measured at an activity of 7.9 MBq with trig 1 for 1160 s.

For the image reconstructions, a voxel pitch of 0.25 mm, 16 iterations and 32 subsets were used, a Gauss filter of approximately 0.17 mm (FWHM) was applied after each subset, and a slice thickness of 20 mm was chosen. Two profiles through these slices
were extracted: one profile going through the rods with a diameter of 0.9 mm and 1.2 mm, and a second profile through the rods with a diameter of 0.8 mm and 1.0 mm (Figure 7.1b). The peak-to-valley values were calculated for each peak using the profiles. The peak height was divided by the mean height of the two adjacent valleys or, for the first and last peak, the height of the single adjacent valley.

7.3.4.2. FDG Rabbit-Sized Phantom:

For the rabbit-sized phantom (Figure 7.1c), $T_C = -5^\circ C$, $V_{ov} = 2.5 V$ and val 28 ph were used. A CW of 1.5 ns was used for both trig to account for the diameter of the activity distribution.

For the first experiment using this phantom, the axes of the cartesian grid on which the rods are located were aligned with the axes of the transversal plane of the scanner (see section 7.5.5 and Fig. 7.12). The trig 3 measurement was started with an activity of 3.8 MBq for a measurement time of 1542 s. Approximately 14 min later, the phantom was measured at an activity of 3.0 MBq using trig 1 for 1018 s.

For a second experiment, the phantom was rotated around the axial axis by 9° with respect to the first experiment to break the alignment of the phantom axes with the scanner gaps (see discussion section 7.5.5). For the trig 1 measurement, an activity of 13.8 MBq was used and measured for a duration of 924 s. Trig 3 was measured approximately 8 min later with an activity of 11.9 MBq for 708 s.

For the image reconstructions, a voxel pitch of 1 mm, 16 iterations and 8 subsets were used, a Gauss filtering after each subset of 0.7 mm (FWHM) was applied and a slice thickness of 10 mm chosen.

7.4. Results

The detailed results of all measurements using the point sources and the mouse-sized scatter phantom are listed in the supplement (Table A.1, Table A.2 and Table A.3). Graphs were extracted to show the behavior of a performance parameter as a function of $V_{ov}$, system $T_{op}$ and activity. The difference of $T_C$ and the system’s $T_{op}$ was approximately 5°C–10°C under operation mainly depending on $T_C$, trig and the activity (for all measurements both values are reported in the supplement). Improvements and degradations are reported as relative changes.

7.4.1. Measurement of the Breakdown Voltage

The mean and standard deviation of $V_{bd}$ for all sensor tiles was determined as $23.02 \pm 0.12 V$ at $T_{op} = 15^\circ C$ and its dependence on $T_{op}$ as $17.1 \pm 1.0 mV/K$ (Fig. 7.2). $T_{op}$ of one detector stack could not be read out due to a broken sensor and was omitted for the evaluation. Nonetheless, $V_{bd}$ was saved for the applied values of $T_C$ for this detector stack as well.
7. PET Performance Evaluation of the Preclinical Configuration

Figure 7.2.: Histogram of the dependence of the breakdown voltage on temperature of all tiles of the system, except for one tile with a faulty temperature sensor. (reprinted from Schug et al. (2016), DOI3.0)

7.4.2. Possible Operating Parameters

Due to the current limitation on the $I_{DDA}$ line, using trig 1 was limited to low temperatures and low activities. $T_C = 5^\circ\text{C}$ ($T_{op} = 13.77 \pm 1.35^\circ\text{C}$) was the highest of the tested temperatures which allowed a stable operation of trig 1 using $V_{ov} = 2.5 \text{ V}$. The highest possible activity was 36.74 MBq. The other trig could be used without restrictions for all tested operation conditions.

7.4.3. System Energy Resolution

The exemplary energy spectrum for coincident singles obtained from a measurement with the FDG-filled scatter phantom for an activity of 8.41 MBq with $\Delta E/E = 12.39\%$ is shown in Fig. 7.3.

Using the $^{22}\text{Na}$ sources at the default benchmark point (see Methods 7.3.3.1), $\Delta E/E$ for trig 2, trig 3 and trig 4 was measured as 12.75 %, 12.75 % and 12.85 %. Increasing the $V_{ov}$ from 2.5 V to 3 V improved $\Delta E/E$ relatively by 1%–2% (Figure 7.4a and Figure 7.4b).

For constant $V_{bias}$, decreasing $T_C$ from 15 $^\circ\text{C}$ down to $-5^\circ\text{C}$ ($T_{op}$ from $\sim 21^\circ\text{C}$ down to $\sim 3^\circ\text{C}$) improved $\Delta E/E$ relatively by $\sim 2.5\%$–3.5\% (Figure 7.4c and Figure 7.4d). In the evaluated $T_{op}$ range, trig 1 showed an approximately twofold stronger dependence.
7.4. Results

Figure 7.3.: Exemplary and unfiltered system energy spectrum of coincident singles applying the COG-ACE algorithm requiring a minimum of 100 photons from a measurement with the FDG-filled mouse-sized scatter phantom with an activity of 8.41 MBq. The Gaussian fitted to the spectrum to evaluate $\Delta E/E$, is plotted in the used fit range. (reprinted from Schug et al. (2016), Θ3.0)

For constant $V_{ov}$, the dependence of $\Delta E/E$ on $T_{op}$ was smaller and was measured as a relative change of $\sim$1% for a comparable change in $T_{op}$ (Figure 7.4e). $\Delta E/E$ for trig 4 was relatively $\sim$1% worse compared to trig 2 and 3 for all operating conditions.

$\Delta E/E$ determined with the measurement of the mouse-sized scatter phantom as a function of activity is shown in Figure 7.4f. It degraded relatively by $\sim$9% from low activities to 100 MBq for all trig. Trig 1 showed an $\Delta E/E$ which was relatively $\sim$1% worse compared to the other trig.

7.4.4. Coincidence Resolution Time

Using the $^{22}$Na sources at the default benchmark point (see Methods 7.3.3.1), the system’s CRT using the NE for trig 2, trig 3 and trig 4 was measured as 450 ps, 562 ps and 1.3 ns, respectively. Increasing $V_{ov}$ from 2.5 V to 3 V improved the CRT up to $\sim$9% (Figure 7.5a and Figure 7.5b). Higher val showed a stronger improvement.

For constant $V_{bias}$, decreasing $T_{C}$ from 15 °C down to $-5$ °C ($T_{op}$ from $\sim$21 °C down to $\sim$3 °C) improved the CRT values up to 15%–20%. When operating at a $T_{op}$ of 4.48 ± 1.45 °C and 13.41 ± 1.32 °C, trig 1 delivered a CRT of 258 ps and 272 ps (Figure 7.5c and Figure 7.5d). For constant $V_{ov}$, the dependence of CRT on $T_{op}$ was mainly eliminated (Figure 7.5e). The CRT values measured at $T_{C} = 15$ °C ($T_{op} \approx 20.5$ °C) were lower than the ones obtained at all other $T_{op}$. The trig 1 showed a
7. PET Performance Evaluation of the Preclinical Configuration

Figure 7.4.: $\Delta E/E$ of the whole insert measured with the $^{22}$Na point sources is shown as a function of $V_{ov}$ in (a) for different trig and in (b) for different val. It is shown as a function of $T_{op}$ for a constant $V_{bias}$ in (c) for different trig and in (d) for different val. For a constant $V_{ov}$, it is shown as a function of $T_{op}$ in (e) for different trig. Measured with the FDG-filled scatter phantom, it is shown in (f) as a function of activity for different trig and val. (reprinted from Schug et al. (2016), ©3.0)
degradation of the CRT value when measuring $T_{\text{op}} = 13.77 \pm 1.35 \degree C$ compared to the other $T_{\text{op}}$. The CRT of the WE was $15\% - 20\%$ worse compared to the NE.

Using the mouse-sized scatter phantom, the CRT as a function of activity is shown in Figure 7.5f. The CRT degraded linearly by about $3\% - 5\%$ from small activities to 100 MBq. Trig 1 showed a more than twofold stronger dependence.

### 7.4.5. Sensitivity

The prompts rate for the five $^{22}$Na point sources at the default benchmark point (see Methods 7.3.3.1) was measured as 60 kcps using the NE and 124 kcps for the WE. This results in a sensitivity of $1.0\%$ and $2.1\%$ for the given distribution of point sources. Increasing the $V_{\text{ov}}$ from 2.5 V to 3 V improved the sensitivity only for trig 4. The other trig lost up to $10\%$ sensitivity (Figure 7.6a). For high val increasing the $V_{\text{ov}}$ was beneficial. Low val, on the other hand, lost sensitivity (Figure 7.6b).

For constant $V_{\text{bias}}$, decreasing $T_{\text{op}}$ improved the sensitivity for almost all operating parameters. Only the sensitivity for trig 2 to 4 degraded when going from $T_{\text{op}} \approx 11.5 \degree C$ to $T_{\text{op}} \approx 3.0 \degree C$ and applying the NE (Figure 7.6c and Figure 7.6d). For constant $V_{\text{ov}}$, lower $T_{\text{op}}$ were beneficial for all trig (Figure 7.6e). Especially the sensitivity of trig 1 was strongly dependent on $T_{\text{op}}$. It showed a loss of $\sim 35\%$ at $T_{\text{op}} = 4.86 \pm 1.42 \degree C$ up to $\sim 65\%$ at $T_{\text{op}} = 13.77 \pm 1.35 \degree C$ compared to the higher trig.

Using the mouse-sized scatter phantom, the scatter fraction was measured to be $\sim 6\%$ for the NE and $\sim 16\%$ for the WE. It showed a slight increase as a function of activity (Figure 7.7a). For the NE it was almost independent of the used trig and val. For the WE, the maximal differences were within a relative band of $\sim \pm 15\%$.

The random fraction of the system was dependent on the used energy window and the CW applied (Figure 7.7b). It can be roughly approximated with a linear dependence on the activity of $\sim 0.2\%/\text{MBq} - 0.5\%/\text{MBq}$.

The NECR curves of the mouse scatter phantom showed different peak NECRs dependent on the trig and val (Figure 7.7c). The peak NECR was for all parameters beyond 25 MBq. Using WE, trig 2 and 3 with a val of at least 28 ph, peak NECRs of about 280 kcps – 320 kcps were measured. For higher trig and val the peak NECR shifted to activities of up to 50 MBq.

The trues sensitivity curve for the mouse scatter phantom is shown in Figure 7.7d. For low activities, an approximately linear decrease in trues sensitivity could be observed, followed by a stronger decline of the sensitivity.
Figure 7.5.: The CRT measured with the $^{22}$Na point sources is shown in (a) as a function of $V_{ov}$ for different trig and in (b) for different val. It is shown for a constant $V_{bias}$ as a function of $T_{op}$ in (c) for different trig and in (d) for different val. For a constant $V_{ov}$, it is shown as a function of $T_{op}$ in (e) for different trig. Measured with the FDG-filled scatter phantom, it is shown in (f) as a function of activity for different trig and val. (reprinted from Schug et al. (2016), \(\Theta^3.0\))
7.4. Results

Figure 7.6.: The sensitivity for the $^{22}$Na point sources (Table 7.1) is shown as a function of $V_{ov}$ in (a) for different trig and in (b) for different val. It is shown for a constant $V_{bias}$ as a function of $T_C$ in (c) for different trig and in (d) for different val. For a constant $V_{ov}$, it is shown as a function of $T_C$ in (e) for different trig. (reprinted from Schug et al. (2016), ☢3.0)
Figure 7.7.: (a) the scatter fraction curves for the mouse scatter phantom for a constant $V_{ov} = 2.5 \text{ V}$ and $T_C = 0^\circ \text{C}$ for different trig and val. The two bands for the different energy windows can clearly be distinguished. (b) the random fraction for the mouse scatter phantom for a constant $V_{ov} = 2.5 \text{ V}$ and $T_C = 0^\circ \text{C}$ for different trig and val. (c) the NECR curves for the mouse scatter phantom for a constant $V_{ov} = 2.5 \text{ V}$ and $T_C = 0^\circ \text{C}$ for different trig and val. (d) the trues sensitivity for the same measurements. (reprinted from Schug et al. (2016), DOI: 10.1001/jamaopa.2016.308)
7.4.6. FDG Mouse-Sized Hot-Rod Phantom

The results and statistics for the mouse-sized hot-rod phantom measurements are listed in Table 7.2. The measurements normalized for the same amount of decays during the measurement time are shown for trig 3 and trig 1 in Fig. 7.8 (a) and (b) and those normalized for the same number of coincidences in Fig. 7.8 (c) and (d). None of the measurements showed a benefit of the ToF reconstruction.

The profile lines through the slices, as defined in Fig. 7.1, are shown for 0.8 mm and 1.0 mm rods in Figure 7.9a and for 0.9 mm and 1.2 mm rods in Figure 7.9b. As the profiles did show a systematic dependency of the peak-to-valley values on the position and did not differ significantly for the different measurement settings and reconstructions, only a combined mean peak-to-valley value for each rod size of all the shown profiles is reported. The extracted mean peak-to-valley values and their standard deviations are $1.24 \pm 0.15$, $1.47 \pm 0.18$, $1.87 \pm 0.19$ and $2.32 \pm 0.28$ for rod sizes of 0.8 mm, 0.9 mm, 1.0 mm and 1.2 mm, respectively.

7.4.7. FDG Rabbit-Sized Phantom

For the measurement with the axes of the Cartesian grid of the phantom aligned with the axes of the transversal plane of the scanner, the results and statistics are listed in Table 7.3. The measurements normalized for the same amount of decays during the measurement time are shown in Fig. 7.10 (a) and (b) and those normalized for the same number of coincidences in Fig. 7.10 (b) and (c). The untrimmed trig 3 measurement with more than threefold the number of counts compared to the trig 1 is shown in Fig. 7.10 (d).

For the measurement in the tilted position, the results and statistics are listed in Table 7.4. The measurements normalized for the same amount of decays during the measurement time are shown in Fig. 7.11 (a) and (b) and those normalized for the same number of coincidences in Fig. 7.11 (c) and (d).

For both phantom orientations, the trig 1 measurements (Fig. 7.10 (b), Fig. 7.11 (b) and (d)) showed a benefit of the ToF reconstruction.
Table 7.2.: Statistics for the hot-rod phantom measurement. (reprinted from Schug et al. (2016), ☞3.0)

<table>
<thead>
<tr>
<th>trig</th>
<th>normalized to</th>
<th>activity</th>
<th>system $T_{op}$</th>
<th>meas. time</th>
<th>FDG decays</th>
<th>LORs</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a)</td>
<td>3</td>
<td>all</td>
<td>9.0 MBq</td>
<td>3.52 ± 1.38°C</td>
<td>762 s</td>
<td>6.48 × 10⁹</td>
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<tr>
<td>(b)</td>
<td>1</td>
<td>decays</td>
<td>7.9 MBq</td>
<td>3.38 ± 1.29°C</td>
<td>875 s</td>
<td>6.48 × 10⁹</td>
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<tr>
<td>(c)</td>
<td>3</td>
<td>counts</td>
<td>9.0 MBq</td>
<td>3.52 ± 1.38°C</td>
<td>640 s</td>
<td>5.49 × 10⁹</td>
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<tr>
<td>(d)</td>
<td>1</td>
<td>all</td>
<td>7.9 MBq</td>
<td>3.38 ± 1.29°C</td>
<td>1160 s</td>
<td>8.41 × 10⁹</td>
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Figure 7.8.: Transversal slices through the reconstructed hot-rod phantom. The voxel pitch is 0.25 mm. The slice thickness is 20 mm. The complete datasets of trig 1 and trig 3 (all) are truncated for comparison: trig 3 all matches trig 1 decays in terms of the number of tracer decays and trig 3 counts matches trig 1 all in terms of the number of coincidences (Table 7.2). The third column shows the absolute difference multiplied with a factor of 5 between the two reconstructions for each measurement. (reprinted from Schug et al. (2016), ☞3.0)
Figure 7.9.: Profiles of the hot-rod phantom through the (a) 0.8 mm and 1.0 mm rods and (b) 0.9 mm and 1.2 mm rods. (reprinted from Schug et al. (2016), ©Elsevier)
Table 7.3.: Statistics for the rabbit-sized phantom measurement. (reprinted from Schug et al. (2016), 3.0)

<table>
<thead>
<tr>
<th>trig</th>
<th>normalized activity</th>
<th>system $T_{op}$</th>
<th>meas. time</th>
<th>FDG decays</th>
<th>LORs</th>
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<tbody>
<tr>
<td>(a) 3 decays</td>
<td>3.8 MBq 3.85 ± 1.14 °C</td>
<td>779 s</td>
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<td>15.88 × 10⁶</td>
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</tr>
<tr>
<td>(b) 1 all</td>
<td>3.0 MBq 4.83 ± 1.39 °C</td>
<td>1018 s</td>
<td>2.79 × 10⁹</td>
<td>9.90 × 10⁶</td>
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</tr>
<tr>
<td>(c) 3 counts</td>
<td>3.8 MBq 3.85 ± 1.14 °C</td>
<td>478 s</td>
<td>1.75 × 10⁹</td>
<td>9.90 × 10⁥</td>
<td></td>
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<tr>
<td>(d) 3 all</td>
<td>3.8 MBq 3.85 ± 1.14 °C</td>
<td>1542 s</td>
<td>5.23 × 10⁹</td>
<td>30.24 × 10⁶</td>
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Figure 7.10.: Transversal slices through the reconstructed rabbit-sized phantom. The voxel pitch is 1 mm. The slice thickness is 10 mm. The complete datasets of trig 1 and trig 3 (all) are truncated for comparison: trig 3 decays matches trig 1 all in terms of the number of tracer decays and trig 3 counts matches trig 1 all in terms of the number of coincidences (Table 7.3). The third column shows the absolute difference multiplied with a factor of 5 between the two reconstructions for each measurement. (reprinted from Schug et al. (2016), 3.0)
Table 7.4.: Statistics for the rabbit-sized phantom measurement in the tilted position. (reprinted from Schug et al. (2016), Θ3.0)

<table>
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<tr>
<th>trig</th>
<th>normalized</th>
<th>activity</th>
<th>system $T_{op}$</th>
<th>meas. time</th>
<th>FDG decays</th>
<th>LORs</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a)</td>
<td>all</td>
<td>11.9 MBq</td>
<td>3.49 ± 1.15 °C</td>
<td>708 s</td>
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<td>$43.47 \times 10^6$</td>
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<tr>
<td>(b)</td>
<td>decays</td>
<td>13.8 MBq</td>
<td>3.66 ± 1.26 °C</td>
<td>606 s</td>
<td>$7.99 \times 10^9$</td>
<td>$26.70 \times 10^6$</td>
</tr>
<tr>
<td>(c)</td>
<td>counts</td>
<td>11.9 MBq</td>
<td>3.49 ± 1.15 °C</td>
<td>652 s</td>
<td>$7.38 \times 10^9$</td>
<td>$40.10 \times 10^6$</td>
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<tr>
<td>(d)</td>
<td>all</td>
<td>13.8 MBq</td>
<td>3.66 ± 1.26 °C</td>
<td>924 s</td>
<td>$11.89 \times 10^9$</td>
<td>$40.10 \times 10^6$</td>
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</table>

Figure 7.11.: Transversal slices through the reconstructed rabbit-sized phantom measured in the tilted position. The voxel pitch is 1 mm. The slice thickness is 10 mm. The complete datasets of trig 1 and trig 3 (all) are truncated for comparison: *trig 3 all* matches *trig 1 decays* in terms of the number of tracer decays and *trig 3 counts* matches *trig 1 all* in terms of the number of coincidences (Table 7.4). The third column shows the absolute difference multiplied with a factor of 5 between the two reconstructions for each measurement. (reprinted from Schug et al. (2016), Θ3.0)
7.5. Discussion

ΔE/E and CRT are comparable to results shown with similar scintillators on the PDPC TEK platform (Dueppenbecker et al. 2011; Degenhardt et al. 2012). It can concluded that the Hyperion-II D data acquisition platform provides a stable clocking and voltage environment on a system level. In other studies, it was shown that the platform is capable of being operated simultaneously inside an MRI (Wehner et al. 2014; Wehner et al. 2015; Weissler et al. 2015). In the following chapters further investigations on the PET performance during MRI operation will be presented.

7.5.1. Possible Operating Parameters

The current limitation on the I_{DDA} line introduces limitations on the possible operating parameters. High operating temperatures cause high I_{DDA}s. In combination with low trig, a high DCR will produce noise triggers which increases the power consumption and dead time of the DPCs. T_C = 5°C (T_{op} = 13.77 ± 1.35°C) was the highest temperature applied using trig 1 which allowed a stable operation. Furthermore, trig 1 was only applicable up to activities of 36.74 MBq due to the current limitation on the I_{DDA} line. Even without these restrictions, trig 1 should not be used at T_{op} ≥ 5°C–10°C as this introduces significant dead time. The higher trig are more robust to high temperatures but still benefit from low temperatures, especially in terms of sensitivity. Limits of the platform due to the saturation of the GbE interfaces are discussed in section 7.5.4.

7.5.2. Energy Resolution

ΔE/E of ~12.7% was very stable for all combinations of parameters applied. At this level, the scanner outperforms ΔE/E shown on other preclinical systems (Inveon: 14.6% (Bao et al. 2009), PET Component of the NanoPET/CT: 19% (Szanda et al. 2011), LabPET: 25% (Bergeron et al. 2014)). A good energy resolution allows to discriminate photopeak from scattered events. The temperature dependency was smaller for constant V_{ov}, as expected. The slight degradation towards higher activities can most likely be attributed to pile-up effects.

7.5.3. Coincidence Resolution Time

The CRT for trig 1 is the best that has been shown for a system with a high-resolution pixelated scintillator configuration so far. However, the CRT values obtained with trig 2 and 3 still outperform, to our knowledge, commercial preclinical systems available today (Inveon: 1.22 ns (Lenox et al. 2006), PET Component of the NanoPET/CT: 1.5 ns–3.2 ns (Szanda et al. 2011), LabPET: ~9 ns (Bergeron et al. 2014)).
7.5. Discussion

Generally, the CRT improved with increasing $V_{ov}$. The effect was higher for high val as the noise induced DPC hits get a smaller statistical weight when determining the final CRT. The CRT for the WE is expected to be worse as no energy-dependent walk correction for the time stamps was performed.

One measurement with constant $V_{bias}$ at $T_C = -5^\circ C$ ($T_{op} = 3.21 \pm 1.15^\circ C$), $V_{ov} = 2.5\, V$, val 52ph and trig 2 showed a deviation in terms of CRT from the expected behavior (see Figure 7.5d and Table A.1 measurement 11 and 12). Our only explanation is that the configuration of the system was not applied as expected. The measurement with constant $V_{ov}$ at $T_C = 15^\circ C$ ($T_{op} \approx 20.5^\circ C$) showed a better CRT performance than the ones obtained at all other temperatures (see Table A.2 measurements 21–24). This behavior can only be explained with a faulty determination of $V_{bd}$ at this temperature leading to a different effective $V_{ov}$ compared to the other measurements.

7.5.4. Sensitivity

A higher $V_{ov}$ increases the PDE of the DPCs as well as the DCR and cross talk. Therefore, increasing the $V_{ov}$ for low val causes more dark noise events to be validated and thus increases the dead time reducing the system’s sensitivity. If a high val is applied, not all DPCs of low-energy events may be validated and a higher $V_{ov}$ increases the probability to reach the validation threshold and thus increases the system’s sensitivity.

The random fraction measured with the mouse-sized scatter phantom is low compared to commercially available systems (Goertzen et al. 2012). This is due to the superior CRT performance and the resulting possible narrow CW. The scatter fraction measured with the small RF Tx/Rx coil is comparable to the lowest values obtained for other preclinical systems (Goertzen et al. 2012). The slight increase of the determined scatter fraction towards high activities can only be explained by fluctuations in the evaluation method, e.g. random estimation, as the scatter fraction should be independent of the activity.

The NECR peak values strongly depended on the chosen trig and val. For the used raw DPC sensor data mode, the GbE interfaces are the bottleneck of the maximum rate of sensor data, the system was able to deliver. If the limit is reached, hit data is statistically thrown away on individual SDMs which are in saturation. This explains why the system showed a stronger decline of the trues sensitivity and NECR when reaching this limit. Measurements with one or more SDMs in saturation should be avoided as hit data is lost depending on the number of hits recorded per SDM. This can lead to activity-dependent loss rates for SDMs, especially if the activity is not symmetrically distributed around the isocenter of the scanner. Therefore, artifacts in the estimated trues rate, randoms rate, scatter fraction and NECR for measurements with SDMs in saturation are most likely caused by data loss. A peak NECR of $\sim 280\, \text{kcps} - 320\, \text{kcps}$ at activities of 30 MBq–55 MBq delivers good sensitivity for
most preclinical applications. Processing and compression of sensor data in firmware should allow to push the peak NECRs to higher values at higher activities until the detector-stack-to-SDM-communication interface or the sensor itself are saturated.

The sensitivity of trig 1 was significantly lower compared to the higher trig for all $T_{op}$ using the COG-ACE crystal identification method. With the employed light sharing, a statistical crystal identification method such as maximum-likelihood estimation could be used to recover the sensitivity loss of trig 1. This, however, would probably occur at the cost of $\Delta E/E$ and CRT performance.

### 7.5.5. Image Spatial Resolution and Benefit of ToF

In the 2D slice of the mouse-sized hot-rod phantom, the scanner was able to separate the 0.8 mm rod region, with the exception of the two rods closest to the center of the phantom which were not resolved. All 0.9 mm rods were separable and clearly identifiable. Although not yet determined according to the NEMA NU 4-2008 standard, the spatial resolution of the scanner seems comparable to the best values reported for other preclinical systems (Goertzen et al. 2012). Trig 1 and trig 3 delivered almost the same peak-to-valley value which indicates that the reconstruction was most likely not limited by statistics. Furthermore, no observable benefit of a reconstruction using the ToF information for neither the trig 1 nor the trig 3 measurement could be shown. This is not surprising, as the CRT of trig 1 (\(~260\) ps) translates to a spatial resolution along the LOR of 39 mm which is still larger than the mouse-sized hot-rod phantom. The better CRT may be used to reduce the random fraction at the cost of sensitivity (Eriksson and Conti 2015).

For the rabbit-sized phantom, trig 1 with ToF information showed a clear benefit due to the large object diameter. Especially in regions of overlapping horizontal and vertical gaps of the system’s geometry that are parallel to the symmetry axes of the Cartesian grid of the phantom, ToF information helped to improve the image quality (Fig. 7.12). Trig 3 did not show an observable improvement when using ToF information for the reconstruction. The trig 3 reconstructions using the complete statistics, which was more than threefold the number of coincidences compared to trig 1, were not able to deliver a comparable image quality to trig 1 with ToF information.

Even though the rotated phantom measurement showed a more homogeneous image quality over the whole area of the phantom, there are still some artifacts visible around the central region (Fig. 7.11). They are significantly reduced by the trig 1 measurement with ToF information.

The measurements using the rabbit-sized phantom suggest an improvement in image quality by ToF information which cannot be compensated by a non-ToF measurement with higher statistics. The cause might be the non-homogeneous image spatial resolution of the scanner which has a directional dependency. It has to be mentioned that the phantom with rods on a Cartesian grid is a very artificial distribution of activity.
Figure 7.12.: Transversal cross-section through the gantry. The LYSO crystal array outlines are drawn in light blue and the light guide in green. The sensor tile is sketched in red. The rabbit-sized phantom is shown at the measured untitled position which is not centered along the $y$-axis. In gray are plotted the gaps in horizontal and vertical direction, and parallel to the symmetry axes of the Cartesian grid of the phantom and intersecting the activity distribution. (reprinted from Schug et al. (2016), ©2016)
7. PET Performance Evaluation of the Preclinical Configuration

A smoother activity distribution containing only some lesions might show a different behavior of the image quality.

A detailed evaluation of the image quality in terms of SNR is ongoing and will be part of the full NEMA NU 4-2008 characterization.

7.6. Conclusion

The robust COG-ACE algorithm presented in the previous chapter was applied to raw DPC sensor data captured with the Hyperion-II\textsuperscript{D} scanner using a wide range of operating parameters. The system and applied algorithm showed very stable PET performance results under a wide range of operating parameters. The presented initial evaluation of the PET performance results in a good understanding of the system and its behavior under a variety of parameters.

Aggressive voltage settings only have very minor benefits for the energy and timing performance of the system compared to a conservative choice of $V_{ov} = 2.5$ V (relative change $< 10\%$). Higher voltages can be used to increase the sensitivity for trig 4 and high val. Lower trig and val, on the other hand, lose sensitivity at aggressive voltage settings. It can be concluded that it is not beneficial to use aggressive $V_{ov} > 2.5$ V for the presented imaging applications.

Low $T_{op}$ are beneficial for all operation parameters. To apply the trig 1, the DPCs should be operated at $T_{op} \lesssim 10$ °C as otherwise the dead time causes a significant loss of sensitivity, especially in the presented application using light sharing. Even lower temperatures are preferable to keep the sensitivity loss at a minimum. Trig 2 and 3 still deliver CRTs of about 440 ps and 550 ps while being more robust to higher temperatures and should be the preferred choice for most preclinical applications. It could be shown that the CRT of $\sim 260$ ps for trig 1 does outperform the trig 3 setting for a rabbit-sized activity distribution. For a mouse-sized phantom, the ToF information of trig 1 did not help to improve the image quality noticeably. It can be concluded that trig 1 should only be the preferred choice if the diameter of the activity distribution is large ($\gg 40$ mm) to benefit from the ToF information.

Using light sharing, one should use low val to increase the probability for all DPCs to be validated that are required for crystal identification (see previous chapter). On the other hand, low val lead to the generation of many DPC hits and the large amount of data lead to a saturation of the GbE interfaces at activities of about 25 MBq – 30 MBq. If high-activity measurements are performed (> 50 MBq – 60 MBq), high val give a better NECR performance as the as the current limit given by the GbE interfaces is shifted to higher activities. Compression or processing of raw DPC sensor data on detector stack and/or SDM level will help to remove this bottleneck.

For the Hyperion-II\textsuperscript{D} scanner in the presented configuration equipped with six detector stacks per SDM and using the raw DPC sensor data mode, the measurement settings listed in Table 7.5 are suggested.
Table 7.5.: Recommended measurement settings when using the Hyperion-II^D scanner to capture the raw DPC sensor data and approximate values for the expected performance. (reprinted from Schug et al. (2016), 3.0)

<table>
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<th>scenario</th>
<th>$T_{op}$</th>
<th>$V_{ov}$</th>
<th>trig</th>
<th>val</th>
<th>$\Delta E/E$</th>
<th>CRT</th>
<th>$\sim$ NECR peak</th>
</tr>
</thead>
<tbody>
<tr>
<td>low activity ($&lt; 30$ MBq)</td>
<td>$&lt; 15^\circ C$</td>
<td>2.5 V</td>
<td>2/3</td>
<td>28 ph</td>
<td>12.7%</td>
<td>440 ps/550 ps</td>
<td>280 kcps(40 MBq)</td>
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<td>high activity ($&lt; 60$ MBq)</td>
<td>$&lt; 15^\circ C$</td>
<td>2.5 V</td>
<td>2/3</td>
<td>37 ph</td>
<td>12.7%</td>
<td>440 ps/550 ps</td>
<td>300 kcps(55 MBq)</td>
</tr>
<tr>
<td>high temperature</td>
<td>$&lt; 25^\circ C$</td>
<td>2.5 V</td>
<td>4</td>
<td>28 ph</td>
<td>13.0%</td>
<td>1300 ps</td>
<td>not measured</td>
</tr>
<tr>
<td>large object ($\phi \gg 40$ mm)</td>
<td>$&lt; 10^\circ C$</td>
<td>2.5 V</td>
<td>1</td>
<td>28 ph</td>
<td>12.8%</td>
<td>260 ps</td>
<td>120 kcps(25 MBq)</td>
</tr>
</tbody>
</table>

7.7. Outlook

Based on the findings presented in this chapter, a few sets of parameters will be selected and a scanner characterization following the full *NEMA NU 4-2008* standard will be conducted. The ToF benefit will be evaluated in terms of SNR gain using standardized phantoms. The interference study between the Hyperion-II^D platform and a 3-T MRI is ongoing (Wehner et al. 2014; Wehner et al. 2015; Weissler et al. 2015) and the influence of simultaneous operation on the PET performance will be investigated in the next chapters.

With the unique possibility to capture raw DPC sensor data, the Hyperion-II^D scanner allows to study a wide range of different processing methods since they can be implemented in flexible software-based frameworks and allows to evaluate these methods and their parameters for exactly the same PET measurement. Currently, a ML algorithm is being evaluated and compared to the processing and performance presented in this and the previous chapter.
8. Hyperion-II$^D$ Clinical Configuration

The Hyperion-II$^D$ platform was equipped with scintillator crystal arrays with a pitch of 4 mm. This clinical configuration was built up to investigate a one-to-one-coupled readout scheme which corresponds to a detector stack design which might be used for whole-body PET applications. Furthermore, this configuration is expected to offer a better timing performance and energy resolution which allows a further characterization of the platform especially with a higher sensitivity to degradations induced by a simultaneous operation inside an MRI.

The difference in the detector stack design and the used data processing techniques used are described in the following sections. A more detailed motivation for the PET/MRI interference study with the clinical configuration is given as well.

8.1. Clinical Detector Stacks

The Hyperion-II$^D$ platform is described in detail in chapter 5. In this and the following chapters the platform is evaluated using the clinical scintillator geometry (section 5.1.1.2).

As a reminder, the clinical configuration employs detector stacks (Dueppenbecker et al. 2012b) equipped with a pixelated LYSO crystal scintillator array with $8 \times 8$ crystals, 10 mm height and a pitch of 4 mm. This leads to a one-to-one coupling of each crystal to a single readout channel. As for the preclinical configuration, up to six sensor stacks can be mounted onto a singles-detection module (SDM) in a $2 \times 3$ arrangement (Weissler et al. 2012a).

8.1.1. Upgrade of the Detector Stack Hardware

The found vulnerabilities of the PET performance to gradient switching (Wehner et al. 2014; Wehner et al. 2015; Weissler et al. 2015) lead to an investigation of the cause and an upgrade of the IF board (Düppenbecker et al. 2016).

The original version and the new version of the IF board were investigated and compared on an imaging capable scanner employing the clinical scintillator configuration (this evaluation is presented in chapter 10).
8.2. Processing for the Clinical Configuration

As a one-to-one coupling of scintillator crystal to DPC pixel is realized, very simple crystal identification algorithms can be used. Furthermore, the data from very dim lit pixels is not needed and therefore a high validation threshold can be used. As for the preclinical configuration, the neighbor triggering capabilities of the DPCs were not used.

DPC hits are temporally clustered using a cluster window of 40 ns and the crystal bin was identified from the highest photon count of the cluster. Pixel photon values are corrected for saturation and the energy was calculated using the four pixels of the DPC housing the main pixel discarding all other photon values of the cluster. Based on the ratio of the main pixel compared to the total photon value in the cluster, a detector scatter rejection can be implemented by requiring a minimum fraction of the total photons to be captured by the main pixel.

For the clinical configuration, a time alignment for each crystal is feasible due to the much lower number of crystals compared to the preclinical configuration (for the preclinical configuration only a general delay value for each of the 900 crystal positions was fitted; section 6.2.3).

8.3. PET Performance Degradation During Simultaneous PET/MRI Operation

As mentioned before, the detailed PET/MRI interference studies presented in (Wehner 2016; Wehner et al. 2014; Wehner et al. 2015) revealed a PET performance vulnerability to MRI gradient switching. Therefore, the here presented PET/MRI interference investigations focus on gradient-intense sequences. In chapter 10 the full gradient characterization for the z-gradient is performed using the same protocol as implemented and used in (Wehner 2016; Wehner et al. 2014; Wehner et al. 2015). For comparison reasons normal imaging sequences are investigated as well.
9. Two Module PET Performance Evaluation during MRI Operation (Clinical Config.)

The content of this chapter is subject of the following paper, of which I am the main author. Content has been copied, rearranged, reformulated and details have been added.


9.1. Introduction

Two SDMs fully equipped with clinical detector stacks (section 5.1.1) and a readout based on PDPC’s DPCs which are ToF-capable and operated in a 3-T MRI system are presented. The focus is on gradient stress tests as used in Wehner et al. (2014) and Wehner et al. (2015) which show the strongest influence on the PET performance (Catana et al. 2008; Weirich et al. 2012).

9.2. Methods

In this investigation, two SDMs fully equipped with clinical detector stacks were used. They were placed horizontally facing each other at two different distance configurations inside the MRI: first, the so called gantry position and second, a maximum distance position. At the gantry position, the distance between the modules (crystal-to-crystal) was 217.6 mm. This is the default distance when using the Hyperion-II D gantry (Fig. 9.1). At the maximum distance position, the SDMs were moved inside the MR bore as far as possible to the inner wall of the bore (the approximate distance is 410 mm). The gradient field strength is expected to be higher at this position which might lead to stronger interferences.

The DPCs were operated at a cooling temperature of 0 °C leading to 5 °C–10 °C measured on the sensor tile under operation. Conservatively, 20% of the worst cells were disabled and an overvoltage of $V_{ov} = 2.0$ V and 2.5 V was used. To obtain the best time stamp performance, trigger scheme 1 (first photon trigger) and a high validation threshold of 52 photons (validation scheme in hexadecimal notation: 0x00:0R) (Philips
Two modules are mounted on a gantry (gantry position) in horizontally opposite positions with a distance of 217.6 mm measured between crystals. In a second arrangement, they are placed in maximum distance inside the MR bore of approximately 410 mm (maximum distance position). (reprinted from Schug et al. (2015a), 3.0)
Digital Photon Counting 2015; Tabacchini et al. 2014) was used. A narrow energy window of $511 \pm 50$ keV was used (this is narrower than the narrow energy window used in the previous investigations on the preclinical configuration), and to further improve the time stamp performance, detector scatter events were rejected by requesting a minimal light fraction of the main pixel of more than 65% of the photon sum of all DPCs of a cluster.

By using a $^{22}$Na point source in the isocenter of the modules, the CRT of the scanner is evaluated during and in the absence of MR sequences.

As described in Wehner et al. (2014), several stress tests with switching gradients were performed. Demanding sequences with a high gradient strength and duty cycle based on a normal EPI sequence was used (EPI factor: 49, gradient strength: 30 mT/m, slew rate: 192.3 mT/m/ms, TE/TR: 12/25 ms and switching duty cycle: 67% with gradients in $x$-, $y$- and $z$-direction).

For each gradient test PET data was recorded for approximately 3 min and the MR sequence was applied in a time window of 1 min in the middle of the measurement window. The energy spectrum and timing difference histogram of the two SDMs was determined in 40 s time windows before, during and after the MR sequence. The energy resolution was determined by iteratively fitting a Gaussian to the energy spectrum in the range of $-0.5$ FWHM to 1 FWHM around the photo peak. In the same way, a Gaussian was iteratively fitted to the timing difference histogram to match a range of $-0.5$ FWHM to 0.5 FWHM around the peak. The degradation of the energy resolution and CRT during the MR sequence to the values before and after the sequence were computed as relative differences.

In Wehner et al. (2014) it was shown that a loss of sensor data due to gradient switching before singles processing could not be measured. A loss of singles was caused only by the degradation of the energy resolution. The loss of singles depends on the selected energy window in conjunction with the induced degradation. It was shown that a large energy window lead to no loss of singles. These findings are consistent with the measurements shown in this chapter. Therefore, singles rate losses were not investigated in detail for this experiment as the underlying platform is the same. Only the loss of coincident prompts for the most aggressive setting for the given energy window will be stated as it shows the highest losses. The coincident rate losses are investigated for a full ring configuration in the next chapter, though.

9.3. Results

Inside the $B_0$ field when no further MR operation was performed the energy resolution was determined to be 11.5% (FWHM) and the CRT 250 ps (FWHM) for an overvoltage of $V_{ov} = 2.0$ V. Applying an overvoltage of $V_{ov} = 2.5$ V yielded an energy resolution of 11.2% (FWHM) and a CRT of 240 ps (FWHM).
Figure 9.2.: The time difference histogram of the two modules as a function of time for measurements of 3 min length per gradient with a gradient sequence in the middle of the measurement of 1 min. The upper histograms show measurements using the gantry position and an overvoltage of $V_{ov} = 2.0 \text{ V}$. The lower histograms are obtained using the maximum distance of the SDMs (maximum distance position) and an overvoltage of $V_{ov} = 2.5 \text{ V}$. The columns from left to right show measurements with a high demanding gradient switching sequence in $x$, $y$ and $z$ direction. At the beginning and the end of the MR sequence, binning artifacts might be observed. White bins have no entries. (reprinted from Schug et al. (2015a), ΘΩ3.0)
Figure 9.3.: The time difference histogram of two modules in gantry position as a function of time for a measurement of 3 min length with a z-gradient sequence in the middle of the measurement of 1 min. An overvoltage of $V_{ov} = 2.5$ V is applied. At the beginning and the end of the MR sequence, binning artifacts might be observed. White bins have no entries. (reprinted from Schug et al. (2015a), \textcopyright 3.0)

The results of the gradient influence are listed in Table 9.1. Histograms for time differences between the two SDMs as a function of time are shown in Fig. 9.2 and Fig. 9.3. The energy histogram for the measurement with the SDMs mounted on the gantry (gantry position) and using an overvoltage of $V_{ov} = 2.5$ V is shown in Fig. 9.4. The $x$-gradient did not show any influence on the energy or timing performance for any of the positions and applied overvoltages. At the gantry position using an overvoltage of $V_{ov} = 2.0$ V during the $y$- and $z$-gradient sequences, the energy resolution was degraded by 0.7\% and 4.1\%, the CRT by 20\% and 25\%, respectively. At an overvoltage of $V_{ov} = 2.5$ V the $z$-gradient sequence degraded the energy resolution by 3.3\% and the CRT by 30\% to 314 ps. When the SDMs were placed closest to the gradient coils at the maximum distance inside the MR bore (maximum distance position), the energy resolution was degraded by 0.4\% and 9.2\% (Fig. 9.4), the CRT by 26\% to 302 ps and 52\% to 365 ps when applying an overvoltage of $V_{ov} = 2.5$ V for $y$- and $z$-gradient sequences, respectively.

For the most aggressive scenario (maximum distance position, $z$-gradient) prompt losses of 3\%–4\% for the selected energy window were observed. No loss of unfiltered singles could be measured.
Table 9.1.: Determined energy and timing resolution (CRT) for the different measurements (positions = gantry position, maximum distance position, overvoltages) under different gradient conditions (no gradients, maximum \(x\)-gradient, maximum \(y\)-gradient and maximum \(z\)-gradient). In addition to the resolution values, the degradation with reference to the measurement without MR activity is calculated. For all experiments, the trigger scheme 1 was used. (reprinted from Schug et al. (2015a), 3.0)

<table>
<thead>
<tr>
<th>Position</th>
<th>OV / V</th>
<th>Condition</th>
<th>Energy resolution FWHM / %</th>
<th>Energy resolution Degradation</th>
<th>CRT FWHM / ps</th>
<th>CRT Degradation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gantry</td>
<td>2.0</td>
<td>no grad.</td>
<td>11.5</td>
<td>no significant degradation</td>
<td>250</td>
<td>no significant degradation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>max. X</td>
<td>11.5</td>
<td></td>
<td>250</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>no grad.</td>
<td>11.5</td>
<td></td>
<td>251</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>max. Y</td>
<td>11.6</td>
<td>0.7 %</td>
<td>303</td>
<td>20 %</td>
</tr>
<tr>
<td></td>
<td></td>
<td>no grad.</td>
<td>11.5</td>
<td></td>
<td>253</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>max. Z</td>
<td>11.9</td>
<td>4.1 %</td>
<td>317</td>
<td>25 %</td>
</tr>
<tr>
<td></td>
<td>2.5</td>
<td>no grad.</td>
<td>11.2</td>
<td></td>
<td>241</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>max. Z</td>
<td>11.6</td>
<td>3.3 %</td>
<td>314</td>
<td>30 %</td>
</tr>
<tr>
<td>max. distance</td>
<td>2.5</td>
<td>no grad.</td>
<td>11.2</td>
<td>no significant degradation</td>
<td>240</td>
<td>no significant degradation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>max. X</td>
<td>11.1</td>
<td></td>
<td>240</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>no grad.</td>
<td>11.2</td>
<td></td>
<td>240</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>max. Y</td>
<td>11.2</td>
<td>0.4 %</td>
<td>302</td>
<td>26 %</td>
</tr>
<tr>
<td></td>
<td></td>
<td>no grad.</td>
<td>11.2</td>
<td></td>
<td>241</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>max. Z</td>
<td>12.2</td>
<td>9.2 %</td>
<td>365</td>
<td>52 %</td>
</tr>
</tbody>
</table>
9.4. Discussion and Conclusion

Energy resolution and CRT degradations could be observed during demanding gradient sequences. The $x$-gradient did not show any measurable influence on the performance whereas the $y$-gradient showed a clear influence. $z$-gradient switching shows the largest influence on the performance of the two modules. This can be explained by the orientation of the SDMs inside the MR bore and the resulting magnetic flux going through the main PCB (Wehner et al. 2015).

![Energy histogram](image)

Figure 9.4.: The energy histogram around the photo peak is shown for two modules at closest position to the gradient system inside the MRI system (maximum distance position) using an overvoltage of $V_{ov} = 2.5\, V$. In dashed black the energy histogram for a measurement without gradient activity is shown. In continuous red the energy histogram for the MR sequence with a maximum $z$-gradient activity is shown. The energy resolution is degraded by 9.2%. (reprinted from Schug et al. (2015a), ©3.0)

A ripple on the bias voltage during gradient switching was observed. It is assumed that this ripple is responsible for the observed energy degradation during gradient switching, as the applied bias voltage directly influences the photon detection efficiency. A photon detection efficiency variation introduces a variation in measured energy values, which, in turn, leads to a decrease in energy resolution.

No loss of sensor data could be measured. Unfiltered single rates did not show any influence. Count rate losses of prompts were caused by degradation of the energy resolution (Fig. 9.4) in conjunction with the narrow energy window (Wehner et al. 2014). This behavior was observed for an APD based system as well (Weirich et al. 2012).

Although the DPC-based PET detector operated stable under MR conditions, it was shown that its timing and energy performance is sensitive to gradient switching. So
far, no evidence that the performance degradations can be ascribed to the DPC itself could be found. The MR sequence used was optimized purely for continuous gradient switching with maximum possible slew rates and is not useful for diagnostic MRI. The measurements represent an temporal averaging of distortions for this worst-case scenario. The degradation for common MR sequences is expected to be far minor and probably negligible for most standard imaging protocols. The highest duty cycle for imaging sequences shown in Weissler et al. (2014) are smaller than 20 % which leads to a smaller fraction of PET data influenced due to gradient switching compared to the sequence shown in this experiment. Nevertheless, for future system designs – especially if the detector is placed closer to the gradient system and higher magnetic field strengths – these effects should be considered to enable simultaneous PET/MR without performance tradeoffs between both modalities.

The underlying Hyperion-II\textsuperscript{D} platform proofed to deliver good timing performance and energy resolution both during MR silence and during highly demanding MR gradient sequences. A DPC-based fully digital PET modules with a clinical scintillator configuration was successfully operated in a 3-T MRI system achieving a CRT of 240 ps and an energy resolution of 11.2 %.

9.5. Outlook

A full PET ring using 10 SDMs and a total of 20 detector stacks in the clinical configuration is investigated in the next chapter. Dedicated synthetic gradient sequences will be used in order to get a better understanding of the influence of gradient system’s parameters on the PET performance degradation. Count-rate losses are investigated and the improvements using an upgraded version of the IF board. The upgraded IF board adresses the problem caused by the observed voltage ripples. The new version is expected to be more robust under gradient-intense sequences.
10. Full Ring PET Performance and MRI Compatibility Evaluation (Clinical Conf.)

The content of this chapter is subject of the following paper, of which I am the main author. Content has been copied, rearranged, reformulated and details have been added.

D. Schug et al. (2015c). “PET performance and MRI compatibility evaluation of a digital, ToF-capable PET/MRI insert equipped with clinical scintillators”. In: Physics in Medicine and Biology 60.18, p. 7045. DOI: 10.1088/0031-9155/60/18/7045

10.1. Introduction

In previous studies, the MR compatibility of the Hyperion-II\textsuperscript{D} platform was investigated in detail on the MRI as well as on the PET side: a decent performance on both imaging modalities was found. However, a sensitivity of our PET electronics to gradient switching resulting in a degradation of the energy and timing performance (coincidence resolution time, CRT) was revealed (Wehner et al. 2014; Wehner et al. 2015). As these studies were performed with a detector configuration suitable for preclinical imaging (1 mm crystal pitch, light guide, preclinical configuration, Figure 5.2a) which does not allow for the best possible timing performance achievable with the Hyperion-II\textsuperscript{D} platform, the influence of the gradient switching on a test setup equipped with a detector employing a clinical scintillator configuration (4 mm crystal pitch, one-to-one coupled, clinical configuration was tested; Figure 5.2b) two PET modules in coincident mode (presented in the previous chapter). Due to the highly improved CRT of about 240 ps, a degradation of about 30\% was found. Moreover, a test with the PET modules at a position which is clinically more relevant, namely closer to the cover of the MRI bore and thus closer to the gradient coils, showed a degradation of about 52\%. As the PET platform with its good timing performance is interesting for clinically driven PET systems, this gradient compatibility study was extended in three ways: first, in the building phase of a copy of the Hyperion-II\textsuperscript{D} scanner with the preclinical crystal configuration, a prototype PET ring with the clinical crystal configuration was built. Second, the impact of the gradient switching on this prototype was tested using the synthetic gradient test protocols as presented in Wehner et al. (2015). As the degradation of the energy and timing resolution can be
associated with an instability of supply voltages, the prototype scanner was equipped with an improved version of the IF board (building the interface between a sensor tile and the PET module’s main PCB) yielding a more stable voltage supply in a third step. This modified hardware was evaluated in the same way and compared with the original version.

In addition, the PET performance of the prototype scanner was evaluated in more detail: a sensitivity profile was acquired, the configuration in an high-activity scenario was tested, and the energy and timing performance for different sensor configurations was measured. Imaging experiments were performed using a hot-rod phantom to evaluate the spatial resolution and a demonstration experiment was conducted using a rabbit-sized phantom to show the ToF capabilities of the PET platform. Since the clinical demonstrator existed only for a short period of time, only an initial PET performance evaluation was conducted. A full characterization according to NEMA NU 2-2012 (clinical) or NEMA NU 4-2008 (preclinical) was not possible.

### 10.2. Materials

#### 10.2.1. Hyperion-II D PET insert

In this experiment detector stacks in the clinical configuration are used (section 5.1.1.2). A clinical detector stack consists of a pixelated scintillation crystal array of $8 \times 8$ optically isolated LYSO crystals with a height of 10 mm and a pitch of 4 mm. Although thicker crystals with a height of about 20 mm–30 mm are commonly used for clinical PET systems, 10 mm thick crystals were chosen for three reasons: firstly, to aim for the maximum possible CRT performance and secondly, the system’s sensitivity was not the main focus of the investigation. Thirdly, thicker crystals intensify the parallax error in the event positioning, especially with the rather small system bore of the Hyperion-II D insert compared to clinical whole-body systems. Crystals with a thickness commonly chosen for clinical whole-body PET systems with a much larger bore would therefore not be an appropriate choice.

Each sensor tile is connected to an FPGA-based control and readout board (IF board) (Dueppenbecker et al. 2012b) (Figure 10.1a). The FPGA configures and reads out each individual DPC of the sensor tile. Besides that, the supply voltages, in particular the bias voltage $V_{\text{bias}}$ defining the operating voltage of the SPADs, are controlled by this FPGA.

As mentioned in the introduction, the original hardware version of the IF board (employed in all investigations presented in the previous chapters) and an improved version of the IF board is used. An additional voltage regulator necessary to stabilize the voltage supply of the FPGA, as well as an additional feed forward capacitor used to reduce a ripple on the bias voltage, were incorporated on the improved IF
10.2. Materials

Figure 10.1.: (a) The detector stack consists of an IF board, the sensor tile and a crystal array. (b) The SDM is equipped with two detector stacks. (reprinted from Weissler et al. (2012b), © 2012 IEEE)

board design (Details on the hardware improvements to the IF-Board are described in Düppenbecker et al. (2016) and are neither part nor in the scope of this thesis).

In contrast to the previous works, only one of the three possible detector rings was equipped by mounting $2 \times 1$ detector stacks (Figure 10.1b) on a singles-detection module (SDM) (Weissler et al. 2012a) and ten of these PET modules were used to build up the PET ring. The resulting PET FOV has an axial extent of 32 mm and a transaxial crystal-to-crystal spacing of 217.6 mm. As already stated in the introduction, the clinical configuration as described here was an intermediate step created during the build-up of a fully populated preclinical PET insert.

10.2.2. MRI system

To test the influence of the switching gradients on this clinical prototype, a clinical Philips Achieva 3-T MRI system equipped with a Dual Quasar gradient system was used. This gradient system employs two gradient amplifiers which allows to increase the available gradient slew rate up to 200 T/m/s. The MRI system was running software release 3.2.1.0 and a system patch implementing the synthetic gradient test protocols as described in Wehner et al. (2015) was installed. For MRI acquisition, the PET insert was equipped with dedicated PET-transparent radio-frequency transmit and receive (RF Tx/Rx) coils (Fig. 5.15). Mainly a small mouse coil (12-leg birdcage resonator, high-pass version) with an inner diameter of 46 mm was used. To measure a large rabbit-sized phantom, a larger RF Tx/Rx coil with an inner diameter of 160 mm was installed.

10.2.3. Phantoms and Test sources

Two kind of radioactive PET phantoms were used: point sources as well as fillable phantoms.
The point sources were used to calibrate the PET scanner and to evaluate the basic PET performance parameters such as energy and timing resolution for the different sensor configurations applied. Up to five $^{22}$Na NEMA cubes with an edge length of 10 mm, an active area of 0.25 mm in diameter with an activity of 1.0 MBq – 1.3 MBq were used.

Three different phantoms which were filled with an FDG solution were used. A tube with a diameter of 10 mm and a length of 25 mm was used to test the behavior of the system at high activities. Two custom-made structured phantoms served to investigate the spatial resolution and to demonstrate the ToF benefits of the system. To determine and investigate the spatial resolution of the system, data from a hot-rod phantom with several structured regions with rod diameters and spacings of 1.0 mm, 1.5 mm, 2.0 mm, 2.5 mm, 3.0 mm and 4.0 mm surrounded by a ring of activity with an outer diameter of 43 mm was acquired. To assess the benefits of ToF image reconstruction, a large rabbit-sized, high-contrast phantom with an outer diameter of 114 mm was used. It is the same phantom that was used in the PET performance evaluation of the preclinical system (see chapter 7 and Figure 7.1c). The structured insert of the phantom provided a regular rod structure. The rods were aligned on a Cartesian grid, had a diameter of 3 mm and a height of 20 mm. The center-to-center spacing of two adjacent rods were two times the diameter.

10.3. Methods

10.3.1. PET system configuration and processing parameters

The cooling temperature of the PET system was set to $-5^\circ$C leading to a temperature of about $0^\circ$C – $5^\circ$C measured under operation on the sensor tiles.

For this operating temperature, we measured the breakdown voltage $V_{bd}$ of each sensor tile whereas $V_{bd}$ is defined as the bias voltage at which the SPADs start to breakdown. The bias voltage applied during operation is the sum of $V_{bd}$ and an additional overvoltage $V_{ov}$. A conservative value of $V_{ov} = 2.5$ V was used. To reduce the dark noise of the sensor tile, 20% of the cells showing the highest dark count rates were disabled.

As a validation configuration of the DPCs, the validation scheme 0x00:0R yielding a threshold of 52 photons was applied. The validation length was set to 10 ns and the integration time was chosen to be 165 ns. The neighbor-triggering capabilities of the DPCs were not used (Schug et al. 2012).

Pixel photon values were corrected for saturation and DPC hits were temporally clustered using a default cluster window of 5 ns. Exploiting the one-to-one coupling, the scintillating crystal was identified from the pixel with the highest photon count of the cluster. Afterwards, the energy was calculated using the photon sum of the four pixels of the DPC comprising the main pixel. To improve the time stamp performance
10.3. Methods

and reject detector scatter and pile up events, a minimal light fraction of the main pixel of more than 60% of the total photon sum of all DPC pixels of a cluster is required. This decreases the system’s sensitivity.

A narrow energy (NE) window of 461 keV – 561 keV was used to obtain the best timing performance and a wide energy (WE) window of 250 keV – 625 keV was applied to yield a higher sensitivity. Those filters were applied before performing a coincidence search with a sliding CW. A CW of 5 ns was used for measurements acquired with low activities. For measurements using higher activities, the CW was reduced down to 500 ps – 1000 ps. Coincident events with more than two singles were discarded.

10.3.2. Computation of the Energy Resolution and CRT

The energy resolution was determined using the energy spectrum of accepted coincident singles. A Gaussian was fitted using a fit range of $-0.5$ FWHM to $1$ FWHM around the photopeak, whereby no background removal or modeling was performed. The FWHM used was determined by an initial, preliminary Gaussian fit.

The CRT was calculated by evaluating the FWHM of the histogram of the measured time differences corrected for the known source positions. As for the energy resolution, a Gaussian fit was performed in the fit range of $-0.5$ FWHM to $0.5$ FWHM around the peak. Again, no background modeling or removal was applied and the FWHM used for the fit range was determined using an initial, preliminary fit.

10.3.3. MRI Compatibility Investigations

The MRI compatibility of the Hyperion-II platform equipped with preclinical detector stacks was investigated in Wehner et al. (2014), Wehner et al. (2015), and Weissler et al. (2015). Based on these results, the clinical scintillator configuration as described in section 5.1.1.2 was investigated using two PET modules each equipped with six detector stacks in coincidence in the previous chapter 9. In these works, the interaction of the PET hardware with the gradient system, especially the $z$-gradient, was identified as the main and almost solely interference phenomena on the PET side resulting in a PET performance degradation. Starting from those results, in this chapter the influence of the gradient system on the CRT and energy resolution was evaluated using realistic imaging protocols as well as synthetic gradient stress tests. These protocols are described in more detail in Wehner et al. (2015).

To have the highest sensitivity for the CRT degradation under gradient stress tests and to obtain the best CRT possible, a point source configuration was used which consisted of $5 \ ^{22}\text{Na}$ point-like sources with a combined activity of 5.59 MBq distributed along the $z$-axis (axial). This allowed a very precise determination of the CRT as each LOR can be unambiguously assigned to one of the point sources.

Using this source configuration, the clinical configuration with the original IF board was tested: first, five MRI imaging sequences were applied (sequence parameters are...
Table 10.1.: Overview of the imaging sequences applied (T1WATSE = T1-weighted turbo spin echo sequence (TSE), T2TSE = T2-weighted TSE sequence, T1WFFE = T1-weighted fast field echo (FFE, gradient echo) sequence, T2WFFE = T2-weighted FFE sequence, EPI7 = FFE sequence with echo planar imaging (EPI) readout (acceleration factor = 7)). The following abbreviations were used: TR = Repetition Time, TE = Echo Time, TF = Turbo Factor, FA = Flip Angle, VS = Voxel Size, ST = Slice Thickness, MS = Matrix Size, MSR = Maximum Slew Rate, MSDC = Maximum Switching Duty Cycle. (reprinted from Schug et al. (2015c), 3.0)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>T1WATSE</th>
<th>T2TSE</th>
<th>T1WFFE</th>
<th>T2WFFE</th>
<th>EPI7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mode</td>
<td>2D</td>
<td>2D</td>
<td>3D</td>
<td>3D</td>
<td>2D</td>
</tr>
<tr>
<td>TR/TE / ms/ms</td>
<td>500/20</td>
<td>2000/100</td>
<td>12/2.3</td>
<td>12/8.1</td>
<td>35/16</td>
</tr>
<tr>
<td>TF</td>
<td>6</td>
<td>12</td>
<td>-</td>
<td>-</td>
<td>7</td>
</tr>
<tr>
<td>FA</td>
<td>90°</td>
<td>90°</td>
<td>35°</td>
<td>40°</td>
<td>25°</td>
</tr>
<tr>
<td>VS / mm²</td>
<td>0.25 × 0.25</td>
<td>0.25 × 0.25</td>
<td>0.45 × 0.4</td>
<td>0.25 × 0.25</td>
<td>0.25 × 0.25</td>
</tr>
<tr>
<td>ST / mm</td>
<td>320 × 312</td>
<td>320 × 312</td>
<td>200 × 200</td>
<td>320 × 320</td>
<td>320 × 315</td>
</tr>
<tr>
<td>X grad. MSR / T/m/s</td>
<td>126</td>
<td>87</td>
<td>125</td>
<td>45</td>
<td>188</td>
</tr>
<tr>
<td>X grad. MSDC</td>
<td>1.0%</td>
<td>0.9%</td>
<td>6.5%</td>
<td>19.6%</td>
<td>7.5%</td>
</tr>
<tr>
<td>Y grad. MSR / T/m/s</td>
<td>193</td>
<td>86</td>
<td>120</td>
<td>65</td>
<td>188</td>
</tr>
<tr>
<td>Y grad. MSDC</td>
<td>1.2%</td>
<td>1.4%</td>
<td>5.2%</td>
<td>15.7%</td>
<td>8.4%</td>
</tr>
<tr>
<td>Z grad. MSR / T/m/s</td>
<td>71</td>
<td>30</td>
<td>50</td>
<td>29</td>
<td>110</td>
</tr>
<tr>
<td>Z grad. MSDC</td>
<td>0.8%</td>
<td>0.9%</td>
<td>6.5%</td>
<td>11.8%</td>
<td>2.8%</td>
</tr>
</tbody>
</table>

summarized in Table 10.1), whereby the sequence parameters were motivated by clinical imaging protocols preinstalled at the MRI system. T1- and T2-weighted turbo spin echo (TSE) sequences (T1WATSE and T2TSE), T1- and T2-weighted fast field echo (FFE, gradient echo) sequences (T1WFFE and T2WFFE) as well as an FFE based echo planar imaging (EPI) sequence (EPI7, acceleration factor = 7) were applied. Secondly, synthetic gradient test sequences as sketched in Fig. 10.2 were used. The sequence gives full control over the gradient system, meaning that gradient strength, slew rate, switching duty cycle as well as switching direction are accurately adjustable. Using this sequence, all combinations of three different gradient strengths (GS) (10 mT/m, 20 mT/m, and 30 mT/m), five different switching duty cycles (SDC) (20%, 40%, 60%, 80%, and 100%) defined as the percentage in which the gradients are in a switching state (see Fig. 10.2) and five slew rates (SR) (25 T/m/s, 50 T/m/s, 100 T/m/s, 150 T/m/s, and 200 T/m/s) were tested. As switching direction, the z-axis was chosen in all experiments as previous experiments showed the highest PET performance degradation in relation to this direction.
10.3. Methods

![Diagram of gradient test sequence](image)

Figure 10.2.: Sketch of the newly implemented gradient test sequence: it gives complete control over the gradient system meaning that strength, slew rate, switching direction as well as asymmetries or duty cycle can be adjusted accurately. (reprinted from Wehner et al. (2015), #3.8)

Each parameter set defined one MRI test sequence which was applied during PET acquisition in a time window of 20 s length. The resulting PET data was gated taking a small safety margin of 2 s into account. One measurement cycle comprised five different gradient parameter sets (constant GS, constant SDC and varying SR) yielding 15 individual PET data acquisitions for all 75 gradient test parameter sets. The energy resolution and CRT were determined for each gradient test parameter set and compared to reference measurements which were acquired without gradient activity (before and after the MRI sequence). PET performance changes are calculated as relative changes and the statistical uncertainty was obtained from the aforementioned fit. For the PET data acquisition containing the worst case gradient sequences (SDC = 80%, GS = 30 mT/m), the coincidence rate over time was evaluated to study the impact on the count rate performance. Besides this worst-case scenario, a measurement series with a SDC of 20% and GS of 30 mT/m is shown which is used to make a comparison to the results presented by Weirich et al. (2012) and approximately matches the gradient parameters of that work.

After upgrading the platform with the improved IF board, these experiments were repeated to evaluate the updated platform.

10.3.4. PET Performance Evaluation

To get a better understanding of the PET performance, some basic investigations were carried out with the upgraded platform. These investigations range from measurements using point sources to determine typical performance parameters up to measurements with structured phantoms to demonstrate the imaging capabilities of the clinical configuration.
10.3.4.1. Point Source Measurement

As for the MRI compatibility investigation, the five $^{22}$Na point-like sources with a combined activity of 5.53 MBq were distributed centrally along the axial axis (positions: $(x, y, z) \approx \{(-11.9, -3.1, -9.2), (-0.7, -10.4, -8.1), (-2.0, -4.2, 0.0), (9.0, -6.7, 5.1), (-3.2, 1.6, 9.5)\}$ mm). All different trigger schemes (1 – 4) were configured consecutively and PET data was recorded for approximately 5 min for each trigger scheme. The energy resolution, CRT as well as the prompt rate was determined for both energy windows and each measurement. With respect to the prompt rate, a signal region of 10 mm around the nominal source positions was selected and the resulting rate was regarded as the trues rate (motivated by the NEMA NU4-2008 standard).

10.3.4.2. Sensitivity Profile

To acquire a sensitivity profile, one $^{22}$Na point-like source with an activity of 1.1 MBq was moved axially through the center of the FoV in approximately 1 mm steps. At each position, PET data was acquired for at least 1 min and the trues rate was determined as the prompt rate in a 3D signal region with a radius of 10 mm around the nominal source position (motivated by the NEMA NU4-2008 standard). Then, the trues sensitivity was calculated by dividing the trues rate by the source’s activity whereby the latter was corrected for the branching ratio of the $^{22}$Na $\beta^+$ decay which is 0.906. The entire measurement series was measured in two parts on separate days. The PET data was processed with a cluster window of 2 ns and a coincidence window of 1 ns.

10.3.4.3. High Activity Measurement

To test the behavior of the system at high activities, an FDG-filled cylindrical volume was used. It was placed in the axial center of the scanner with an offset in the transaxial plane at the position $x = 2.69\text{ mm}$, $y = 13.28\text{ mm}$. At the beginning of the experiment, the activity of the phantom was approximately 200 MBq. Measurements down to about 45 MBq were performed.

During the FDG decay, trigger schemes 1-3 were used for measurements of approximately 30 s, whereby trigger scheme 1 was only characterized at lower activities due to power consumption and current limitations on the power supply chain. The acquired data sets were processed with a cluster window of 2 ns, a CW of 500 ps and both the NE and the WE window were applied. To estimate the trues and randoms rate, a signal region with a radius of 20 mm around the central axis of the cylinder of the activity volume was defined. Since the phantom is not compliant with the NEMA NU 4-2008 standard, a scatter rate was not calculated. The trues rate is determined by the prompts rate obtained in the signal volume corrected for the randoms rate. The randoms rate was estimated from the measured singles and prompts rate as proposed in Oliver and Rafecas (2012) in the stated signal region. The randoms signal region is comparable to the randoms region defined for a mouse-sized scatter phantom in
Table 10.2.: Bed positions, activities and measurement times of the measurement of the rabbit-sized phantom. (reprinted from Schug et al. (2015c), 3.0)

<table>
<thead>
<tr>
<th>axial bed position</th>
<th>activity</th>
<th>duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0 mm</td>
<td>15.74 MBq</td>
<td>606.5 s</td>
</tr>
<tr>
<td>−16.5 mm</td>
<td>14.50 MBq</td>
<td>311.6 s</td>
</tr>
<tr>
<td>−32.0 mm</td>
<td>13.96 MBq</td>
<td>306.0 s</td>
</tr>
<tr>
<td>15.1 mm</td>
<td>13.36 MBq</td>
<td>310.5 s</td>
</tr>
<tr>
<td>32.0 mm</td>
<td>12.62 MBq</td>
<td>320.0 s</td>
</tr>
</tbody>
</table>

the NEMA NU 4-2008 standard and the evaluation should shield comparable results with regards to the randoms rate. As an equivalent to the noise equivalent count rate (NECR) without accounting for scattered events, the square of the trues rate divided by the difference of the trues rate and randoms rate was calculated.

10.3.5. Imaging Experiments

To demonstrate the spatial resolution of the clinical configuration, the hot-rod phantom providing various rod size sections was used and measured for 2264.8 s with an activity of 9.81 MBq.

The rabbit-sized phantom was measured in five bed positions to cover the whole phantom with the FoV of the PET insert (see Table 10.2). For this phantom, an image reconstruction once with ToF information and once without was performed.

All imaging experiments have been conducted using the trigger scheme 1. The acquired raw PET data were processed with a cluster window of 2 ns and a CW of 1 ns.

10.3.5.1. Image Reconstruction

For the image reconstruction, a 3D reconstruction (Salomon et al. 2011; Salomon et al. 2012) implementing an OSEM algorithm (Hudson and Larkin 1994) was used.

For the image reconstruction of the smaller hot-rod phantom, self normalization was used, but neither scatter nor attenuation was accounted for. In contrast, scatter and attenuation were modeled for the larger rabbit-sized phantom using an artificial cylindrical attenuation map. An isotropic reconstruction voxel size of 0.5 mm, 32 iterations with 8 subsets were without filtering the activity distribution at any point. For the ToF capabilities of the image reconstruction, a ToF kernel of 215 ps for trigger scheme 1 is assumed.

2D image slices are shown for the different imaging experiments. The slice thickness used is 1 mm for the hot-rod phantom and 15 mm for the rabbit-sized phantom.
10.4. Results

10.4.1. MRI Compatibility Investigations

10.4.1.1. Original IF board

The results of the PET performance degradation induced by imaging sequences are listed in Table 10.3. With respect to the energy resolution, only the T2FFE sequence showed a measurable degradation of about $0.58 \pm 0.25 \%$. For the CRT measurements, only the EPI7 sequence had a measurable impact. A degradation of $2.95 \pm 0.70 \%$ was observed. In contrast to these two measurements, all other imaging protocols did not provoke a significant performance degradation ($p \geq 5 \%$).

The degradation maps of the synthetic gradient stress tests are shown in Fig. 10.3. The worst degradation of the energy resolution was measured as $5.1 \pm 0.3 \%$ for a GS of 30 mT/m, a SR of 200 T/m/s and a SDC of 80%. For the CRT, the worst degradation was observed for a GS of 30 mT/m, a SR of 200 T/m/s and a SDC of 60% as $33.9 \pm 1.2 \%$.

For the PET acquisition containing the gradient test parameter set which provoked the highest energy resolution degradation (GS of 30 mT/m and a SDC of 80% and SRs ranging from 25 T/m/s – 200 T/m/s), the relative coincidence rate as function of time is shown in Fig. 10.4. Here, a drop of the coincidence rate of about 2% was observed for the highest SR applied, namely 200 T/m/s, the value for which the highest energy resolution degradation was found, too. For the next smaller SR of 150 T/m/s, the coincidence count rate drop is halved to about 1% and all further test sequences with lower SR did not show a measurable decline of the coincidence rate.

In addition to that, the relative coincidence rate as function of time for the gradient stress tests with a GS of 20 mT/m and a SDC of 20% and SRs ranging from 25 T/m/s – 200 T/m/s is shown in Fig. 10.5 for comparison reasons. For these parameters, no measurable count rate losses could be observed.

10.4.1.2. Improved IF board

The PET performance degradation measurements obtained with the prototype scanner equipped with the improved IF boards during the application of the imaging sequences are listed in Table 10.4. No significant degradation of the energy resolution or the CRT was measured ($p \geq 10 \%$) in all cases.

The degradation maps acquired using the gradient stress test are depicted in Fig. 10.6. With the improved IF board, the gradient stress tests did not cause a significant degradation of the energy resolution or the CRT.

For comparison reasons, the relative coincidence rate as function of time for the gradient stress tests with a GS of 30 mT/m and a SDC of 80% and SRs ranging from 25 T/m/s – 200 T/m/s is shown in Fig. 10.7. In contrast to the measurement shown with the original IF boards, no drop of the coincidence rate was measurable.
Table 10.3.: Energy and CRT degradations for the imaging sequences measured with the original IF board. The *no sequence* row is used as a reference to calculate the degradation as relative change for the imaging sequences. (reprinted from Schug et al. (2015c), Ψ03.0)

<table>
<thead>
<tr>
<th>MRI sequence</th>
<th>$\Delta E/E$ (FWHM)</th>
<th>rel. deg.</th>
<th>CRT</th>
<th>rel. deg.</th>
</tr>
</thead>
<tbody>
<tr>
<td>no sequence</td>
<td>11.360 ± 0.011 %</td>
<td>213.0 ± 0.6 ps</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1WATSE</td>
<td>11.396 ± 0.024 %</td>
<td>0.32 ± 0.23 %</td>
<td>212.2 ± 1.4 ps</td>
<td>−0.36 ± 0.70 %</td>
</tr>
<tr>
<td>T2WTSE</td>
<td>11.370 ± 0.023 %</td>
<td>0.09 ± 0.23 %</td>
<td>213.1 ± 1.4 ps</td>
<td>0.05 ± 0.70 %</td>
</tr>
<tr>
<td>T1WFFE</td>
<td>11.378 ± 0.023 %</td>
<td>0.15 ± 0.23 %</td>
<td>215.4 ± 1.2 ps</td>
<td>1.12 ± 0.66 %</td>
</tr>
<tr>
<td>T2WFFE</td>
<td>11.426 ± 0.025 %</td>
<td>0.58 ± 0.25 %</td>
<td>214.0 ± 1.3 ps</td>
<td>0.49 ± 0.68 %</td>
</tr>
<tr>
<td>EPI7</td>
<td>11.366 ± 0.023 %</td>
<td>0.05 ± 0.23 %</td>
<td>219.4 ± 1.3 ps</td>
<td>2.95 ± 0.70 %</td>
</tr>
</tbody>
</table>

Figure 10.3.: Degradation maps of the gradient stress test measured with the original IF board. The top row shows the energy resolution degradation and the lower row the CRT degradation. Each column shows the degradation maps for a fixed gradient strength. Individual degradation maps show the degradation for different slew rates and switching duty cycles. (reprinted from Schug et al. (2015c), Ψ03.0)
Figure 10.4.: Relative coincidence rate over time for 5 s time bins acquired with the platform equipped with the original interface boards. The time periods with gradient stress test sequences with a GS of 30 mT/m and a SDC of 80 % for different SRs ranging from 25 mT/m/ms – 200 mT/m/ms are marked in grey. (reprinted from Schug et al. (2015c), *3.0*)

Figure 10.5.: Relative coincidence rate over time for 5 s time bins acquired with the platform equipped with the original interface boards. The time periods with gradient stress test sequences with a GS of 20 mT/m and a SDC of 20 % for different SRs ranging from 25 mT/m/ms – 200 mT/m/ms are marked. This evaluation is used as a comparison to the results presented in Weirich et al. (2012). (reprinted from Schug et al. (2015c), *3.0*)
Table 10.4.: Energy and CRT degradations for the imaging sequences measured with the improved IF board. The no sequence row is used as a reference to calculate the degradation as relative change for the imaging sequences. (reprinted from Schug et al. (2015c), Ø3.0)

<table>
<thead>
<tr>
<th>MRI sequence</th>
<th>ΔE/E (FWHM)</th>
<th>rel. deg.</th>
<th>CRT</th>
<th>rel. deg.</th>
</tr>
</thead>
<tbody>
<tr>
<td>no sequence</td>
<td>11.388 ± 0.013 %</td>
<td>213.0 ± 0.7 ps</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1WATSE</td>
<td>11.427 ± 0.023 %</td>
<td>0.34 ± 0.23 %</td>
<td>213.7 ± 1.2 ps</td>
<td>0.30 ± 0.66 %</td>
</tr>
<tr>
<td>T2WTSE</td>
<td>11.385 ± 0.022 %</td>
<td>−0.02 ± 0.23 %</td>
<td>214.4 ± 1.2 ps</td>
<td>0.63 ± 0.64 %</td>
</tr>
<tr>
<td>T1WFFE</td>
<td>11.415 ± 0.025 %</td>
<td>0.24 ± 0.25 %</td>
<td>213.2 ± 1.3 ps</td>
<td>0.09 ± 0.69 %</td>
</tr>
<tr>
<td>T2WFFE</td>
<td>11.349 ± 0.024 %</td>
<td>−0.34 ± 0.24 %</td>
<td>214.1 ± 1.3 ps</td>
<td>0.51 ± 0.70 %</td>
</tr>
<tr>
<td>EPI7</td>
<td>11.398 ± 0.024 %</td>
<td>0.09 ± 0.24 %</td>
<td>214.7 ± 1.3 ps</td>
<td>0.80 ± 0.68 %</td>
</tr>
</tbody>
</table>

Figure 10.6.: Degradation maps of the gradient stress test measured with the improved IF board. The top row shows the energy resolution degradation and the lower row the CRT degradation. Each column shows the degradation maps for a fixed gradient strength. Individual degradation maps show the degradation for different slew rates and switching duty cycles. (reprinted from Schug et al. (2015c), Ø3.0)
Figure 10.7.: Relative coincidence rate over time for 5 s time bins acquired with the platform equipped with the improved interface boards. The time periods with gradient stress test sequences with a GS of 30 mT/m and a SDC of 80 % for different SR ranging from 25 mT/m/ms−200 mT/m/ms are marked in grey. (reprinted from Schug et al. (2015c), ©3.0)

10.4.2. PET Performance Evaluation

10.4.2.1. Point Source Measurement

The results of the point source measurements are summarized in Table 10.5: while the energy resolution is almost the same for all trigger settings with approximately 11.4 %, the CRT depends on the trigger scheme and ranges from 215 ps for trigger scheme 1 and the NE window to 621 ps for trigger scheme 4 and the WE window. The sensitivity loss associated with trigger scheme 1 is approximately 5 %−6 % compared to the sensitivity obtained with trigger schemes 2-4. For all trigger schemes, the CRT using the WE window is about 10 % worse compared to the CRT with the NE window. The sensitivity of the WE window is about 77 % higher compared to the NE window.

10.4.2.2. Sensitivity Profile

Fig. 10.8 shows the axial sensitivity profile of the scanner measured with trigger scheme 1 for the NE and WE window. The NE window shows an isocenter sensitivity of 0.41 ± 0.01 % and the WE window 0.71 ± 0.01 %.

10.4.2.3. High Activity

Measurements were recorded between ~ 46 MBq−193 MBq for trigger scheme 3 and between ~ 44.5 MBq−163 MBq for trigger scheme 2. The trigger scheme 1 showed
Table 10.5.: Results for the measurements using 5 point sources and applying different trigger schemes. Both energy windows were applied. The trues rate was evaluated as the prompt rate in a 10 mm signal region around the nominal positions of the point sources. (reprinted from Schug et al. (2015c), 3.0)

<table>
<thead>
<tr>
<th>energy window</th>
<th>trigger scheme</th>
<th>CRT / ps</th>
<th>$\Delta E/E$ / %</th>
<th>trues / kHz</th>
</tr>
</thead>
<tbody>
<tr>
<td>461 keV – 561 keV</td>
<td>1</td>
<td>215.2 ± 0.4</td>
<td>11.381 ± 0.007</td>
<td>11.990 ± 0.006</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>279.1 ± 0.5</td>
<td>11.358 ± 0.007</td>
<td>12.731 ± 0.006</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>332.7 ± 0.6</td>
<td>11.356 ± 0.007</td>
<td>12.751 ± 0.006</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>557.0 ± 1.1</td>
<td>11.355 ± 0.007</td>
<td>12.814 ± 0.006</td>
</tr>
<tr>
<td>250 keV – 625 keV</td>
<td>1</td>
<td>232.4 ± 0.4</td>
<td>11.384 ± 0.006</td>
<td>21.331 ± 0.008</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>307.3 ± 0.4</td>
<td>11.367 ± 0.006</td>
<td>22.498 ± 0.009</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>363.4 ± 0.5</td>
<td>11.366 ± 0.006</td>
<td>22.527 ± 0.009</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>621.1 ± 0.9</td>
<td>11.360 ± 0.006</td>
<td>22.411 ± 0.009</td>
</tr>
</tbody>
</table>

Figure 10.8.: Sensitivity profile of a centered $^{22}$Na source moved axially through the scanner. The trues sensitivity is defined as the LORs within a signal region of 10 mm around the nominal source position. The profile is shown for the NE window (461 keV – 561 keV) and WE window (250 keV – 625 keV) and has been measured in two parts. (reprinted from Schug et al. (2015c), 3.0)
stability problems at high activities and only allowed a stable operation at an activity of $\sim 42.1 \text{ MBq}$. For the other two measurements with trigger scheme 1 at $\sim 49.5 \text{ MBq}$ and $\sim 58.3 \text{ MBq}$ one detector stack was not operational due to the high power consumption and did not deliver any hit data resulting in a lower sensitivity of the scanner. Nonetheless, these measurements allowed a determination of the energy resolution and CRT of the scanner. Two measurements with trigger scheme 2 and 3 were conducted between those two trigger scheme 1 measurements. Both measurements deliver a CRT which is unexplainably worse than the expectation based on the other trigger scheme 2 and 3 measurements. As a result, the activity range including those four measurements showing either a sensitivity loss due to a missing detector stack or an unexplainable degradation of the CRT is marked with a grey shaded bar in the result plots (Fig. 10.9).

The energy resolution as function of activity is depicted in Figure 10.9a. It degrades linearly by about 2.9 $\%$ $\text{MBq}^{-1}$ (measured relatively).

The CRT as function of activity is shown in Figure 10.9b for all trigger schemes. Depending on the trigger setting and the energy window used, the CRT degrades relatively towards higher activities by $0.27 - 0.41$ $\%$ $\text{MBq}^{-1}$.

The sensitivity for the cylindrical activity distribution and the defined signal region as function of activity is shown in Figure 10.9c, where a decline in sensitivity can be observed with increasing activity.

The random fraction evaluated in the described signal region as function of activity is presented in Figure 10.9d and shows a linear increase for the WE window of 0.138 $\%$ $\text{MBq}^{-1}$ and for the NE window of 0.114 $\%$ $\text{MBq}^{-1}$ for trigger schemes 2 and 3.

The ratio of the trues rate squared and the difference of the trues rate and the randoms rate is measured as function of activity and shown in Figure 10.9e, whereby the rates are evaluated in the signal region. This measure does not peak in the evaluated activity range.

10.4.3. Imaging Experiments

10.4.3.1. Phantoms

The reconstructed images from the hot-rod phantom with rod sizes of 1.0 mm – 4.0 mm and a ring of activity surrounding the structured region shows clear rod separation down to 2.0 mm for a slice thickness of 1 mm (Fig. 10.10). The 1.5 mm region can not be resolved properly anymore in this phantom.

The large rabbit-sized phantom was reconstructed without (Figure 10.11a) and with the application of a ToF kernel (Figure 10.11a). In both cases, 2D slices with a slice thickness of 15 mm are presented. The reconstruction with ToF information shows a clear improvement. Image artifacts, which are caused by the PET ring geometry, are visible in the case of non-ToF reconstruction. They are resolved when the ToF information is included in the reconstruction.
Figure 10.9: Results of the high-activity measurement plotted as function of activity for the energy resolution (a), the CRT (b), the trues rate (corrected for randoms) in a signal region 20 mm around the central axis of the activity phantom (c), the random fraction evaluated in the same signal region as the prompt rate (d) and the trues rate squared over trues rate minus randoms rate (e). The gray area marks the measurements which were conducted with the system in an unstable condition. (reprinted from Schug et al. (2015c), $\Theta$3.0)
10. Full Ring PET Performance and MRI Compatibility Evaluation (Clinical Conf.)

Figure 10.10.: (a) MRI image of the hot-rod phantom (acquired with the T2WTSE sequence). (b) 2D slice of the PET reconstruction (OSEM, attenuation correction, 32 iterations, 8 subsets). A 0.5 mm voxel pitch and ToF information with a ToF kernel of 215 ps were used. The shown slice thickness is 1 mm. (reprinted from Schug et al. (2015c), ☞3.0)

Figure 10.11.: 2D slices of the multi-bed reconstruction (OSEM, attenuation correction, 32 iterations, 8 subsets) of the rabbit-sized phantom. A 0.5 mm voxel pitch was used and the shown slice thickness is 15 mm. For the reconstruction shown in the left image, no ToF information was used during reconstruction (a). In a second reconstruction, the ToF information with a ToF kernel of 215 ps was used (b). (reprinted from Schug et al. (2015c), ☞3.0)
10.5. Discussion

10.5.1. MRI Compatibility Investigations

The MRI compatibility of the Hyperion-II\textsuperscript{D} platform equipped with preclinical LYSO crystal arrays was investigated in Wehner et al. (2014), Wehner et al. (2015), and Weissler et al. (2015): the high resolution scintillator configuration in conjunction with a light guide and the employed trigger scheme 3 delivered an energy resolution of 12.87\% and a CRT of 555 ps. Using the synthetic gradient stress tests as described above and in Wehner et al. (2015), a maximum degradation of the energy resolution of about 5.8\% and the CRT of about 14.3\% was provoked. Especially the CRT degradation played a subordinate role in the preclinical scenario (in combination with a mouse Tx/Rx RF coil), as the extent of the objects under investigation are too small in order to profit from ToF-PET.

In a configuration with rather clinical parameters, in which e.g. trigger scheme 1 is applied to provide a much better CRT, ToF-PET gains importance. With a superior CRT performance, the influence of the gradient switching is expected to become more substantial. Moreover, an investigation using trigger scheme 1 is expected to be more sensitive to gradient switching. As a result, a first evaluation of two modules equipped with clinical detector stacks was conducted with respect to gradient switching (see chapter 9). There, a demanding sequence with a high gradient strength and duty cycle based on a normal EPI sequence (EPI factor: 49, gradient strength: 30 mT/m, slew rate: 192.3 T/m/s, TE/TR: 12/25 ms and switching duty cycle: 67\% with the gradient in z-direction) was used as presented in Wehner et al. (2014). The better timing resolution proved to offer a higher sensitivity to the degradation induced by the gradient sequence compared to the preclinical LYSO crystal configuration. Whereas, the energy calculation in the one-to-one coupled readout scheme proved to be more stable. The degradations measured were 3.3\% for the energy resolution and 30\% for the CRT for two modules mounted on the standard Hyperion-II\textsuperscript{D} gantry.

The investigations presented in this chapter were extended to a full-ring geometry allowing for an initial PET performance evaluation of the clinical crystal configuration as discussed earlier. In addition, the full synthetic gradient test protocol was applied in order to investigate the degradation phenomena in detail. The maximum degradations found are $5.1 \pm 0.3\%$ for the energy resolution and $33.9 \pm 1.2\%$ for the CRT. For the imaging scenarios tested, the degradation levels are more than one order of magnitude smaller compared to the maximum degradation level observed. This is expected, as the SDCs of the imaging sequences are below 20\% (cf. Table 10.1 and (Wehner et al. 2015)). For the test sequences causing the highest energy resolution degradation, a loss of coincident events of about 2\% was observed. This loss is caused by the event filtering with the NE window in combination with the degradation of the energy resolution. A loss of raw detector signals was not observed (Wehner et al. 2014;
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Wehner et al. (2015). In contrast to that, the CRT degradation did not cause a loss of events in this measurement as a very large CW was employed.

Based on these studies, the reason of the degradations was investigated, identified and addressed by improving the interface board (Düppenbecker et al. 2016). The improved interface boards were installed and tested on the prototype scanner equipped with clinical scintillators presented in this chapter. The upgraded platform did not show any measurable PET performance degradation in terms of energy resolution, CRT and count rate performance even under the most demanding synthetic gradient test sequences. Hence, the Hyperion-II platform equipped with the improved interface boards is expected to deliver the same PET performance outside and inside an MRI system even under the most demanding gradient sequences without measurable degradations. The interference tests presented in this chapter were conducted on a demonstrator with a bore size which is small compared to a whole-body PET insert. In case of a whole-body system, the bore would be larger and the PET modules would be placed closer to the gradient coils and would therefore experience a higher magnetic flux of the gradient fields. Experiments with modules at this maximum position were presented in chapter 9. There, the increased magnetic flux led to e.g. a CRT degradation of up to ∼50% in contrast to the worst degradation level of 30% measured at the nominal position. As also discussed in Wehner et al. (2015), the degradation scales with the magnetic flux density and therefore with the proximity to the gradient coils. Although the improve IF-board were not tested at the maximum position, a serious performance degradation is not expected as the degradation worsening (without the hardware fix) between the nominal and maximum position was less than a factor of 2 and because no discontinuous scaling behavior of the degradation levels with the distance to the gradient coils was observed.

Only few other groups investigated the influence of MR operation on the PET performance at the level of detail presented here and in the previous works of our group. In Weirich et al. (2012), the influence of gradient sequences on the count rate for the Siemens 3T MR-BrainPET scanner has been investigated. The highest reduction of the count rate was observed for a z-gradient with a GS of 20 mT/m, SR of 154 mT/m/ms and a SDC of 10.6%. An energy window of 420 keV – 580 keV and a CW of 12 ns was used. The observed coincident count rate loss was reported as 1.2%. A comparable investigation with the Hyperion-II platform equipped with the original interface board and comparable gradient sequence parameters are shown in Fig. 10.5 and does not show a loss of coincident events for the given sets of gradient parameters.

Therefore, it is recommended to scan the full parameter space of the gradient system in order to acquire the full understanding of the influence of the gradient system on the PET performance, as MR imaging sequences may not be sensitive enough to show degradations and only investigate a single set of parameters of the gradient system. This might be in particular critical, as this level of investigations does not allow a reliable compatibility investigation. In case of more demanding imaging experiments,
degradations might occur which were not observed in the supposed compatibility investigations. In contrast, synthetic test protocols as discussed in Wehner et al. (2015) and applied in this work allow to distinguish between gradient switching direction and the influence of each parameter of the gradient system and do not include any RF induced interferences, which might lead to degradation of the PET performance, as well. Hence, a more detailed understanding of interference phenomena becomes possible.

10.5.2. PET Performance Evaluation

10.5.2.1. Point Source Measurement

The timing resolutions obtained with the scanner are the best values obtained with an imaging-capable MR-compatible PET system. Because of the one-to-one readout scheme, the photon density on a single DPC pixel is increased in comparison to a light-sharing readout scheme as used for the preclinical Hyperion-II(D) scanner. This results in a lower CRT degradation going from trigger scheme 1 to higher trigger schemes (as shown in chapter 7). Moreover, since the one-to-one coupling does not need to combine hit data of multiple DPCs and because consequently higher validation thresholds are chosen, the sensitivity does only degrade by about 5% when trigger scheme 1 is configured (in comparison to higher trigger schemes). In contrast to that result, we measured a sensitivity loss of about 40% with similar cooling temperature and operating voltages on the preclinical scanner exploiting a light-sharing readout scheme (chapter 7). However, even for the clinical scintillator configuration, the sensitivity loss is expected to be higher if the insert is operated at higher temperatures.

10.5.2.2. Sensitivity Profile

The sensitivity profile shows the expected triangular shape and the measurements taken on two separate days match nicely showing the reproducibility and stability of the investigation.

10.5.2.3. High Activity

Trigger scheme 1 showed problems when operated at activities above 43 MBq. This has been observed before for the platform equipped with preclinical LYSO crystal arrays (chapter 7). Origin of this restriction is the increased power consumption associated with trigger scheme 1: the required current strength reaches the current limitations implemented on stack level. This results in a supply voltage drop and prohibits the operation of trigger scheme 1 above the mentioned activity. Trigger schemes 2 and 3 are not affected by this limitation and can be operated without degradations up to the highest activities investigated. The only exception are two measurements taken between the problematic trigger scheme 1 measurements. The
exact cause of the slight CRT degradations for these two measurements could not be identified. As there are trigger scheme 2 and 3 measurements before and after the problematic measurements, one can conclude that both measurements are affected by a misconfiguration of the system’s operational parameters which could not be identified in the later data analysis. A further analysis is not possible because the clinical scintillator configuration was only installed for a short period of time. Therefore, a repetition of the high activity measurement is not possible.

The energy resolution and CRT only show slight degradations towards the highest measured activities. The degradation coefficient of the energy resolution with the activity is only a third of the coefficient measured with the platform equipped with preclinical LYSO crystal arrays (chapter 7). The corresponding coefficient for the CRT is on the same level for both readout schemes.

With only two stacks per SDM, the employed one-to-one coupling and higher validation threshold, the raw data rate per SDM is much lower compared to the fully equipped preclinical SDMs. Up to activities of almost 200 MBq no saturation effects were observed. Such saturation effects were observed for the preclinical configuration with six stacks at activities of about 25 MBq–55 MBq depending on the trigger and validation scheme (chapter 7).

The sensitivity shows a decline, most likely due to pile up effects which could be reduced with a more sophisticated clustering and coincidence processing. The randoms fraction is very low due to the narrow coincidence window and stays below 2.7% even up to the highest activities and largest energy windows investigated. The NECR (without accounting for scatter) does not show the peak in the measured activity range.

10.5.3. Spatial resolution

As expected, the spatial resolution of the PET scanner is in the range of half the crystal array’s pitch: the hot-rod phantom shows rod separation down to at least 2 mm. However, the 1.5 mm rods cannot be resolved anymore. The presented scanner configuration is expected to provide a spatial resolution in the order of 2 mm.

10.5.4. ToF Benefit for Reconstruction

As demonstrated by the imaging experiments presented in Fig. 10.11, adding the ToF information to the reconstruction clearly improves the visual impression of the image. Artifacts associated with the PET scanner’s geometry can be substantially reduced. As expected from ToF-PET, the SNR improves with increasing CRT performance depending on the diameter of the activity distribution. This effect was also shown for the preclinical configuration (chapter 7).
10.6. Conclusion

The PET performance of the Hyperion-II\textsuperscript{D} platform in the presented configuration with the improved IF board design, the clinical crystal configuration and using the preclinical gantry geometry seems not to be harmed in any measurable degree by the operation of the employed 3-T MRI scanner even under the most extreme conditions the system is able to generate. This is a promising result if the platform should be used to built up gantries with a different geometry or if the PET modules should be integrated directly next to the gradient coils where they might experience stronger gradient field strengths.
11. Summary and Conclusion

In this thesis the Hyperion-II\textsuperscript{D} PET insert was calibrated and its performance evaluated outside an MRI and during simultaneous MRI operation. Two different scintillator configurations of the detector stack were investigated, a preclinical configuration aimed at high resolution preclinical imaging and a clinically motivated configuration with larger crystals but better performance in terms of energy and timing resolution.

In chapter 6 the processing that is used for the preclinical detector configuration is presented in detail. The employed COG algorithm was restricted to operate only on channels that are within a defined ROI. This ensures a stable set of input channels and leads to a reliable crystal identification. As an enhancement, up to two sets of input channels are accepted per scintillator element resulting in a superior sensitivity while maintaining the crystal identification, energy resolution and timing performance.

In the next chapter (chapter 7) the PET performance of the preclinical insert (scintillator pitch of 1 mm with light guide) was evaluated applying the calibration and processing methods presented in the previous chapter. For a wide range of operating parameters, such as temperature and the applied voltage, as well as DPC configuration parameters, a detailed analysis of the PET performance was investigated. It could be shown that the PET performance is very stable over a wide range of different operating scenarios demonstrating the robustness of the developed processing techniques. The obtained performance values are superior or in the range of the best commercially available preclinical PETs. Especially the CRT of the system using the first trigger scheme with 260 ps is the best value that has been shown for a high-resolution preclinical imaging capable system. With this CRT, a clear benefit of ToF information in terms of image quality could be shown for a rabbit-sized activity distribution introducing ToF to preclinical PET applications.

Besides the preclinical detector configuration a clinically motivated (scintillator pitch of 4 mm, one-to-one coupled) was investigated. With this detector configuration the PET performance during simultaneous MRI operation was evaluated with focus on gradient-intense sequences.

In a first study, two fully equipped modules were operated in coincidence inside an MRI (chapter 9). Here, a clear vulnerability, especially to an artificial z-gradient sequences, could be shown. This PET performance degradation was relatively larger due to the better performance that can be achieved with the clinical detector configuration. This proved that this configuration is more sensitive to investigate the MRI compatibility of the Hyperion-II\textsuperscript{D} platform.
11. Summary and Conclusion

In a second step the clinical configuration was implemented in a full-ring (chapter 10), imaging-capable demonstrator. With this scanner, a detailed investigation of the PET performance degradation for a fully configurable z-gradient sequence was performed. The sequence allows to fully control the parameters of gradient system and thus allows a detailed investigation of a possible vulnerability. Degradations of the energy resolution and the CRT were reported and it could be shown that an improved version of the IF board of the detector stack allowed to completely solve the problem of degrading PET performance. This is a very promising result that shows that the upgraded Hyperion-II$^D$ is not influenced by the harshest MRI sequences the employed system is able to produce and should enable even higher integrations of the PET insert with the MRI system.

The calibration and processing techniques developed in this thesis were also applied in an in-vivo imaging campaign. Mice were imaged simultaneously with PET and MRI. The results are presented in Weissler et al. (2015) and Weissler (2016) showing that the system, the data acquisition and processing as well as the PET/MRI compatibility allow a wide range of advanced preclinical PET/MRI investigations and giving a very promising prospect of a development of the technology towards clinical applications.
Acknowledgements

First and foremost, I would like to thank Professor Volkmar Schulz who gave me the opportunity to work in his department on the topic of digital PET and the integration of it with MRI. He supported my work every step of the way while still leaving a lot of freedom to define the direction of research on my own. I would also like to thank Professor Fabian Kiessling, the head of the institute of Experimental Molecular Imaging. I thank Professor Achim Stahl who kindly agreed to serve as the second referee for this thesis.

Without my dear colleagues and fellow PhD students the Hyperion-II\textsuperscript{D} PET scanner would certainly not have been finished in time and would not have turned out to be such a great success. Björn Weissler, Pierre Gebhardt and Peter Düppenbecker already worked on the predecessor of the current platform. Their skills and knowledge about how to design and construct an MR-compatible readout architecture were the foundation for the success of the project. I learned and still learn a lot from them.

The same is true for the fellow PMI PhD students who were already at the institute or joined more or less at the same time as I did: Yannick Berker, Benjamin Goldschmidt and Jakob Wehner. Furthermore, I would like to thank Torsten Solf, Christoph Lerche and André Salomon for sharing their vast expertise on a large variety of PET-related topics.

Marcel Straub, who works on MPI, is a dear colleague who, besides his own research, always keeps the IT and network infrastructure of the group running smoothly. Patrick Hallen joined in the mid of my PhD and is a great reinforcement and support for the PET physics group of PMI.

The very gifted young students Nicolas Groß-Weege, Dennis Klöpping and Christian Ritzer showed a great enthusiasm for physics and it was a privilege for me to work with them.

With all of these brilliant researchers it was a great pleasure to work with and spend time besides work on various conferences and other off-work activities. I hope that we continue with some of them.

A big thanks goes to Thomas Frach, Ralf Schulze and Ben Zwaans from Philips Digital Photon Counting who have always been very supportive and helpful with discussing details about the digital SiPM, data acquisition and processing.

Last but not least, I would like to thank my family. My parents, on whose unwavering support I could always count on, not only during my studies. And my own small family, Eva and Leni, who always manage to remind me of the important things in life.
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Seifert, S., G. Van der Lei, H. T. Van Dam, and D. R. Schaart (2013). “First characterization of a digital SiPM based time-of-flight PET detector with 1 mm spatial resolution”. In: Physics in medicine and biology 58.9, p. 3061. DOI: 10.1088/0031-9155/58/9/3061.


Weissler, B. et al. (2015). “A Digital Preclinical PET/MRI Insert and Initial Results”. In: Medical Imaging, IEEE Transactions on 34.11, pp. 2258–2270. ISSN: 0278-0062. DOI: 10.1109/TMI.2015.2427993.


A. Supplemental data

A.1. Co-Authored Publications

During my work as a PhD I co-authored the following publications (including peer-reviewed and non-peer-reviewed publications).

P. M. Düppenbecker et al. (2016). “Development of an MRI-compatible digital SiPM detector stack for simultaneous PET/MRI”. In: Biomedical Physics & Engineering Express 2.1, p. 015010. DOI: 10.1088/2057-1976/2/1/015010

B. Goldschmidt et al. (2016). “Software-Based Real-Time Acquisition and Processing of PET Detector Raw Data”. In: IEEE Transactions on Biomedical Engineering 63.2, pp. 316–327. ISSN: 0018-9294. DOI: 10.1109/TBME.2015.2456640


B. Weissler et al. (2015). “A Digital Preclinical PET/MRI Insert and Initial Results”. In: Medical Imaging, IEEE Transactions on 34.11, pp. 2258–2270. ISSN: 0278-0062. DOI: 10.1109/TMI.2015.2427993


### A.2. Measurement Details

Table A.1.: All measurements performed for the preclinical PET performance evaluation (chapter 7) with the $^{22}$Na point like sources (distribution and activities listed in Table 7.1 and constant $V_{\text{bias}}$. A measurement id is used to identify a specific measurement (meas.). The measurement parameters: cooling temperature ($T_C$), overvoltage ($V_{ov}$), trigger scheme (trig), validation scheme (val) and the used energy window (EW) are stated for each evaluation of a measurement. The energy resolution and CRT are stated as FWHM and the sensitivity is calculated from the ratio of the prompt rate and the activity of the point sources corrected for the branching ratio of the $^{22}$Na $\beta^+$ decay of 0.906. (reprinted from Schug et al. (2016), ⓒ03.0)

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continued on next page
Table A.1 – continued from previous page

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<th>trig val</th>
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<th>$\Delta E/E$</th>
<th>CRT sens.</th>
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<td>544 ps 0.99 %</td>
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<td>540 ps 0.97 %</td>
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### A. Supplemental data

Table A.1 – continued from previous page

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<th>val</th>
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Table A.2.: All measurements performed for the preclinical PET performance evaluation (chapter 7) with the $^{22}$Na point like sources (distribution and activities listed in Table 7.1 and constant $V_{ov}$. A measurement id is used to identify a specific measurement (meas.). The measurement parameters: cooling temperature ($T_C$), system operating temperature ($T_{op}$), overvoltage ($V_{ov}$), trigger scheme (trig), validation scheme (val) and the used energy window (EW) are stated for each evaluation of a measurement. The energy resolution and CRT are stated as FWHM and the sensitivity is calculated from the ratio of the prompt rate and the activity of the point sources corrected for the branching ratio of the $^{22}$Na $\beta^+$ decay of 0.906. (reprinted from Schug et al. (2016), 3.0)

<table>
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<tr>
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<th>$T_C$</th>
<th>system $T_{op}$</th>
<th>$V_{ov}$</th>
<th>trig</th>
<th>val</th>
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<td>ph</td>
<td>NE</td>
<td>12.57%</td>
<td>576 ps</td>
<td>1.03%</td>
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Table A.3.: All measurements for the preclinical PET performance evaluation (chapter 7) performed with the mouse-sized scatter phantom. A measurement id is used to identify a specific measurement (meas.). The measurement parameters: source activity (activity), system operating temperature ($T_{op}$) for a cooling temperature of $T_C = 0^\circ C$, trigger scheme (trig), validation scheme (val) and the used energy window (EW) are stated for each evaluation of a measurement. The energy resolution and CRT are stated as FWHM. The prompt rate (prompts), random fraction (randoms), scatter fraction (scatter), trues sensitivity (sens) and NECR are evaluated following the NEMA NU 4-2008 standard. (reprinted from Schug et al. (2016), 3.0).

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<th>CRT</th>
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<th>sens</th>
<th>NECR</th>
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<td>NE</td>
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<th>EW</th>
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<th>prompts</th>
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A. Supplemental data
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<td>1 17 ph NE</td>
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continued on next page
## A. Supplemental data

Table A.3 – continued from previous page

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