

UNIVERSITY OF LJUBLJANA
FACULTY OF MATHEMATICS AND PHYSICS
DEPARTMENT OF PHYSICS

Matic Orehar

**DEVELOPMENT OF FLAT PANEL DETECTORS
FOR TIME-OF-FLIGHT POSITRON EMISSION
TOMOGRAPHY**

DOCTORAL THESIS

ADVISER: assist. prof. dr. Rok Dolenec

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UNIVERZA V LJUBLJANI
FAKULTETA ZA MATEMATIKO IN FIZIKO
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Matic Orehar

**RAZVOJ DETEKTORJEV ZA POZITRONSKO
EMISIJSKO TOMOGRAFIJO Z MERITVIJO
ČASA PRELETA V PLOŠČATI GEOMETRIJI**

DOKTORSKA DISERTACIJA

MENTOR: doc. dr. Rok Dolenec

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Pro Deo et patria.

Razvoj detektorjev za pozitronsko emisijsko tomografijo z meritvijo časa preleta v ploščati geometriji

IZVLEČEK

Pozitronska emisijska tomografija (PET) je modaliteta slikanja v nuklearni medicini, ki omogoča slikanje fizioloških procesov v telesu pacienta. Ena izmed smeri razvoja detektorjev za PET je uporaba meritve časa preleta v rekonstrukcijah slik. Za izboljšavo časovne ločljivosti (CTR) je potrebna izboljšava vsakega dela detektorja. Z izboljšavo CTR se odprejo nove možnosti v izdelavi PET skenerjev, na primer odprta geometrija in ploščata geometrija detektorjev. Slednji bi lahko privedli do več prednosti pred konvencionalnimi cilindričnimi skenerji; glavno med njimi bi bilo znižanje cene naprave. Nova geometrija privede tudi do mnogih novih izzivov v uporabi in evalvaciji zmogljivosti skenerjev.

Optimizacija zasnove skenerjev je bila izvedena z Monte Carlo simulacijami. Različne konfiguracije skenerjev so bile primerjane z referenčnim skenerjem z uporabo več metrik za oceno kvalitete slike tako s standardnimi kot tudi novimi fantomi. Zaradi izzivov, ki jih predstavlja ta geometrija, predvsem napaka zaradi paralakse in nepopolne kotne pokritosti, so bili pri rekonstrukciji upoštevani dodatni popravki poleg študije različnih rekonstrukcijskih parametrov. Eksperimentalne meritve so bile opravljene z enim parom detektorskih elementov. Cilj meritev je bila karakterizacija scintilatorjev in fotodetektorjev ter ocena učinkov eksperimentalnih parametrov kot so napetost na fotodetektorju, mediji za optično sklopitev in oprema za zajem na izmerjeno časovno ločljivost.

Ključne besede: Pozitronska emisijska tomografija, meritev časa preleta, Monte Carlo simulacije, koincidenčna časovna ločljivost, eksperimentalne meritve

Development of flat panel detectors for time-of-flight positron emission tomography

ABSTRACT

Positron emission tomography (PET) is an imaging modality in nuclear medicine primarily focused on imaging physiological processes within the body of a patient. One of the focuses in the development of PET detectors is the use of time-of-flight (TOF) information during image reconstruction. In order to achieve improvements in coincidence time resolution (CTR) every part of the detector requires improvement. As the CTR is improved, new possibilities emerge in the construction and use of PET scanners, such as open geometry and flat panel scanner configurations. The latter design could bring several advantages over the conventional cylindrical scanners, the principal being the reduction of the cost of the device. The new geometry also introduces several new challenges both in use and assessment of the scanner.

The optimisation of the novel scanner design was performed using Monte Carlo simulations, where various scanner configurations were compared to a reference scanner using various performance metrics for image quality with both standard and novel phantoms. As the novel geometry presented new challenges, such as the increased parallax error and reduced angular coverage, additional corrections were considered during image reconstruction alongside the study of various parameters used in the reconstruction process. Experimental measurements were performed using a pair of detector elements, with the aim of characterisation of the scintillators and photodetectors and evaluating the effects of the experimental parameters such as different bias voltages, optical coupling agents and acquisition hardware on the measured CTR.

Keywords: Positron emission tomography, Time-of-flight, Monte Carlo simulations, Coincidence time resolution, Experimental measurements

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1. Introduction

Positron emission tomography (PET) is an imaging modality in nuclear medicine that enables the observation of physiological functions and processes through the use of positron emitting radiopharmaceuticals injected into the patient. Afterwards the two high-energy 511 keV photons resulting from the annihilation of the positron need to be detected. By detecting a large number of such events by a scanner consisting in general of a ring of scintillator detectors, it is possible to reconstruct the approximate distribution of the radiopharmaceuticals throughout the body of the patient. PET is characterised by a high degree of specificity compared to anatomical imaging techniques such as computed tomography (CT), making it easier to distinguish between, for example, cancerous growths and healthy soft tissues. On the other hand PET performs worse in terms of spatial resolution and signal-to-noise ratio (SNR) compared to CT. As the modalities provide complementary information, they are used in tandem to provide more relevant diagnostic information. CT images are also utilised during the reconstruction of PET images themselves for various corrections.

Detectors in PET scanners comprise a scintillation crystal, the property of which is to convert part of the energy of the 511 keV photons into photons mostly in the visible part of the spectrum. The crystal is coupled to a photodetector, which converts detected photons into electrical pulses and amplifies them. Further amplification, processing and reading is performed by front-end electronics. In order to detect annihilation events, at least two detectors facing each other are required, with the event originating in the volume of space betwixt the two detectors, referred to as the line of response (LOR).

By measuring the difference between the time of arrival of the two 511 keV photons, it is possible to further localise the event along the LOR. The time-of-flight (TOF) information used in the reconstruction algorithm improves the SNR of the reconstructed image. The coincidence time resolution (CTR) of PET scanners is limited by the various parameters of the detector and its constituents. This includes both the timing characteristics and physical dimensions of the scintillators and the timing and noise characteristics of the photodetectors and front-end electronics. The development and optimisation is conducted on all levels of the detector, with the underlying properties of the scintillators being considered the physical limits of achievable CTR.

Improved CTR on the order of 100 ps enables novel configurations of PET scanners including open geometry and flat panel detector designs. The latter present a substantial move away from the conventional cylindrical PET scanners and may bring several advantages. For example, the flat panel detectors could reduce the cost of the scanner due to a lower amount of used material and lower number of detector elements. The flat panel scanners could be modular, meaning that panels could be placed in different configurations around the patient and the distances could be ad-

justed for each specific clinical case, optimising the sensitivity and spatial resolution of the scanner and allowing flexibility in the coverage of the subject from imaging a single organ with a pair of opposing panels to total-body coverage or a four panel configuration. The scanners could also be made smaller or even mobile and would not necessitate a dedicated room for the PET scanner. The open geometry would allow for the scanners to be used, for example, during hadron therapy for monitoring or planning. The flat panel design also brings forth several challenges associated with the unusual scanner geometry, including the incomplete angular sampling and the exacerbation of the parallax effect for the oblique LORs. The former of which can be addressed with the use of TOF information during image reconstruction.

PET remains one of the important imaging modalities in medicine for instance in the fields of oncology and neurology. The imaging instrumentation exhibits a great potential for improvement, which may lead to better individual patient outcomes as well as improve clinical situation with, for example, increased patient throughput. It is, however, also important to understand how various parameters of PET scanners affect the performance metrics. The significance is increased further as the parameters for the novel scanner designs begin deviating from the most common parameter values to a larger degree, making the current simulation studies less reliable and relevant.

Both the challenges and advantages of detectors currently in development, including the flat panel PET scanner design, necessitate comprehensive evaluation of the performance of such scanners and the effects of various parameters (for example detector element dimensions). For the purpose of optimisation of the detector performance, Monte Carlo simulations of various scanner configurations and parameters were performed, making use of different phantoms and sources of activity, both following the established standard for the evaluation of PET scanners and adding to it where deemed necessary.

The novel flat panel geometry also presented challenges for image reconstruction, requiring a study and optimisation of various reconstruction parameters and even additional corrections, leading to an improvement in the studied image quality metrics. The results were compared to the performance of a reference scanner based on a conventional modern high-end scanner used in clinical practice.

The simulations also served as the basis for the experimental measurements, which were performed using the simplest PET setup, consisting of a single pair of annihilation detectors and entailed performance characterisation of the photodetectors and fast scintillators. The focus of the experimental measurements was primarily on the light yield of scintillator crystals and the CTR of the setup. The effect of various parameters on the two metrics were evaluated, including different scintillation crystals, optical coupling agents, photodetectors, electronics and acquisition hardware.

Chapter 2 presents the theoretical background for PET imaging and an abridged history of development of PET. Chapter 3 presents the methodology for evaluating the performance of PET scanners and the simulation framework, along with the explanation of the experimental setup and measurements. The results for both the simulations and experimental measurements are presented in chapter 4 and are further commented on in chapter 5. A conclusion and future prospects are presented in chapter 6.

2. Positron Emission Tomography

Positron emission tomography (PET) is an imaging modality in nuclear medicine that enables imaging of various physiological functions through the use of positron emitting radiopharmaceuticals.

Radiopharmaceuticals comprise a biologically active compound, a radioisotope, and a connecting link between them. A solution of the radiopharmaceutical is injected into a patient, after which it is distributed throughout the body as determined by the pharmacokinetics of the specific radiopharmaceutical and patient physiology. The quantity of the radiopharmaceutical decreases with time as both the radionuclides decay and the body of the patient expels the radiopharmaceutical. The patient is placed in a PET scanner, conventionally a ring of annihilation detectors. As the radioisotopes decay, they emit positrons which interact with electrons in the surrounding matter and after undergoing an annihilation event produce two back-to-back photons, with the energy of each being 511 keV, corresponding to rest masses of the electron and positron. When both photons are detected in coincidence, the annihilation event can be localised to the line connecting the two detectors that detected the photons, referred to as line of response (LOR). In a more practical sense, a true event can be detected as long as it comes from the cuboid-shaped area between the two detectors in the most basic case of two parallel detectors.

Radioisotopes that decay via β^+ decay are produced mostly using cyclotrons in which charged particles are accelerated into a target. As the particles collide with the target nuclei with sufficiently high energies, they cause nuclear reactions, transmuting the target nuclei. For example in a (p,n) reaction, a proton is accelerated into the target nuclei, which captures it and releases a neutron, thereby changing its atomic number while retaining the same number of nucleons. An example of such a target is water, in which ^{18}O is transmuted into ^{18}F , an isotope of fluorine commonly used in various radiopharmaceuticals for PET.

Another method of production of radionuclides is through the use of generators in which a parent radionuclide decays into the desired daughter radionuclide, providing a longer-lasting and replenishing supply of the desired product. The parent may still be obtained using cyclotron production. Use of generators is more common in single-photon emission computed tomography, specifically with the $^{99\text{m}}\text{Tc}$ generator.

The most commonly used radiotracer in PET is fluorodeoxyglucose (FDG). The compound is analogous to glucose, where one of the hydroxyl groups is substituted with ^{18}F . Its uptake within the body of a patient reflects that of regular glucose and is in that way used as a marker for glucose metabolism. Despite the similarity to glucose, FDG is not metabolised within the body. Instead, ^{18}F decays into $^{18}\text{O}^-$, which obtains a hydrogen ion from the environment and the FDG molecule becomes a regular glucose molecule and is metabolised within the body. The most common use cases for FDG are the diagnosis and staging of cancer in oncology, and diagnosis

of neurological diseases and disorders such as various types of dementia and epilepsy.

A detector element in PET scanners is constructed from a scintillator crystal, which converts a high energy photon into multiple photons in the visible spectrum. These are detected by a photodetector, usually a photomultiplier tube or a silicon photomultiplier and converted into an electronic signal read out and processed by electronics.

In general any detected photons that fall within a coincidence timing window can be considered as possible coincidence events. The window is usually a couple of nanoseconds wide. With advancements in technology it is possible to measure time of detection of annihilation photons with the coincidence time resolution (CTR) in the range of a few 100 ps. This measurement can be used during reconstruction in a technique called time-of-flight (TOF) PET. This information localises the event, meaning that without TOF information the event was assigned a uniform probability across the entire LOR inside the field of view (FOV). TOF instead gives a Gaussian probability distribution with the width of the distribution corresponding to the CTR.

The most common PET scanner design comprises detector modules arranged in a cylindrical configuration with an inner diameter of about 80 cm. This standard design enables acquiring the data for all azimuthal angles simultaneously. The patient is translated along the axis of the scanner using a motorised bed in order to acquire data for a larger portion or even the entirety of the patient body in what is called a whole-body scan. The bed positions partly overlap to compensate for the lower sensitivity at the edges of the axial FOV of the scanner. Detector modules can be placed in a variety of ways, including a regular cylindrical placement or a hexagonal placement. Geometry can also be open, meaning that part of the azimuthal angle is not covered. In this case the detector either has to be rotated in order to acquire full tomographic information or TOF information has to be used to compensate for the incomplete angular coverage.

PET scanners can be developed for special use cases, affecting the geometry of the system. For example a dedicated brain scanner can have a smaller radius and smaller detector elements, both of which improve the spatial resolution of the scanner. Another example is a breast imager using two panels for imaging under compression of the tissue. Such a scanner can be constructed at a much lower cost, as it uses much less material than a full ring scanner and doesn't require a motorised bed. It is also portable. Both of these examples therefore aren't considered whole-body scanners and can only image specific parts of the body.

Another type of scanner design accommodates small animals. They are mostly used for research purposes such as assessing and optimising the performance of new techniques and radiopharmaceuticals. As the subjects for this type of scans are much smaller than human patients, the biggest obstacle is the requirement for improved spatial resolution and sensitivity. As the diameters of such systems are much smaller (on the order of 15 cm) than whole-body scanners for human use, the effect of acollinearity is already mitigated to some extent. To further improve the spatial resolution the cross-section of the crystals is reduced and to mitigate the effect of the depth-of-interaction (DOI) effect, crystal length is reduced as well. Due to the required FOV being much smaller for animal scanners, high geometric efficiency can be achieved without substantially increasing scanner cost.

Another area of development in PET scanners is in the direction of extending

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the axial FOV of the scanners. For example Siemens Biograph Vision Quadra has an axial FOV of 106 cm, four times as much as a more standard Siemens Biograph Vision 600 scanner [1]. A more extreme version of the long axial FOV scanner is the total-body scanner, for example United Imaging uEXPLORER, which has the axial FOV of 194 cm [2] and covers the entirety of the patient body at once. In both of these cases the patient may be imaged without any bed motion, as the entire area of interest falls within the FOV. One of the main advantages of such a design is the increase in sensitivity due to the increased geometric coverage, which can be utilised in a number of different ways. The time to acquire the same amount of data from a scan of a patient is decreased, or in the same amount of time an image with a higher SNR can be acquired. Alternatively a lower amount of activity needs to be injected into a patient to acquire an image of the same quality without an increase in imaging time. Some combination of all three may be optimised for a given clinical problem. With the increase of demand for PET imaging, the increased patient throughput facilitated by the long axial FOV scanners can be an attractive consideration [3]. Shorter scans would also improve patient comfort and reduce motion based image artefacts. Another area of interest is kinetic imaging. Ordinary whole-body scanners are already capable of performing dynamic imaging protocols but are restricted to a relatively small area, such as a single organ. Extended scanners on the other hand are capable of performing these studies on multiple organs or the entire body simultaneously and may bring new insights into disease states and the characteristics of the radiopharmaceutical.

Different imaging techniques can be used complementarily in hybrid imaging. Low SNR and spatial resolution of PET can be compensated by using an anatomical imaging modality such as computed tomography (CT) or magnetic resonance imaging (MRI). CT images are also used in the reconstruction of PET images to for attenuation and scatter correction.

2.1 Interaction of High Energy Photons and Electrons with Matter

In PET the interactions of high energy photons with matter can be regarded as collisions with electrons. One type of such interactions is the photoelectric effect. In such case the photon deposits all of its energy to an electron and disappears. The photoelectron is ejected from the atom if the energy of the photon is larger than the binding energy of the electron in that atom. The remainder of the energy is converted to the kinetic energy of the photoelectron. The photon is most likely to be ejected from the innermost shell of the atom if the photon energy is sufficient. The vacancy in the shell leads to the emission of characteristic X-rays. In biological material the binding energies and the energies of characteristic X-rays are much lower than the 511 keV photon energy and range up to a couple of keV. For elements with higher atomic numbers these energies can range up to about 100 keV.

The second type of interaction relevant in PET is Compton scattering. In this case the photon doesn't deposit its entire energy and doesn't disappear. Instead, it is deflected. The energy and angle of deflection of the photon are connected by the equation:

$$E'_\gamma = \frac{E_\gamma}{1 + \frac{E_\gamma}{m_e c^2}(1 - \cos \theta)}, \quad (2.1)$$

where E'_γ is the energy of the scattered photon, E_γ the energy of the incident photon, m_e the mass of the electron, c the speed of light and θ the angle of deflection of the photon. The photon thus deposits the most energy to the electron when $\theta = 180^\circ$. The interaction typically happens with electrons in the outer shell of the atom. Because the binding energy is much lower than E_γ it can be ignored in the equations and the electrons regarded as free. In this case the energy of the electrons is calculated by subtracting the photon energies $E_e = E_\gamma - E'_\gamma$. The differential cross-section is given by the Klein-Nishina formula and describes the angular distribution of scattered photons with higher energies leading to lower deflection angles.

Another type of interaction is pair production. In this case from a photon in the electric field of an atomic nucleus or an electron, a pair consisting of an electron and a positron are created. The lower energy limit of the photon for such an interaction is the sum of masses of both particles, which would be 1.022 MeV or twice the energy of annihilation photons. Such an event therefore cannot take place due to annihilation photons originating from β^+ decay. It could only occur in the context of PET if the decaying radionuclide or one of its decay products would have another decay mode in which a sufficiently energetic γ ray was emitted.

Interaction probabilities and linear attenuation coefficients of all these types of events depend on the density of the material. Effective atomic number of the material and the energy of the photons affect the cross-sections for each event type, with photoelectric effect dominating at lower energies and higher effective atomic numbers. Dominant interactions for photons with different energies depending on atomic number are shown in figure 2.1. The attenuation of a narrow beam of photons is described by the equation

$$I = I_0 (1 - e^{-\mu x}), \quad (2.2)$$

where I is the number of photons that had undergone an interaction, I_0 the total number of photons, x the thickness of the material and μ the linear attenuation coefficient. The attenuation coefficient is different for each of the types of interactions and can be combined into a total attenuation coefficient by adding them together linearly $\mu_{\text{TOT}} = \mu_{\text{PE}} + \mu_{\text{CS}}$.

After photons deposit some or all of their energy to electrons, those also lose their energy through different mechanisms as they move through material. Positrons also lose their energy in the same manner after they are emitted from nuclei, the difference being that they undergo an annihilation event after losing most of their energy.

Electrons lose their energy through interactions with atoms of the surrounding material via electric force. In a simplified explanation that can be seen as collisions with electrons. These collisions can either put the atom in an excited state or cause the electrons to be ejected from the atom and ionising it. The secondary electrons then also behave in the same manner. These interactions mostly occur with outer shell electrons.

Electrons can also interact with the nuclei of the atom. In this type of interaction an electron's path is deflected and it loses a part of its energy through bremsstrahlung in which the energy is emitted in the form of electromagnetic radiation. The ratio of

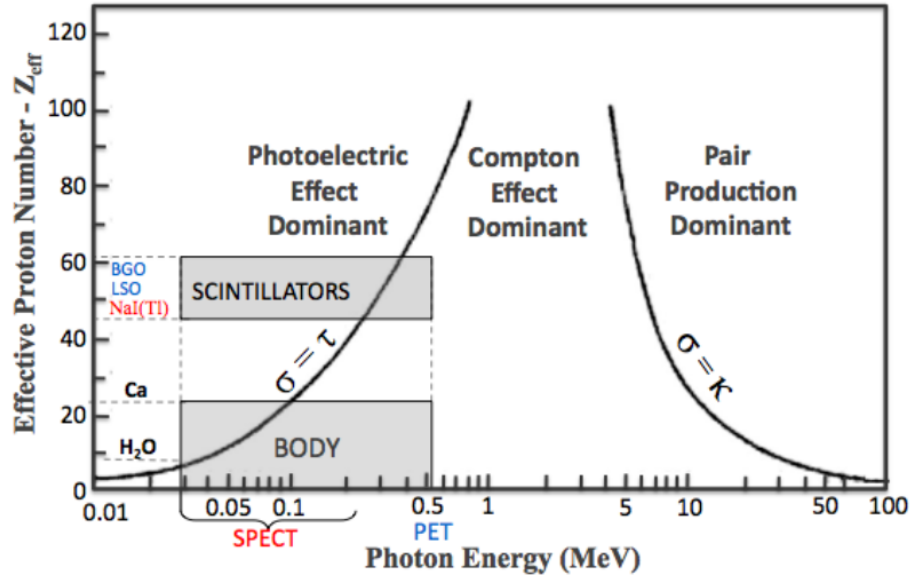


Figure 2.1: Dominant photon interactions depending on the atomic number and photon energies. Grey boxes show typical domains encountered in nuclear medicine for both PET and Single-photon emission computed tomography. For PET specifically, the dominant interaction for the incident photons is always Compton scattering both in the body and the scintillator crystals. Taken from [4].

energy lost due to collisions and due to radiation losses depends on electron energy and the atomic number of the material, with higher energy and atomic number meaning more radiation losses. For electrons obtaining their energy from the 511 keV photons in PET the radiation losses are much smaller than losses due to collisions.

In case the electron travels faster than the phase velocity of light inside a medium (speed of light divided by the refractive index) the electron releases photons of Cherenkov radiation. This type of radiation in the context of PET accounts for a negligible amount of energy losses but may open interesting detection concepts in some cases.

2.2 PET Performance Parameters

2.2.1 Event Types

Different types of events are recorded by the PET scanner. A true coincidence is an event in which both photons from the same annihilation event are detected by the system. It is the only desired event type. A scattered event occurs when one or both of the photons undergo a scattering event and is then detected by a detector element that is not in line with the true LOR. The scattering can occur either in the patient or in any part of the scanner. Intra-crystal scattering that ends with the photon being absorbed inside the crystal does not count as a scattered events. Similarly, if multiple detector elements are grouped together in a module, any event that scatters only within the scintillator crystals of the module is still considered a true coincidence event. This greatly increases the sensitivity of a PET scanner at the cost of spatial resolution. The location of the true interaction point is approximated using for example energy weighted centroid calculation. On the other hand, if a

photon was scattered within the crystal and then escaped, such an event would still be characterised by the correct LOR but it cannot be distinguished from one that had been scattered within the patient and then detected. Some scattered events can be disregarded during reconstruction if the measured energy of the event falls outside the energy window of the system. Scattered events introduce a background to the reconstructed image, concentrated around the centre of the imaged object and lead to the deterioration in image contrast.

Random coincidences are events where the two detected photons originate from different annihilation events leading to the assignment of an incorrect LOR. Rate of these events depends on the width of the coincidence window and is roughly proportional to the square of injected activity. In reconstructed images random coincidences contribute a kind of uniform background across the FOV which deteriorates image contrast and the accuracy of quantification.

2.2.2 Spatial Resolution

Spatial resolution of a PET scanner is determined mainly by three contributions: dimensions of detector elements, contributions due to positron range and the acollinearity of the emitted high-energy photons. Regarding the dimensions of detector elements, the full width at half maximum (FWHM) of the resolution for a pair of detectors with the width d ranges from $d/2$ at the midpoint between a detector pair to d at the face of one of the detectors.

Positrons emitted during β^+ decay have non-zero kinetic energy, which they lose through interactions with surrounding charged particles. The annihilation event therefore takes place in a different location than the original position of the radionuclide and the emission of the positron. The travelled distance depends on the initial energy of the positron and the medium, and typically ranges between 1 mm and 20 mm [5] in water. Interactions with charged particles do not only decrease the velocity of positrons but also change their direction. The effective range of positrons is thus described by the root mean square value, which ranges between 0.1 mm and 3 mm in water for positrons with the maximum possible energy encountered in PET, meaning that for most emitted positrons the values are even lower.

The positron can undergo an annihilation event before losing its entire momentum. In order to satisfy the conservation of momentum, the two annihilation photons are not emitted at exactly 180° , which is referred to as noncolinearity or accollinearity. The FWHM of the emission angle distribution is approximately 0.5° . The contribution to spatial resolution is $R_{180^\circ} = 0.0022 \cdot D$, where D is the diameter of a scanner.

Spatial resolution of the entire system, R_{sys} , is approximated with the equation [5]

$$R_{sys} \approx \sqrt{R_{det}^2 + R_{range}^2 + R_{180^\circ}^2}, \quad (2.3)$$

with typical values of each contribution being: $R_{det} = 1.6$ mm for the contribution of the detector dimension, $R_{range} = 0.2$ mm for the contribution due to positron range, and $R_{180^\circ} = 1.7$ mm for the contribution due to accollinearity. The first contribution can be decreased by reducing the width of the detectors, in which case cost is the limiting factor. The third can be reduced by using a scanner with a smaller radius, which requires specialised scanners and limits the spectrum of possible applications of the device. The second is an insurmountable physical barrier

with no clear possibility of mitigation. It is also the smallest contribution. Spatial resolution also varies across the FOV. In part this is due to the variable contribution of the R_{det} .

The other contribution to the deterioration of spatial resolution is the depth-of-interaction effect. For events occurring outside of the centre of the FOV scintillator crystal length also plays a role in spatial resolution besides the width. The slant of the pair of detector elements effectively increases the area from which possible coincidence events can be detected. In other words the apparent width of the crystal is increased and is equal to the orthogonal projection of both the width and the length of the crystal onto the face of the area defined by the LOR. A way to mitigate this effect is to determine the depth at which the photon had interacted within the scintillator crystal. DOI information can be measured, for example, by using multiple photodetectors on a single scintillator crystal, for example on the front and back face. This in turn increases the cost and complexity of the PET scanner.

2.2.3 Sensitivity

The sensitivity of PET scanners is characterised by the intrinsic efficiency of detectors and the geometric coverage of the scanner, which is the solid angle covered by the detectors relative, for example, to a source located at the centre of the FOV. For a pair of detectors, the sensitivity R_{true} is described by the equation

$$R_{\text{true}} = E\epsilon^2 g_{\text{ACD}} e^{-\mu T}, \quad (2.4)$$

where E is the source emission rate, ϵ the intrinsic efficiency of a single detector as described by the dimensionless version of equation 2.2, μ the attenuation coefficient of the imaged object and T its thickness. The parameter g_{ACD} is the geometric efficiency for annihilation coincidence detection, which establishes the proportion of the annihilation photons emitted towards a detector. For a source located at the midpoint and centreline between two opposing detectors g_{ACD} can be approximated as

$$g_{\text{ACD}} \approx \frac{2A_{\text{det}}}{\pi D^2}, \quad (2.5)$$

where A_{det} is the area of one of the detectors facing the source, and the dimension of the detectors is assumed to be small in comparison with the distance between the detectors D . As such, the equation approximates the proportion of the full solid angle covered by the two detectors and a similar approximation can be made for a full ring of detectors as long as the same assumptions hold with the area covered by the detectors being πDh , with h being the axial length of the scanner as shown in the schematic representation in figure 2.2. As such, in order to increase the g_{ACD} of a cylindrical scanner, it has to be either extended in the axial direction (for example, with addition of more rings of detectors), or the diameter of the scanner would need to be decreased. The cylindrical PET scanner geometry is not particularly suitable for the latter. However, a scanner configuration made of a pair of flat panel detectors may take advantage of the geometry and adjust the distance between the opposing detectors for a given clinical problem.

2.3 Detectors

The function of detectors in PET is to convert a high energy photon into an electronic pulse. The detectors comprise the scintillator crystal, a photodetector and read-out

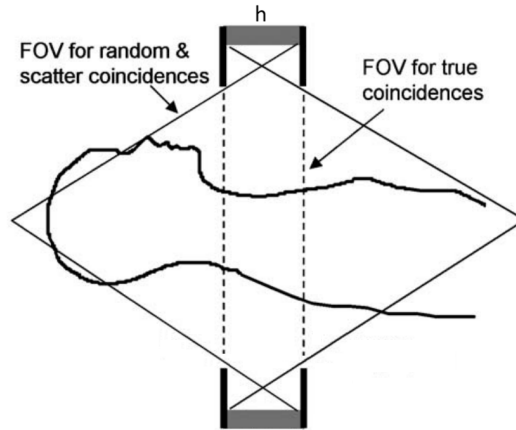


Figure 2.2: Schematic representation of a patient during the acquisition of the PET image. FOVs for different event types are marked. Adapted from [6].

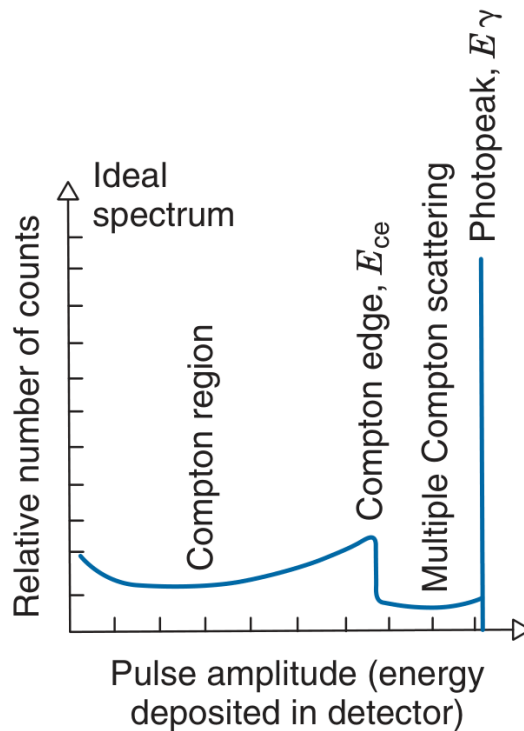


Figure 2.3: Histogram of an ideal pulse-height spectrum for a scintillation detector, showing different regions according to the deposited energy in the detector, with the discrete line representing the deposition of the entire energy of the photon and the lower energy representing the single and multiple scattered events with a very distinct feature called the Compton edge representing the most energy a photon can lose during a scattering event (in other words when the scatter angle is 180°). Taken from [5].

electronics. In an ideal case, such a detector would produce an energy spectrum of incident photons as shown in figure 2.3 where different features are annotated and explained.

The actual resulting measured spectrum is blurred and broadened due to several factors, for example statistical variations in the number of produced photons, variations in the number of detected photons due to imperfect transport and detection efficiency, nonlinearity of the energy response of the scintillator when absorbing photons with different energies, non-uniformity of the photodetector, fluctuations in the voltage of the photodetector, electronic noise and crosstalk. One of the consequences of the blurring is that the photopeak becomes roughly Gaussian in shape. The energy resolution of the detector is determined as the FWHM of the photopeak divided by the photopeak energy as shown in the equation

$$\text{ER} = \frac{\Delta E}{E_\gamma}, \quad (2.6)$$

where ER is the energy resolution expressed in percentage, ΔE the FWHM of the photopeak and E_γ the energy of the photopeak.

2.3.1 Scintillators

Scintillators are materials in which part of the deposited energy from ionising radiation is converted into multiple photons of visible light. The amount of photons is proportional to deposited energy and is a characteristic of the scintillator material. In PET, high energy photons interact with the scintillator via photoelectric effect or Compton scattering, both of which release electrons that cause ionisation through collisions with matter. Scintillators come in forms of organic or inorganic materials.

Organic scintillators come in solid, liquid and gaseous forms with the most common being scintillators dissolved in liquid, and plastic scintillators. Neither see extensive adoption in clinical practice and are mostly confined to experimental settings with the first and most famous example of the use of plastic scintillators on the system level being Jagiellonian PET [7]. Contrary to inorganic scintillators, where scintillation occurs due to the crystalline structure of the material, scintillation of organic scintillators is a characteristic of the molecule, for example butyl PBD dissolved in toluene. In this case the photoelectron excites the molecules of the solvent, which transfer the energy to the scintillator molecule for instance via dipole-dipole interactions. This excites the molecule into an excited singlet state from which it returns to the ground state by emitting a photon.

The most common type of scintillators used in PET are inorganic scintillators. They are used in form of solid crystals that can be either in their pure state or doped with another element to create activator centres and alter the characteristics of the material. Material characteristics of different scintillators must be considered when choosing them. Density of the material determines the efficiency for stopping 511 keV photons. In this metric most inorganic scintillators outperform all organic scintillators with LSO ($\text{Lu}_2(\text{SiO}_4)$), LYSO ($\text{Lu}_{2(1-x)}\text{Y}_{2x}\text{SiO}_5$) and BGO ($\text{Bi}_4\text{Ge}_3\text{O}_{12}$) materials for example being approximately 7 times denser than plastic scintillators. In a similar manner, the effective atomic number, which determines the fraction of photoelectric effect and Compton scattering is several times higher for inorganic scintillators, making them more appropriate for use in PET.

Photon yield of scintillators determines the number of visible photons released per unit of deposited energy and is important for discrimination between true and scattered events, in other words, the energy resolution of the scanner. It also affects the CTR of the system. Other characteristics related to timing are the rise and decay

times of the material, both of which affect the CTR. The decay time is also one of the limiting factors in discriminating between consecutive events due to pile-up. The decay time for fast inorganic scintillators usually ranges in tens of nanoseconds for example 30 ns for LSO:Ce:Ca [8] while rise time ranges in the tens of picoseconds, for example 20 ps for LSO:Ce:Ca. Plastic scintillators on the other hand can reach the decay times of about 1 ns and rise times in the hundreds of picoseconds [9],[10]. Another matter regarding the rise time is Cherenkov radiation. Scintillators can also emit Cherenkov photons which are emitted promptly though in much lower numbers. Those can be used to improve the CTR of the system, for example using BGO crystals [11]. It is also in principle possible to use pure Cherenkov emitters instead of scintillators, which comes with a new set of challenges [12].

The index of refraction is an optical property of the scintillator and is important for optical coupling of the scintillator to the optical window of the photodetector. A high index leads to a higher amount of total reflections of visible photons, as they can hit the face of the scintillator coupled to the photodetector at an oblique angle, for example, the index of refraction for BGO is 2.15 and 1.82 for LSO. The indexes of the scintillator and optical window materials should match as much as possible to enable visible photons passing to the photodetector with the least amount of internal reflections. This is aided by an optical coupling agent connecting the scintillator to the window. The index of refraction also determines whether the scintillator produces Cherenkov photons. The spectrum of emitted visible light is also a characteristic of the scintillator and should overlap with the photon detection efficiency of the photodetector.

Mechanical properties affect the difficulty of handling the scintillators. Some considerations are state of matter, with only solids being used in clinical practice, whether or not the material is hygroscopic, with hygroscopic materials requiring being hermetically sealed, and mechanical stability. Another important metric is the cost of material.

The final choice of material is a compromise between all those characteristics, taking also into account what the desired result is, for example if timing is more important than efficiency for the particular experiment, a plastic scintillator would be preferable over an inorganic one. The choice of material also impacts other parameters, that are not material specific, such as dimensions, number and placement of the scintillators.

2.3.2 Photodetectors

The second part of the detector chain is the photodetector. The most common types used in PET are photomultiplier tubes (PMT) and silicon photomultipliers (SiPMs). In general the function of the photodetector is to convert the pulse of visible light from the scintillator into an electronic pulse.

After a visible photon passes through the optical window of a PMT, it is absorbed in a photocathode, which releases a photoelectron from the substance with a likelihood corresponding to the quantum efficiency of the material for that specific wavelength. Photoelectrons are then focused and accelerated to a positively charged dynode. After an electron collides with the dynode, several secondary electrons are emitted. All of those are then accelerated to the next dynode where the process is repeated. After several stages of dynodes, the electrons are collected at the anode. Typical electron multiplication factors are 3-6 per dynode with the number of dyn-

odes ranging from around 9-12. The total multiplication factor for an example with 10 stages and 4 electrons per dynode would be $4^{10} \approx 10^6$. PMTs suffer from stochastic variations from the first steps of the amplification when the number of electrons is low. These are propagated across the amplification process and are reflected in variabilities in pulse height [13].

SiPMs consist of a grid of single photon avalanche diodes (SPAD) in Geiger mode, each diode or cell is referred to as a pixel with a typical size of tens of micrometres. They are electrically decoupled and are implemented on a common silicon substrate. Each pixel can detect a single photon. The output signal of the SiPM is the sum of all signals of the discharged pixels. The gain of a SiPM is on the order of 10^6 and the quantum efficiency ranges from 0.5 to 0.8 at its peak and is wavelength dependent[14]. SiPMs are typically operated a couple of volts above breakdown voltage, which is on the order of tens of volts. In SPADs a carrier can be produced thermally in the sensitive volume. Such an event produces the same result as a visible photon hitting the cell. This is the main source of noise in SiPMs and is called dark noise. The rate of noise is temperature dependant with higher temperatures causing higher noise and a typical value at room temperature being around 100 kcps/mm². The pulse heights of such events are much lower than those from pulses of light from scintillators in PET. The effect is more noticeable when dealing with Cherenkov radiation, which produces a far lower number of photons.

PMTs differ from SiPMs in many ways, each offering advantages in different areas. The most obvious difference being the much larger size and weight of PMTs. The electrodes must be enclosed in a vacuum and have a shorter operating life. PMTs operate at much higher voltages and currents. All these make PMTs harder to work with. PMTs are affected by external magnetic fields, making PMTs unable to be used in PET/MRI hybrid scanners. PMT pulse heights have a higher degree of variability. SiPMs suffer from dark counts and crosstalk between the cells. SiPMs outperform PMTs with regard to time resolution but are sensitive to operating temperatures. Historically, PMTs were used in most clinical systems, but in more modern scanners, SiPMs are used more commonly due to their more desirable characteristics and also superior performance [15],[16].

2.3.3 Time-of-Flight PET

A possible coincidence event is detected when two annihilation photons are detected within the timing window, which are in general a couple of nanoseconds wide. TOF information refers to the fact, that it is possible to determine the time of arrival of the two photons more accurately than the duration of the coincidence window. Without the use of TOF information, the detected event is only localised to the specific LOR along which it was detected and restricted to the imaged object, while the use of TOF information further localises the event with a Gaussian distribution along the LOR with the width of the distribution corresponding to the CTR. The distance of an event from the central point of a pair of detectors is given by

$$\Delta d = \frac{\Delta t \cdot c}{2}, \quad (2.7)$$

where Δd is the distance from the central point, Δt the time difference between the detection of both events and c the speed of light. The same equation can also be used to estimate the the uncertainty of localisation by replacing time difference with CTR.

The first generation of TOF-PET scanners were built and tested in the early 1980s, with the research on the topic dating even further back. The achieved CTR of those scanners was on the order of 500 ps, which was reported to be enough to obtain a non-uniform SNR gain of about 3-7, dependant on activity [17]. One of the motivations for improving the timing characteristics of PET scanners was to deal with difficulties arising from the use of higher activity levels when imaging with short-lived radioisotopes. The improvement in timing characteristics enabled narrower timing windows, which in turn meant less random coincidences. Faster scintillators also meant a reduction in dead time. Both of these factors along with the use of TOF information in reconstruction contributed to the improvement of SNR of reconstructed images [18].

The first generation of TOF-PET scanners utilised fast scintillators such as BaF₂, which enabled good timing but poor sensitivity. Crystals were coupled 1-1 to photodetectors, limiting the spatial resolution to the size of the photodetector. As the block detector design came into use and more efficient scintillators such as BGO, the 1990s saw a decline in the use of TOF-PET. The revival of TOF-PET was facilitated by the invention and use of LSO and LYSO scintillators in PET devices. The new generation of TOF-PET scanners were able to approximately match the timing performance of the first generation, while avoiding both of the design drawbacks that had resulted in poor sensitivity and spatial resolution of those scanners [19]. The development of TOF-PET scanners continued and recent achievements include CTR of 214 ps [20] and even more recently as low as 189 ps [21] on system level for a clinical scanner.

In experimental setups CTR as low as 58 ps [8] and 32 ps [22] have been reported with a single pair of detectors. Those, however, cannot be easily translated into clinical practice because, the results are obtained using smaller scintillators (or Cherenkov radiation emitters), leading to poor sensitivity and make use of high-frequency electronics which are not scalable or photodetectors not suitable for a clinical scanner. However, the results are important to demonstrate the potential for improvement of TOF-PET scanners.

Every part of the PET detector contributes to the obtained CTR, thus every level of detection requires optimisation in order to improve on the time resolution with a roadmap towards a theoretical limit of 10 ps being proposed [23].

The contribution of the scintillator material properties to the CTR of the PET detector can be approximated with the equation [24]:

$$\text{CTR} = 2.18 \sqrt{\frac{\tau_r \tau_d c}{n}}, \quad (2.8)$$

where τ_r is the rise time, τ_d the decay time, c the speed of light, and n the number of detected photons. Using some the best currently available scintillators (LSO:Ce:Ca), this would lead to a contribution of about 12 ps. Besides the material properties, the dimensions of the scintillator crystal also impact the CTR, with thicker crystals performing worse, leading to a trade-off between sensitivity, CTR and cost.

The electronics [25] and photodetectors [26] also both contribute to the CTR of the system.

The SNR gain due to the use of TOF information can be approximated using the equation [27]:

$$\text{SNR}_{\text{TOF}} = \sqrt{\frac{D}{\Delta d}} \text{SNR}, \quad (2.9)$$

where SNR_{TOF} is the improved SNR, D the thickness of the imaged object and Δd the localisation uncertainty given by equation 2.7. The equation is only valid under very specific conditions, but can be used as a basic approximation.

The gain due to TOF can be utilised in a variety of manners, such as imaging for shorter times, the benefits of which being patient comfort and faster throughput. Another possibility is improved image quality due to higher contrast and lower noise levels, leading to better lesion detectability. The final possibility is imaging using lower injected activities, reducing the radiation burden on the patient and opening the possibility of extending the use of PET to include for example screening tests, or imaging patients more susceptible to the damage of radiation.

2.3.4 Depth-of-interaction

In a detector setup consisting of a scintillator crystal and photodetector, it is generally not possible to accurately determine where exactly inside the crystal the photoelectric interaction took place. For all events detected in a specific detector element, all events are assigned the same interaction position, usually the centre or the front face of the crystal. As long as the event originates along the centreline between a pair of detectors, this only affects the CTR of the system, however, for events originating from other positions, the spatial resolution is also affected. For example, in cylindrical scanners events originating from outside the centre of the FOV deteriorate the spatial resolution. The parallax error is exacerbated by crystal length. DOI encoding enables more uniform spatial resolution across the FOV in all directions [28] and can be performed in different ways, such as having multiple layers of detectors, resulting in a discrete encoding of DOI information, or by utilising dual ended readout detector design, enabling a continuous DOI measurement, with a single layer of scintillator crystals. A continuous DOI measurement can also be performed using a single ended readout with a monolithic scintillator crystal, meaning that the crystal covers multiple photodetectors.

2.3.5 Detector Design

In PET scanners utilising PMT the block design [29] is often employed. Instead of each scintillator crystal requiring its own photodetector, a larger block of the scintillator can be used, partially cut into, for example, 64 elements and coupled to just 4 PMTs. In this way the spatial resolution can be improved without the increase in cost because of the photodetectors, as they are no longer the limiting factor. The location of the interaction within the scintillator can be calculated by comparing all four signals of the PMTs. The number of required PMTs per detector element can be decreased even further with a quadrant sharing approach. With the advent and refinement of SiPMs, the one photodetector per element design is commonly implemented.

The block detector design can also be combined with a phoswich detector design, which employs two different scintillator materials in two layers. By observing the decay time characteristics of the pulse, it is possible to distinguish between the two scintillators, which provides DOI information, however, this is at the cost of TOF information.

Another possible design are the monolithic-based detectors. The basic configuration is similar to the block detector, with the exception that the scintillator crystal is a single continuous and uncut slab. Both PMTs and SiPMs have been used in this detector design with SiPMs being preferred [30]. Photodetector placement has been tested in various configurations including front face, back face, double sided and even lateral side readout [31]. The readout can be simplified by implementation of various projection, logic or multiplexing schemes to reduce the number of signals that need to be digitised. On the other hand, these schemes also negatively affect timing performance. Monolithic detectors in general provide greater sensitivity than pixelated detectors since they have no dead areas and this design also provides DOI information [32], which can be used to improve the quality of reconstructed images by reducing the parallax error. For events in which the 511 keV photon underwent a single or multiple Compton scattering events inside the scintillator before the photoelectric interaction the determination of DOI information is impeded. Each event may trigger multiple photodetectors, making data acquisition more demanding compared to a pixelated detector. This also makes the system more susceptible to event pile-up or dead time as the rate of events increases. System spatial, energy, and time resolution are dependant on the position of the event within the detector and all parameters degrade towards the edges of the detector. In terms of implementation and wider adoption in clinical practice, they would require more complicated calibration and validation procedures in comparison to the pixelated detectors.

2.3.6 Sparse Detector Configuration

In an effort to reduce the required number of detector elements in a given system, sparse configurations have become an area of interest. This refers to any configuration in which detector elements are not tightly packed. The feasibility of retaining clinical image quality whilst reducing the number of detector elements by one half has been demonstrated [33]. In the study every other row of detector elements was removed in either axial or tangential direction and compared to the full detector. Despite the sensitivity being reduced to 25% of the original value, all lesions in the images remained visible, with the caveat that lesions with lower contrast may have posed a greater challenge.

Sparse configurations are more interesting in terms of extending the axial FOV of the scanners without increasing the cost of the scanner. This can for example be accomplished by moving rings of detectors further apart or even employ a chequer-board pattern of detector placement [34]. If the detector rings are spaced too far apart, it leads to gaps in the sensitivity profiles and artefacts in the reconstructed images, especially when TOF information is not used in the reconstruction process. One way to ameliorate the image quality is to employ bed motion during the acquisition of the image.

Another approach to the sparse configuration involves using scintillator crystals with a smaller cross-section than the photodetector. This approach also decreases the cost of the system, as the required amount of scintillator material is reduced despite the fact that the number of detector elements remains the same. Such a configuration has the potential to improve the CTR of the system, as the efficiency of scintillation light collection on the photodetector is improved.

2.3.7 Limited Angle and Flat Panel Scanner Geometry

In some specific cases in PET imaging, a limited angle scanner geometry is preferred, as such an open geometry enables access to the patient, for example in breast imaging, where a clinician may perform a needle biopsy during image acquisition. The incomplete angular sampling in image acquisition causes artefacts in reconstructed images. These can be mitigated either by rotating the scanner or by making use of TOF information. Sufficient CTR enables the recovery of the complete 3D image without artefacts and depends on the angular coverage. For example, 600 ps was demonstrated to be sufficient for a scanner that covers $\frac{2}{3}$ of the azimuthal angle and 300 ps for $\frac{1}{2}$ of the azimuthal angle [35]. Limited angle scanners may also be constructed in a way that allows the scanner to accommodate patient-specific imaging scenarios by bringing the detectors closer or farther apart [36].

A different approach to the limited angle geometry is to relinquish the standard cylindrical geometry altogether and utilise flat panel detectors with popular options involving a configuration of two or four panels around the imaged object. As before, the solution to the artefacts is either rotation of the panels [37] or improvement in CTR in which case it was demonstrated that with CTR below 100 ps a flat panel scanner approaches the performance of a standard modern clinical scanner (which also makes use of TOF with a CTR of about 200 ps) [38].

Much like with sparse configurations, limited angle scanner geometry is also interesting from the point of view of reducing the cost of the device, as it naturally leads to a reduced amount of detector elements in the system. A scanner utilising such flat geometry may be designed in a modular manner, meaning that multiple panels could be placed in a variety of manners such as two or four panels around the imaged object or even multiple consecutive panels creating in essence a long axial FOV scanner. Panels could also be brought closer to the imaged object in order to improve sensitivity and spatial resolution of the system. Sensitivity improves due to increased geometric coverage and spatial resolution improves due to the reduction of the contribution of acollinearity to spatial resolution (and is thus only noticeable if this contribution is comparable to the others or larger). The flat panel scanner configuration could also be designed to be lighter, more compact or even mobile, meaning that it would no longer require a dedicated room for the scanner, though the immediate benefit of that may not be realisable, as a CT scan for attenuation and scatter correction is still required in image reconstruction.

Flat panel designs suffer from the parallax error due to the DOI effect, as even an event originating from around the centre of the FOV can be assigned an incorrect LOR, if the paths of the high energy photons are oblique relative to the panels as shown in figure 2.4. Therefore, it is important to address this issue, which can be done in various ways including having multiple separate layers of detector elements, double sided readout, a phoswich configuration or even a monolithic detector design. Of these the phoswich is the least useful, since CTR is also an important consideration in such a geometry. The simplest solution is to decrease crystal length. This leads to a reduction of sensitivity, which decreases the SNR of the reconstructed image but on the other hand it improves the spatial resolution and also the CTR of the system, both of which are important factors in the flat panel design, with CTR not only compensating for the limited angular coverage but also improving the SNR of the reconstructed image. At the same time it also leads to a reduction in the cost of the system. The use of double sided readout can also be utilised to improve the

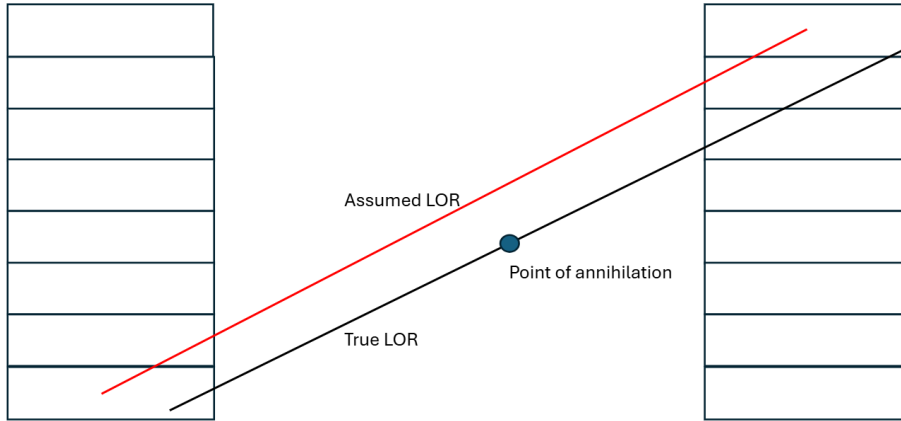


Figure 2.4: An illustration of the parallax error for oblique LORs, where the red line shows the assumed LOR connecting the centres of the two crystals and the black line showing the actual LOR for an extreme example where the 511 keV photons interact near the edges of the crystal.



Figure 2.5: An illustration of the DOI effect on a pair of detector elements. In this case the DOI doesn't affect the LOR but instead the CTR as photons would be detected faster in the left detector.

CTR of the system as the DOI can be accounted for. This is due to the fact that the velocity of the 511 keV photons remains approximately the same as in vacuum, while the phase velocity of the visible photons is determined by the refractive index. Meaning that, for example, a photon might interact near either the face coupled to the photodetector or the opposite face. In the former case the visible light would reach the photodetector sooner as shown in figure 2.5.

2.4 Tomographic Image Reconstruction

In PET imaging the measurement is the number of detected events along each of the LORs connecting each pair of detector elements. These data have to be reconstructed into a 3D array representing the accumulation of the radiopharmaceutical within the body of the patient or a phantom which is then viewable as a set of 2D images as slices across the array. In other words tomographic reconstruction is the calculation of the scalar field representing the distribution of the radiopharmaceutical from the collection of measurements.

Both of the presented reconstruction algorithms are written in their most basic and simplified forms, not taking into account any corrections such as random and scatter correction or normalisation nor does it take into account TOF which can have a significant effect on both the reconstruction process itself as well as on the resulting reconstructed images regarding the image quality.

2.4.1 Lines of Response

LORs can be parametrised as lines with 4 parameters, namely the shortest distance of the LOR projected onto the XY plane from the centre of the FOV p , the angle of the LOR ϕ , the axial position $z = 0.5 \cdot (z_1 + z_2)$ with z_i being the axial position of each detector, and the axial angle θ determined by the ring difference of the detectors. Measurements, where the axial angle θ is not zero can be transformed to the case where $\theta = 0$ in a process called rebinning. This simplifies the reconstruction process into a set of independent 2D reconstructions for each slice of the image.

Planar histograms characterised with p and ϕ are called sinograms, or in case where rebinning was not performed oblique sinograms. Rebinning is done mostly to make reconstructions less computationally intense and also as a way to compress data to reduce memory requirements as the number of sinograms is reduced due to rebinning. There are multiple rebinning algorithms, the most simple being the single-slice rebinning algorithm [39]. More accurate and advanced algorithms include multi-slice rebinning [40] and Fourier rebinning algorithm [41]. Events can also be stored individually as list-mode data, allowing for more data to be stored for each event including, for example, temporal and spatial information.

2.4.2 Filtered Back Projection

A measurement in the form of a sinogram can be expressed with the equation

$$s(p, \phi) = \int \lambda(\mathbf{r}) \delta(\mathbf{r} \cdot \mathbf{n} - p) d\mathbf{r}, \quad (2.10)$$

where λ is the distribution of the sources, δ the Dirac delta, $\mathbf{r}$ position vector and $\mathbf{n}$ a unit vector perpendicular to the LOR. The measurement could be directly projected back to form an image

$$\lambda'(\mathbf{r}) = \int s(p, \phi) \delta(\mathbf{r} \cdot \mathbf{n} - p) d\phi, \quad (2.11)$$

which gives a very blurry image where the blur is inversely proportional to the distance from the centre. The step in this context serves more as the demonstration of the principle of back projection.

The first step in filtered back projection (FBP) algorithm is to perform a Fourier transform (FT) of the measurement s as shown in the equation

$$\begin{aligned} s(k_p, \phi) &= \int e^{-i2\pi k_p p} dp \int \lambda(\mathbf{r}) \delta(\mathbf{r} \cdot \mathbf{n} - p) d\mathbf{r} = \int \lambda(\mathbf{r}) e^{-i2\pi k_p \mathbf{r} \cdot \mathbf{n}} d\mathbf{r} = \\ &= \int \lambda(\mathbf{r}) e^{-i2\pi k_p \mathbf{r} \cdot \mathbf{n}} d\mathbf{r} = \lambda(\mathbf{q}), \end{aligned} \quad (2.12)$$

where $\mathbf{q} = k_p \mathbf{n}$. We arrive at the result of the FT of the distribution of the sources being equal to the FT of the measurement. According to the central slice theorem the FT of the detector function is the same as a line through the Fourier representation of the object at the same angle and going through the centre of the slice. Therefore in theory we could then invert the FT to arrive at the correct distribution λ . However, as data is noisy, the amount of measurements is finite and the Fourier domain is sampled along the polar coordinates, which is denser at

the centre, this leads to artefacts in the reconstructed image as the data has to be interpolated to a rectangular grid.

The next step in FBP is to modify the FT of the original measurement s by multiplying it with the factor k_p and only then performing the inverse FT and finally the back projection as shown in the equation

$$\lambda(\mathbf{r}) = \int d\phi \int dk_p s(k_p, \phi) k_p e^{i2\pi k_p p} \delta(\mathbf{r} \cdot \mathbf{n} - p) = \int d\phi s'(p, \phi) \delta(\mathbf{r} \cdot \mathbf{n} - p). \quad (2.13)$$

Instead of multiplying the FT of the measurement s with the factor k_p , a different filter such as Hanning or Wiener filter can be used instead. This presents a compromise between the finer details of the reconstructed image given by the higher spatial frequencies in the FT of the object and the associated higher levels of noise.

A disadvantage of FBP is that it requires complete angular coverage, making it inappropriate for scanners with open geometry. It is also susceptible to noise associated with low counting statistics.

2.4.3 Iterative Reconstruction Algorithms

Iterative reconstruction algorithms such as the maximum likelihood expectation maximization (MLEM) algorithm work by successively approximating the correct distribution of sources [42]. The initial estimate can be an uniform image, which is then projected forward much like the process of actual imaging. These projection are then compared to the real measured projections from the imaged object and the difference between them is used to adjust the estimated image, whereupon the new estimated image is again forward projected and the process is repeated until the difference between the projection of the estimated image and the measured projections falls below a certain specified level. The iteration is described by equation [43]

$$\lambda_{i'}^+ = \lambda_{i'} \sum_j \frac{Y_j M_{i'j}}{\sum_i M_{ij} \lambda_i} \quad (2.14)$$

where $\lambda_{i'}^+$ is the new estimate, $\lambda_{i'}$ the previous estimate, i each of the pixels, Y_j a measurement, j the LOR, M_{ij} a system matrix giving the probability that an event occurring in location i is detected in the LOR j .

With the increase of the number of iteration the estimation algorithm converges asymptotically towards the real distribution, improving the spatial resolution of the reconstructed image. However, this also induces noise [44]. The optimum number of iterations depends on the specific requirements of the imaging case [45].

The use of TOF information in iterative reconstruction algorithms improves the convergence speed, and the trade-off between SNR and contrast of the reconstructed images. In the case where the number of iterations is low, to reduce the noise of reconstructed images, the faster convergence due to TOF may lead to higher noise in the reconstructed image than in the case where no TOF information was used [46],[47].

To accelerate the reconstruction, the projection data can be split into ordered subsets. The ordered subset expectation maximization (OSEM) algorithm performs partial updates on each subset. An iteration is completed after a single pass across all of the subsets[48]. The OSEM algorithm can introduce additional noise or artefacts.

2.5 Data Corrections

2.5.1 Normalisation

Normalisation refers to the corrections to the variations in collected data arising from the differences in individual detector elements due to their efficiency and also the variations due to the DOI effect, in which oblique LORs are affected. A basic approach to this correction is to have all LORs exposed to a uniform source, for example a rod of activity, which is then rotated along the bore of the scanner. The normalisation factors for each pair of detectors are calculated from the number of detected events for that pair divided by the average number of detected events across all pairs of detectors. The number of detected events for a pair of detectors in an actual measurement is then divided by this normalisation factor. Due to the stochastic nature of radioactive decay, the normalisation factors suffer from statistical errors related to the number of detected events. These errors induce additional noise in the reconstructed images. This technique is used in 2D acquisition, but is less effective in fully 3D acquisition due to the large increase in the number of LORs.

Factors that impede its use are [49]: low activity, which is required to avoid dead-time, leads to very long acquisition times. The increase in sensitivity to scattered events, which have different normalisation factors than true events, can lead to artefacts in reconstructed images. Due to the wide range of rates of events for different pairs of detectors, events may be mispositioned due to pulse pile-up leading to incorrect normalisation factors, seemingly dependant on the rate of events.

A more applicable normalisation scheme includes determining the efficiencies of each detector element separately and the differences in efficiencies of LORs for example due to the angles of incidence and the positions of detectors. The normalisation coefficients are then the product of all separate factors. The measurements are performed using cylindrical phantoms and line sources.

2.5.2 Random Coincidence Correction

The rate of random coincidences can be estimated from a delayed coincidence window [50], meaning that for any event, coincidence events are formed with an event that occurs in a window of time with the same width as with regular events, but delayed for a time interval, that is greater than the width of the window. Consequently, all coincidences formed in this way will be random coincidences. Due to the random nature of such events, the rate of random coincidences will remain the same as it was with the regular coincidence window that is not delayed.

After the number of random events is measured, the correction is performed by subtracting the number of random events from the total events recorded by the regular coincidence window. This correction, however, induces increased statistical noise, as both measurements are subject to stochastic processes and the error for all events is proportional to the square root of the number of events. Therefore, for the best image quality, the number of random events should be minimised, as the correction still leads to a worse image than the case with no random events. The rate of random events depends on the width of the coincidence window and the amount of activity injected into the imaged object. Alternatively, variance reduction techniques can be employed for smoothing the delayed coincidences, which leads to an increase in the processing burden of the imaging case.

Another approach for random coincidence event correction is to measure single

event rates for each detector element. Then the rate of random events for a pair of detectors can be calculated as a product of single rates for each of the detectors and the coincidence window. The correction is then performed the same way as the previous method by subtracting the number of random events. As the rate of single events is significantly higher than the rate of prompt coincidences, this method induces less noise. On the other hand, incorrect estimation of any of the factors can lead to the introduction of bias.

2.5.3 Scattered Coincidence Correction

Scattered events are partly suppressed by the energy window of each of the detectors in the detected coincidence event, but this is not sufficient in recovering image quality. More intricate methods include estimating the number of scattered events from multiple energy windows [51]. Weights can be assigned to events based on their energies, indicating the probability of them being true events. Weights are obtained from Monte Carlo simulations, where event types are known. An even more involved methods includes statistical models to estimate how much of the signal comes from scattered events.

The use of shielding or septa is also possible to decrease the number of scattered events coming from outside the FOV. The most extreme version being 2D acquisition, where each ring of detectors is separated by a septum, causing a large decrease in system sensitivity.

Another approach for obtaining scatter distribution is based on direct calculation. This can be done using either Monte Carlo simulations, which are computationally intense, or faster analytical models operating in single scatter approximation. The distribution of scattered events is estimated using the preliminary emission image and the transmission image together with the Klein-Nishina formula. Afterwards, the scatter projections are calculated and subtracted from the measured projections. The process is performed iteratively. Scatter corrections become more complex with the use of TOF information, but also lead to more accurate results.

Methods so far have corrected for scatter before the final reconstruction, but scatter correction can also be implemented into the reconstruction process using iterative reconstruction algorithms by estimating the amount of scatter during each iteration and including it in the forward projection, then comparing to the measured data. This method is also computationally intense.

Transmission or CT images that are used in scatter and attenuation correction are also subject to scattering errors, which are then propagated when performing scatter and attenuation correction.

2.5.4 Attenuation Correction

As annihilation photons travel through the imaged object, they are attenuated by the material along their path. For an object with thickness d , an event originating at depth x would produce a pair of photons, with one travelling a distance x and the other $d - x$. The probability of both reaching a detector without an interaction is the product of individual probabilities, given by the equation

$$P = e^{-\mu x} e^{-\mu(d-x)} = e^{-\mu d} \quad (2.15)$$

where μ is the attenuation coefficient. The probability does not depend on the location of the event along the LOR. Attenuation correction can be performed

in several ways. Most common have historically been corrections with the use of transmission images and CT images.

Transmission image in PET is obtained by rotating a rod source of activity around the bore of the scanner. A commonly used source is ^{68}Ga , a positron emitter, generated from ^{68}Ge . Two images are captured for attenuation correction. The first is a blank image, where no object is imaged, while the second is performed with the imaged object. The attenuation correction factor is then the ratio between the blank counts and the transmission counts for each LOR.

PET scanners can be coupled with a CT in hybrid PET/CT scanners. This simplifies the process and reduces the time needed for a transmission image. In order to use the CT image for attenuation correction, the CT image pixel values must first be converted into linear attenuation coefficients at 511 keV. This can be done for example by segmenting the CT image into tissue classes based on the pixel values such as for example bone, muscle, and lung. Afterwards these values are substituted with known attenuation coefficients for those tissues. Difficulties arise at the borders between tissues, where a mixture of tissues may be present. Tissue density is also not constant across the same organ.

Another way is to have a continuous mapping from pixel values to attenuation coefficients. A bilinear fit is used to fit the values to attenuation coefficients due to the different energies of the CT and PET imaging, as the probability of photoelectric effect is much higher for tissues with high atomic numbers such as bones or even implants and the lower energy of the photons used in CT.

It is crucial for the CT and PET image to be registered. In the most basic sense operations of translation, rotation, and scaling are applied to the images to align them. The resolution of both images should also match to avoid the partial volume effect. Any movement of the patient leads to artefacts in the reconstructed images. Movement cannot be fully eliminated, as breathing and in general the movements of internal organs cannot be controlled, especially in PET imaging, which takes significantly longer than CT imaging.

A less common type of hybrid imaging scanner is the PET/MRI scanner. In this case the MRI provides the high resolution anatomical information, but as the mechanism behind the imaging is completely different, it cannot be directly used for attenuation correction. Such scanners are attractive, among other reasons, for the reduced radiation burden on the patient.

A way to use magnetic resonance (MR) data is similar to the CT technique by segmenting the tissue into classes and assign predetermined attenuation coefficients [52]. Some tissues like fat and soft tissues can be resolved with this technique, but others, like bone and lung are more problematic, as they produce little MR signal.

Another method is to register the MR data of the patient to an atlas of MRI and CT images to generate a synthetic CT image. Machine learning methods trained on pairs of MR and CT images can be used to predict the CT images.

Alternatively, pure emission-based attenuation correction can be used. This type of correction would benefit non-hybrid scanners the most as it doesn't rely on external anatomical images. One such method is maximum-likelihood reconstruction of attenuation and activity [53]. The limitations of the method include high noise levels and inability to determine absolute values, making quantification problematic. Making use of TOF information can improve the prospects of the method. Some emerging methods also attempt to use scattered data to evaluate the attenuation

map [54].

2.6 Performance Measurements in Positron Emission Tomography

To allow standardisation of performance evaluation of PET scanners the National Electrical Manufacturers Association (NEMA) has published performance measurement standards [55]. These provide detailed procedures to be carried out while evaluating performance.

Evaluation of spatial resolution is performed by imaging and reconstructing point sources in air. This type of measurement does not reflect clinical scenarios but is used as a baseline comparison between different scanners. The width of the reconstructed points is evaluated in the radial, tangential and axial direction. The point sources are placed 1 cm, 10 cm and 20 cm from the centre of the FOV in the transverse direction and at the centre and one-eighth of the axial FOV from the end of the scanner in the axial direction. At least 100000 counts are acquired with activity low enough for the random coincidence rate to be below 5 % of the total event rate. The filtered back projection algorithm should be used for reconstruction and the voxel size of the reconstructed images must be below a third of the FWHM of the reconstructed point source. The FWHM is calculated using interpolation and the maximum using a parabolic fit.

Rates of different event types and count losses are evaluated using a cylindrical polyethylene phantom with a line source. Scatter fraction is the ratio of scattered events to the sum of true and scattered events. The noise-equivalent count rate (NECR) is calculated as the square of the true count rate divided by the total count rate (the sum of true T , random R and scatter S count rates) using the equation

$$\text{NECR} = \frac{T^2}{T + S + R}. \quad (2.16)$$

Sensitivity measurement is performed using a plastic tube phantom filled with water mixed with a positron emitter. This material, however, attenuates the gamma rays. In order to achieve an attenuation free measurement, the phantom is placed into successively larger metal sleeves with known attenuation coefficients. From that, an attenuation free sensitivity value can be extrapolated.

Image quality is evaluated using a roughly body-shaped phantom to simulate a clinical imaging scenario. The phantom is filled with a solution with a specific activity of 5.3 kBq/ml, which serves as the background activity. The phantom contains 6 spheres with diameters of 10 mm, 13 mm, 17 mm, 22 mm, 28 mm, and 37 mm that are filled with four times higher specific activity and are referred to as hot spheres. A central part of the phantom is doesn't contain activity and is filled with a material with low density (0.3 g/ml) to simulate lung tissue. Percent contrast recovery Q is calculated using the equation:

$$Q = \frac{\frac{C_h}{C_b} - 1}{\frac{a_h}{a_b} - 1} \cdot 100\%, \quad (2.17)$$

where C_h is the average number of counts in the region of interest (ROI) of the hot sphere, C_b the average of the counts in the ROI of background spheres of the same size, taken from 60 different positions in the phantom, a_h the activity concentration

in the hot spheres and a_b the activity concentration in the background. The second calculated metric is the percent background variability BV given by the

$$BV = \frac{\sigma_b}{C_b} \cdot 100\%, \quad (2.18)$$

where σ_b is the standard deviation of the counts in the ROI of background spheres.

2.7 Dosimetry and Safety

Ionising radiation causes damage in tissues of the patient. This is utilised in radiotherapy but is a disadvantage in diagnostic modalities (excepting modalities that combine diagnostics and therapy, known as theranostics). The exposure to ionising radiation is characterised with several dosimetric quantities. the most basic of them being absorbed dose D , defined as the energy of the radiation deposited per unit of mass of the absorber, using the unit gray (Gy), defined as joule per kg. The effects of a certain amount of dose are not equivalent for different types of radiation, therefore another quantity named equivalent dose H

$$H = w_r D \quad (2.19)$$

is defined as a product of absorbed dose and a weighting factor for different types of radiation. The factor ranges from 1 for photons, electrons and positrons to 2 for protons and 20 for α particles and heavier ions. For neutrons, the factor is dependant on energy. In PET, therefore, for all types of encountered radiation the factor is 1. The unit for H is sievert (Sv), defined the same as Gy. The third type of dosimetric quantity is the effective dose E , defined as

$$E = \sum_T w_T H_T \quad (2.20)$$

the product of a weighting factor w_T and dose for different organs or tissues, as the same amount of radiation of the same type has a different effect on different parts of the human body.

3. Methods

3.1 Simulations

The simulation work was performed using the Monte Carlo method, utilising open-source GATE software v8.2 [56], a Geant4 Application for Tomographic Emission.

In general the workflow consisted of defining the scanner geometry including the dimension and position of the detector elements, the scintillator material, energy and timing characteristics of the detectors, the readout scheme, and the geometry (material and shape) and activity distribution of the imaged phantom. As the simulation was run, pairs of back-to-back 511 keV photons were produced individually and stochastically according to the defined distribution, with the orientation also being randomly assigned. Generating pairs of photons instead of β^+ decay simplified the workflow, but also affected the results, as the activity didn't change with time and the spatial resolution was improved due to the discarded contribution of the range of the positron before annihilation.

The photons travel through the matter, and may undergo interactions with probabilities based on the medium. The particles are tracked until they are either absorbed (via photoelectric interaction) or else leave the defined area around the scanner, named world, which was set as a cube with the side of 4 m. The physical processes after the absorption of the high energy photons were not simulated. This includes the generation and propagation of visible photons due to scintillation or Cherenkov radiation and also the detection of those photons. This task would increase the computational complexity and intensiveness to an unmanageable degree. The task was simplified by using the digitizer module within GATE, which simulates the characteristics of the detectors and the signal processing chain.

As each instance of the simulated pair of photons is completely independent from any other, the problem is embarrassingly parallel, and the simulation can be split among any number of processor cores to speed up the task and thus follows Gustafson's law. Nevertheless, the simulations can be computationally intensive depending on the desired number of simulated events and the complexity of the simulated phantom.

Two GATE specific systems designated *ecat* and *cylindricalPET* were used for the simulations, with the former being used for systems with crystal level readout and the latter for systems with higher level readouts. The physics list builder mechanism was used for the simulation of physics processes, specifically the *emstandard_opt4* electromagnetic physics list. Production thresholds, the *SetCutInRegion* parameters, were set for photons, electrons and positrons to 1 m for the world, to 0.1 mm for the crystals and were left as default values of 1 mm for the phantoms.

The digitizer was constructed from a series of signal processors in a set order. The first processor was the *adder*, followed by *readout*, where the *depth* was set to

either 2 for *ecat* systems, or to 3 for *cylindricalPET* systems. The energy-centroid readout policy was used for the reference scanner and the winner-takes-all for the rest of the simulated systems. The next processor was energy blurring, where the energy resolution was set. It was followed by the *thresholder* and the *upholder*, which defined the energy window. The final processor was the temporal resolution module, which introduced Gaussian blurring in the time domain. The digitizer constructed the single events, which were then sorted into coincidence events by setting the coincidence timing window and the minimum difference between sectors. In case where more than two singles were found in coincidence, the *takeAllGoods* policy was used, which considered each good coincidence pair, "good" meaning that the events fell within the timing window, and that the sector difference was sufficient.

The density of the scintillator material LSO was set to 7.4 g/cm^3 , consisting of lutetium, silicon and oxygen with the ratio between the three elements in that order set to 2:1:5.

The results of the simulations were saved in CERN ROOT [57] data format containing the coincidence events. The saved data for each event included: the position of the origin of the photon pair, the time and energy information, position of the detected event, the number of Compton scattering events in the phantom and the crystal, and the identity of the crystal in which the photon was detected, as well as the identities of groupings of detector elements into submodules, modules and sectors, where applicable.

3.2 Reconstruction

The reconstruction of the images was performed utilising open-source CASToR software v3.1.1 [58], a customizable and advanced software for tomographic reconstruction. This software was used first to convert the scanner geometry into a format that it can use with the command *castor-GATEMacToGeom*. Then the software was used to convert the CERN ROOT data format files into list-mode data according to the system geometry and the timing characteristics using the *castor-GATERootToCastor* command. Since the data was derived from simulations, it was possible to separate the true events from random and scatter events. Thus, to simplify the workflow and bypass the need for random and scatter correction, only true coincidence events were considered for the reconstructions using the *-t* parameter while converting data into the list-mode format.

CASToR allows for a host of reconstruction parameter settings including the choice of optimisation algorithm, with MLEM always being used in this work. For the projection operators both the classic Siddon projector and the distance-driven projector were utilised for different studies. The number of iterations for reconstruction was chosen per study. Subsets were not utilised. The dimensions and voxel size of the output image were also chosen per study. No image processing modules were employed. To make use of parallelisation, the multicore setting was utilised. Images were saved as binary files along with an associated header file, which contained relevant metadata.

When dealing with physical phantoms, another input into the reconstruction settings was the attenuation map for attenuation correction. The software can also generate a sensitivity image used for normalisation.

With the use of non-standard scanner geometries such as flat panels, some difficulties can be encountered when utilising software made and validated for standard

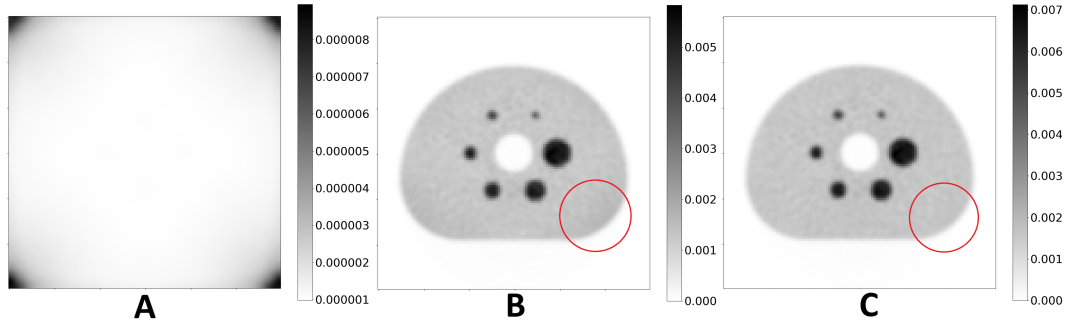


Figure 3.1: Reconstructed image of the homogeneous cube of activity (A). Reconstructed image quality phantom with standard normalisation (B) and with additional normalisation with the homogeneous image (C). The red circle was used to demonstrate the most obvious differences between the images, most pronounced as inhomogeneities at the edge of the reconstructed phantom.

cylindrical systems, therefore, additional normalisation correction was performed along with the CASToR software generated sensitivity image for some of the studies. In those cases, a homogeneous cube of activity in air corresponding to the dimension of the reconstructed image was simulated and reconstructed, which would, in an ideal scenario, be just an image of the same value in each voxel. To eliminate the noise, a wide Gaussian filter was used, smoothing the image. The image of any reconstructed phantom was then divided by this secondary image and multiplied by its mean value. The latter was done to keep the values at about the same value, though it was not a necessary step, as the units in all cases of reconstructed images are arbitrary and not calibrated. An example of additional normalisation is shown in figure 3.1.

As simulations and reconstructions were both computationally complex and intense, they required extensive use of grid computing. The resources were provided by the Slovenian national supercomputing network (SLING) with the HPC Vega [59] cluster.

3.3 Scanner Geometry and Parameters

The flat panel scanners were simulated using various configurations and scanner parameters, with the most common setup being four flat panels with dimensions of $30 \times 30 \text{ cm}^2$, with the crystal pitch (meaning the distance between the centres of neighbouring crystals) being 3 mm and each panel comprising 100×100 LYSO crystals. The distance between the panels was set to 40 cm. The cross-sections of the scintillators used in different simulations were $1.5 \times 1.5 \text{ mm}^2$, $2 \times 2 \text{ mm}^2$, $2.5 \times 2.5 \text{ mm}^2$, and $3 \times 3 \text{ mm}^2$. With the pitch remaining constant, the first three examples lead to a sparse configuration as there was empty space between the detector elements. The different used scintillator crystal lengths were 5 mm, 7.5 mm, and 10 mm. The CTRs of the scanners were set to 75 ps, 100 ps, 150 ps, and 200 ps.

Different readout strategies were explored, mainly crystal and submodule level, the former being the equivalent of a one-to-one pairing between the scintillator crystal and the photodetector and the latter representing several crystals grouped together. The crystal level readout in general sacrifices sensitivity (causing increased levels of noise) for improved spatial resolution, because the submodule level accepts

some of the inter-crystal scattered events and assigns them a location based on the energy deposition within the submodule. In theory it could be possible to construct a system capable of outputting both of those images, conceivably improving diagnoses.

Some of the other configurations include a scanner with the crystal pitch reduced to 2 mm, using only crystals with the $1.5 \times 1.5 \text{ mm}^2$ cross-section (resulting in a larger number of detector elements), scanners with a 2 panel configuration, a long axial FOV scanner with a two panel configuration and the panel dimension of $120 \times 60 \text{ cm}^2$, roughly corresponding to a 4×2 configuration of the original panels for each of the larger panels, with crystal cross-section of $2.5 \times 2.5 \text{ mm}^2$, 10 mm length, and a module level readout. A scanner consisting of the studied detector modules arranged in a more traditional cylindrical geometry was also simulated to demonstrate the potential performance of the improved CTR in a more standard geometry. In this case this was a brain scanner with an even more reduced pitch of 1.6 mm and cross-section of $1.5 \times 1.5 \text{ mm}^2$ for improved spatial resolution.

In order to allow for a clear way of showing results, a naming scheme for the flat panel scanners was implemented. In its most common and basic form it follows the following structure: **CS<cross-section>_L<length>_CTR<CTR>**, where the main scanner parameters are listed. For example CS3_L10_CTR75 would refer to a scanner with the crystal cross-section of $3 \times 3 \text{ mm}^2$, crystal length of 10 mm and a CTR of 75 ps. As most of the configurations use the same crystal pitch, it is omitted from the naming scheme, except when it is not the standard 3 mm. In those cases it is added as a suffix to the name. Another omitted parameter is the number of panels, which is 4 for most scanners and is also added as a suffix when required. The readout level is omitted for crystal level readout and added as a suffix for the submodule level. The suffix tot is added for the long axial field of view scanner, with an additional suffix when axial acceptance of events is limited (for example "tot25" meaning that axial acceptance is limited to 25 cm).

The energy resolution of the simulated scanners was set to 10 % at 511 keV, and the energy window was set from 435 keV to 585 keV. The coincidence window was in most cases set to 2 ns, with the exception being the long axial FOV scanners, where it was increased to 4 ns to avoid possibly losing events originating far from the centre of the FOV. In some cases the axial acceptance was reduced for the long axial FOV scanners to eliminate the artefacts caused by the oblique LORs in reconstruction.

In order to compare the performance of the various flat panel configuration, a standard cylindrical scanner was also simulated, based on the Siemens Biograph Vision 600 specifications as reported in [20] and will be referred to as the reference scanner. The scanner consists of $3.2 \times 3.2 \times 20 \text{ mm}^3$ LSO crystals which were grouped into submodules of 5×5 crystals, those were further grouped into an array of 4×2 in modules, which were combined in arrays of 2×8 into sectors, finally repeated 19 times in a ring with the bore diameter of 78 cm and the axial FOV of 26.3 cm. The total number of detector elements was therefore 60800, with the total scintillator volume being 12.45 dm^3 . The energy resolution and window was set to the same values as for the flat panel scanners, but the coincidence window was increased to 4.7 ns. The CTR was set to 214 ps and the minimum difference between sectors for accepted events was set to 4.

Various scanner configurations and simulated phantoms are shown in figure 3.2.

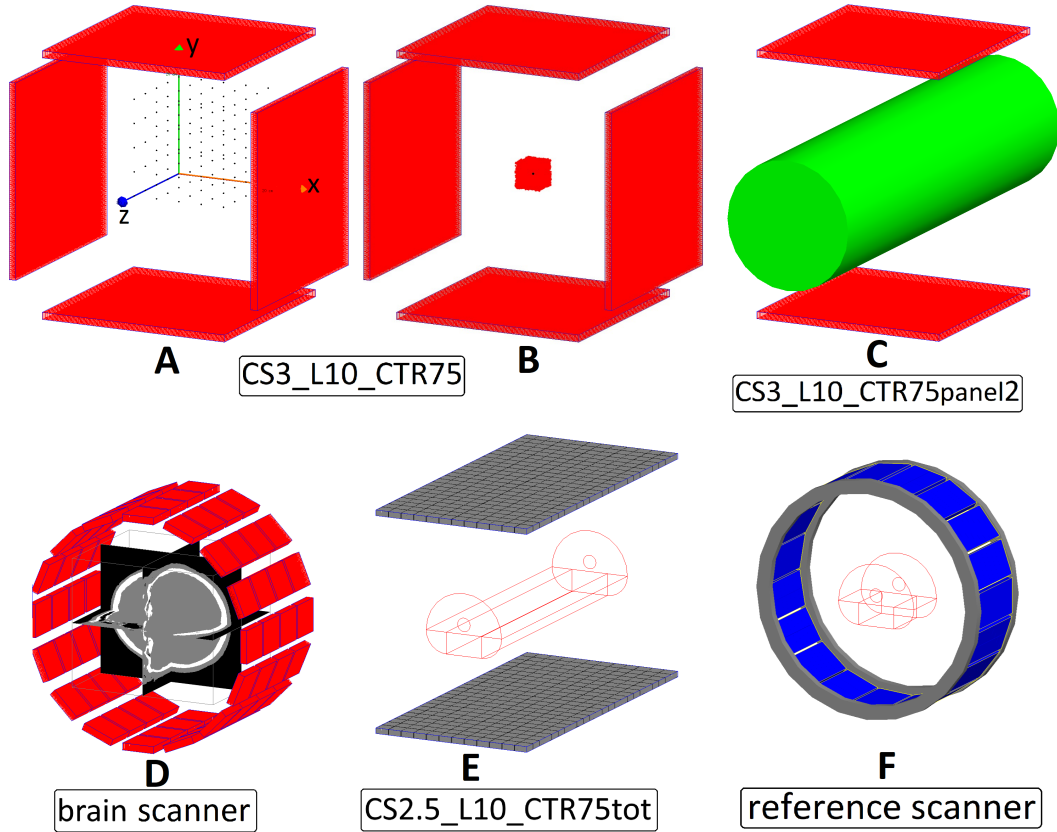


Figure 3.2: Visualisations of scanners and simulated phantoms and sources. (A) a four panel configuration with a grid of point sources and coordinate axes, (B) a four panel configuration with the point source surrounded by a cube of activity serving as background, (C) a two panel system with a cylindrical NECR phantom, (D) brain scanner configuration and the brain phantom, (E) long axial field of view scanner with the extended NEMA image quality phantom, (F) reference scanner with the NEMA image quality phantom. Examples of the naming schemes are included.

3.4 Image Analysis

Reconstructed images were analysed and processed using Python v3.6.9. The binary files were opened using the `open()` comand and read using the `read()` command. Next, it was converted into Float32 format using the `frombuffer` routine in the NumPy package, which interpreted the file as a 1 dimensional array. The images were then converted into the proper 3 dimensional array with the `reshape` routine from the same package.

Where applicable, the images were filtered with a Gaussian filter (`gaussian_filter`) from the SciPy package. The analysis was performed on the voxel level, simply by taking each relevant value into account.

Images were displayed using the Matplotlib library, with `imshow` being used for the display of the 2 dimensional images and `plot` being used for line profiles. The same library was also used for the creation of most other shown figures.

Other processing and analysis steps were described in more detail in relevant sections.

3.5 Simulation Studies

3.5.1 Spatial Resolution

The methods used to assess image quality parameters in standards employed by the industry 2.6 may not be applicable for unconventional systems. The primary difference being the choice of the reconstruction algorithm, as FBP, cannot be easily implemented with flat panel scanners and open geometries. Therefore, contrary to the standard, MLEM reconstruction algorithm was employed. To keep the results comparable, MLEM was used even in the case of more standard cylindrical scanners.

Further, the method for assessing the spatial resolution was developed for cylindrical scanners, providing the assumption that knowing the spatial resolution in the handful of specified positions gives enough information about the spatial resolution of the scanner. In order to test this assumption for the flat panel geometry, a grid of 125 spherical sources arranged in a $5 \times 5 \times 5$ grid were simulated. The source radius was set to 0.1 mm, making them effectively point sources, and they will be referred to as such henceforth. The grid was placed in the first octant of the FOV of the scanner, assuming that the symmetry would yield the same results for each. The distance between each source was set to 37 mm in order to cover almost the entire FOV of the first octant. Source activity was set to 70 Bq, a low value, which reduced the amount of random coincidences.

According to the NEMA standard, the resolution should be reported as FWHM of the line profile of the reconstructed source in the axial, tangential and radial direction. In this case, where most sources do not align with the axes of the scanner, it makes more sense to speak in terms of the resolution in the X and Y directions, coinciding with the reconstructed voxels and the image grid. The Axial or Z direction remains unchanged compared to the NEMA standard for cylindrical scanners.

To more accurately model the spatial resolution of the scanner, the non-collinearity of the annihilation photons was considered by setting the GATE parameter `accolinearity` of the source to 0.5° . However, this specific implementation of the physics is not accurate and causes underestimation of the deterioration of the spatial resolution due to this effect [60]. Because this is not the main contributor to the spatial

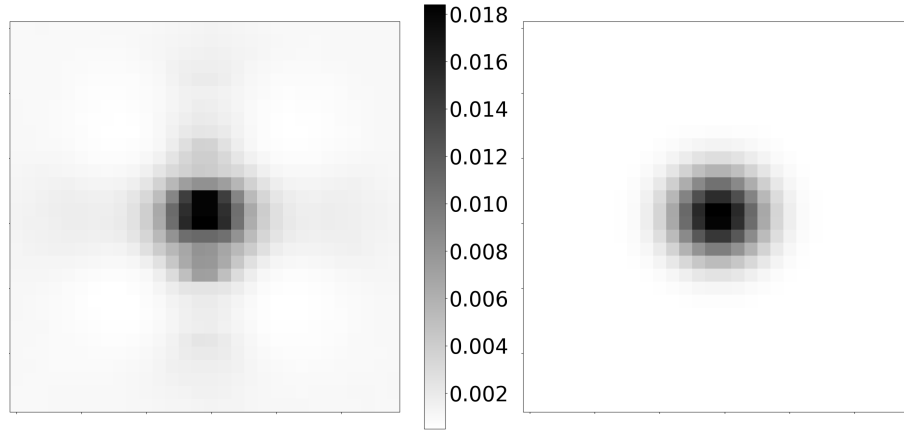


Figure 3.3: An example of a reconstructed point source (left) and the result of the Gaussian fit (right). A 2 dimensional representation is shown in the transverse plane. The source is located in the central plane along the axial direction and moved 1 cm from the centre in the Y direction. The CS3_L10_CTR75 scanner geometry was used for the simulation.

resolution, the results are not affected in a substantial degree. Furthermore, since the panels are generally placed closer together than, for example, the radius of the reference cylindrical scanner, the effect is reduced even further.

In order to evaluate the spatial resolution, the reconstructed image was fitted with a Gaussian function in three dimensions given by the equation

$$f(x, y, z) = A \cdot e^{-\left(\frac{(z-z_0)^2}{2\sigma_z^2} + \frac{(y-y_0)^2}{2\sigma_y^2} + \frac{(x-x_0)^2}{2\sigma_x^2}\right)} + C, \quad (3.1)$$

where A is a constant used for normalisation, as the voxel values in reconstructed images are in arbitrary units, x_0 , y_0 , and z_0 determine the location of the centre of the function, σ_i are the standard deviations in each direction and C is a constant compensating for the background activity.

The resolution was calculated as FWHM from the standard deviations in each direction. This also deviates from the standard used for cylindrical scanners and is used primarily because this method takes the entire reconstructed source into account while performing the fit, instead of just a single linear profile. However, this method is more susceptible to errors, for example in the case where the reconstructed sources do not have a regular Gaussian shape in the sense that the fitted function may not accurately represent the reconstructed image. Though even in those cases the width of the function tended to accurately reflect that of the reconstructed source.

The use of MLEM reconstruction algorithm further leads to complications for two reasons. The first is the impact of the number of iterations on spatial resolution, which in general leads to sharper and noisier images as the number of iterations increases. The second is that when dealing with point sources, the algorithm produces artefacts due to the constraint of non-negativity [61] and can oversharpen the reconstructed image. For that reason the simulations were repeated by adding background activity to each of the point sources (figure 3.2 B). The volume of the warm background was a cube with a side of 4 cm and activity of 28.8 kBq. The

activity level was chosen as a compromise between the computational complexity introduced by this addition in terms of increased requirements for processing time and data storage, the ratio between the reconstructed background and signal height, and acquiring enough data for the reconstruction with a sufficiently low amount of noise or in other words enough events originating from the point source. An example of the reconstructed point source along with the resulting Gaussian fit is shown in figure 3.3.

Another set of simulations were performed in order to examine the effect of voxel size of the reconstructed images on the spatial resolution. For the sake of simplicity, in this case instead of the full grid of 125 point sources only four were simulated and placed according to the NEMA standard with ultimately only a single one being used for the final analysis, positioned in the centre in the axial direction and 10 mm from the centre in the radial direction in which case the analysis once again coincides with the original standard, as the X and Y direction become the same as radial and tangential. The offset from the centre was also important as it avoids the geometric effects that can occur in reconstructed images with point sources in the centre of the FOV. The voxel sizes for the reconstructed images were set to $0.4 \times 0.4 \times 0.4 \text{ mm}^3$, $0.6 \times 0.6 \times 0.6 \text{ mm}^3$, and $0.8 \times 0.8 \times 0.8 \text{ mm}^3$. The effect of the number of iterations on the resolution was also tested with a total of 100 iterations being executed for each voxel size.

3.5.2 Image Quality

With the image quality metric it was possible to conform more closely to the NEMA standard. The NEMA phantom was simulated with both activity and geometry corresponding to the values specified in the NEMA standard. Acquisitions of 1 min simulated time (the equivalent of 1 min scan time with real scanners) were performed for each tested geometry. The reconstructions were performed using the MLEM algorithm with 50 iterations and the voxel size was set to $3 \times 3 \times 3 \text{ mm}^3$. To avoid the partial voxel effect, the images were scaled up by a factor of 10 in X and in Y direction by duplicating each voxel 10 times in essence making each voxel a grid of 10×10 voxels with the same value.

Additional normalisation correction (section 3.2) was performed using the homogeneous cube of activity, the dimensions of which were $36 \times 36 \times 36 \text{ cm}^3$, the same size as the FOV of the reconstructed images in this case. This image was also reconstructed with 50 iterations and the same voxel size. A wide 15 mm Gaussian filter was applied to the homogeneous image in order to lower the noise level, as correcting the original image with a noisy image would induce additional noise. The wide filter can be used because the variations in sensitivity across the FOV are gradual. The reconstructed images of the NEMA phantom were divided by the homogeneous image and multiplied by its mean value.

In order to obtain values for the contrast at different levels of background variability, each image underwent Gaussian filtering with the width of the filter varying from 0 mm (no filter) to 15 mm. Each acquisition was repeated 10 times in order to determine the errors. The effect of number of iterations in the reconstruction algorithm was examined for one of the scanner configurations.

Extended Image Quality Phantom

For the long axial FOV scanner configuration, a modified version of the NEMA phantom was utilised (figure 3.2 E). The modified NEMA phantom retained the basic

shape of the standard phantom but was extended from the normal 18 cm to 100 cm in the axial direction. The hot sources within the phantom were also modified. Only the 10 mm, 13 mm, and 17 mm spheres were kept and were also copied to different axial positions. In the original phantom, the spheres were located 2 cm away from the axial centre but in the modified the same sphere was also replicated 7.5 cm, 30 cm, and 45 cm from the centre. In place where the other three spheres were in the original phantom, three hot cylinders were placed with the same radii as the spheres and the height of 90 cm. The specific activity of the entire phantom was reduced by a factor of 100 because of the increase in the ratio of random events to true, making the data files needlessly large. The purpose of the extended phantom was to determine the variation of the contrast along the axial direction, and how different parameters affect it especially since the scanner geometry used for these simulations was even further away from the standard cylindrical PET scanner, that the reconstruction software was developed for. The contrast was compared in case all coincidences were accepted and in the case of limiting the acceptance along the axial direction to 25 cm. In this way the scanner is reduced to something similar to a moving bed scan with a regular axial field of view scanner, making the reconstruction more predictable. This way the most oblique LORs are taken out of consideration. This is important specifically because most reconstruction software including CASToR does not take into account the oblique paths travelling through neighbouring crystals as can be seen in figure 2.4.

A total of 10 sets of acquisitions were performed, but extended to 6000 s (of equivalent time to the real world scan time) to compensate for the lower activity.

The simulations were performed with the long axial FOV scanner, bearing the designation CS2.5_L10_CTR75tot and described further in section 3.3.

3.5.3 Sensitivity

The acquisition of data for the sensitivity metric was simplified from the NEMA standard, because the simulations can provide an accurate number of detected true events and activity can be simulated without a physical phantom, eliminating the need for attenuation correction. A single point source was simulated at the centre of the axial plane and then moved in axial direction from one edge of the scanner to the other. The movement was done in 1 mm increments and the same number of events was simulated in each case. The number of detected events was divided by the activity of the point source and the simulation time, or in other words the total number of simulated events.

3.5.4 Noise-Equivalent Count Rate

The phantom used in simulations for the NECR metric was a cylindrical polyethylene phantom with a radius of 10 cm and the height of 70 cm. The radius of the line source was 1.6 mm and the length was equal to the height of the phantom. Besides the regular NECR metric, the effect of TOF was also examined as TOF impacts the SNR and can be characterised in a modified metric, the effective NECR (NECR_{TOF}), as defined by the equation

$$\text{NECR}_{\text{TOF}} = \frac{2D}{c\Delta t} \text{NECR}, \quad (3.2)$$

where D is the diameter of the imaged object, Δt the CTR and c the speed of light. The CTR does not impact the measurement itself, but can be used to compare the

effect of TOF information on different configurations, and the comparison to the reference scanner.

3.5.5 Brain Phantom

A realistic high-resolution digital brain phantom based on the BigBrain atlas [62] was simulated for qualitative assessment of a more realistic clinical scenario. The phantom has a 0.4 mm spatial resolution, comprising intricate structures, which serve well when simulating systems which boast high spatial resolution and to compare them as well. Still, for a quantitative result, reconstructed images from different systems can be compared to the original activity map using metrics such as the structural similarity index (SSIM) [63]. The images were reconstructed using the MLEM with 50 iterations and the voxel size was set to $1 \times 1 \times 1 \text{ mm}^3$. The comparison was performed by taking a single slice of the image and cropping it close to the visible reconstructed skull in order to focus only on the relevant portion of the image. Because the spatial resolution of the activity map was higher than that of the reconstructed image, the mean values of two consecutive slices of the activity image were taken for the comparison.

3.6 Experimental Measurements

3.6.1 Coincidence Experimental Setup

Experimental measurements were performed with the simplest PET system setup consisting of two detector elements and a ^{22}Na point source, shown in figure 3.4. Each detector element comprised a scintillator crystal wrapped in polytetrafluoroethylene (Teflon) tape, the purpose of which was to reflect photons of visible light and prevent them from exiting the crystal, increasing the number of detected photons on the photodetector. Except where noted, four layers of Teflon tape were used to wrap the scintillator crystals. The scintillator was coupled to the photodetector via an optical coupling agent, ensuring improved photon transmission to the detector and preventing the crystal from moving to some degree. The following optical coupling agents were used for various measurements:

- Silicon grease (Rexon Components Inc. RX-688)
- Fiber coupling index matching gel (Thorlabs G608N3)
- Optically Clear Adhesive Tape (Thorlabs OCA8146-3)
- Cargille MeltmountTM 1.582

SiPMs were used for the detection of visible photons and were the latest prototype models created by Fondazione Bruno Kessler (FBK) research institution. On the most common used model the surface of the active area was $3 \times 3 \text{ mm}^2$ and was bare (not covered by an optical window). This led to an improvement in photon collection efficiency and consequently the CTR of the setup. On the other hand, the exposed active area was more susceptible to damage and defects (caused by frequent coupling and decoupling of the scintillator crystals) that led to an increase in the noise and dark current and a deterioration in the CTR. The designation of the model used in most measurements was FBK NUV-HD-MT low field, $3 \text{ mm} \times 3 \text{ mm}$, $40 \text{ }\mu\text{m}$ LF-M0 and was used in every measurement except where specified otherwise.

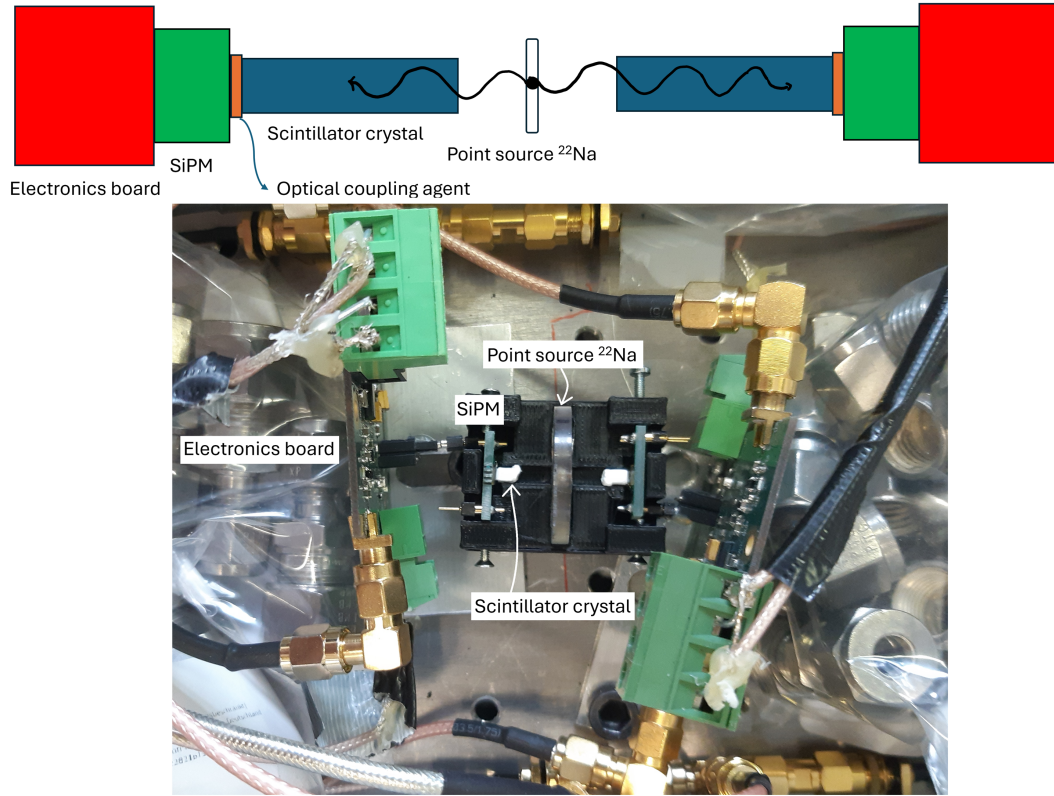


Figure 3.4: Schematic (top) and picture (bottom) of the basic experimental setup comprising two detector elements and a source of activity.

The SiPMs were connected to custom front-end electronics boards, designed specifically for the coincidence experiments and produced by researchers from Institut de Ciències del Cosmos, University of Barcelona. The output from each SiPM was split into two paths, each amplified to a different degree. The signal, which was amplified less was referred to as the energy signal and was primarily used in order to discriminate between events that have undergone the photoelectric effect and those that have undergone scattering. Energy signals were also used for triggering the measurement. The second chain was the time signal and was used for determining the timing of each event.

All of the signals were acquired by oscilloscopes and the waveforms were saved for further analysis. Different oscilloscopes were utilised across the different measurements. For the CTR measurements a high-bandwidth oscilloscope was used, the Teledyne LeCroy LabMaster 10 Zi-A 36 GHz. The DRS4 evaluation board, LeCroy WAVEPRO 7300A and even modular crate electronics were also utilised, though the latter two proved to be insufficient in terms of timing performance to measure CTR below 100 ps, but were still usable for measuring the light output of the crystal samples. Even the most powerful of the oscilloscopes was still limited in the sense of having 8-bit resolution of the digital-to-analogue converter, making it necessary to adjust the vertical scale settings for the acquired waveforms, decreasing the amount of volts per division and thus clipping away the majority of the time signal.

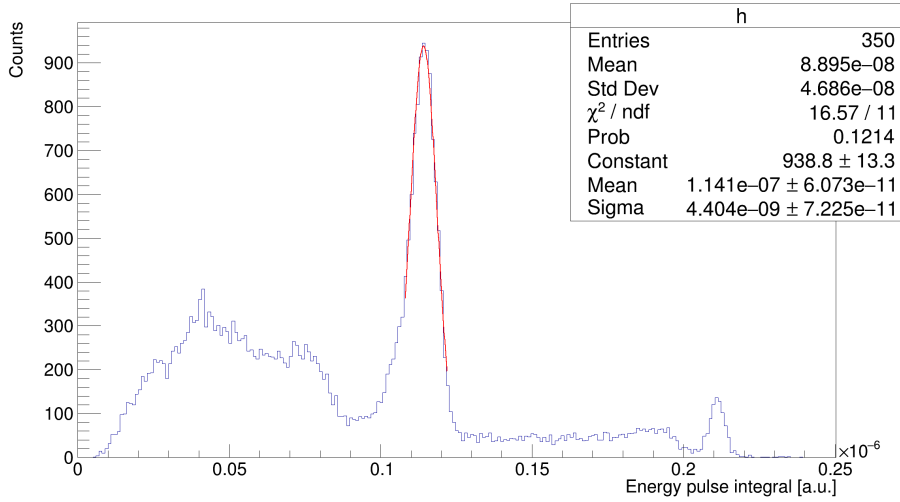


Figure 3.5: Histogram of the integrals of the energy signals, showing the spectrum of the deposited energy of 511 keV photons in the scintillator crystal. The fitted Gaussian function is shown in red over the photopeak. Energies above the photopeak are visible with another small peak corresponding to the 1274.5 keV photon which is also emitted during the decay of ^{22}Na as well as the associated Compton spectrum.

3.6.2 Light Yield Measurements

The coincidence setup was first used to measure the light yield of different scintillator samples. This was done to compare the output of samples made by different producers, one of the important factors when it comes to determining the CTR of the detector (equation 2.8). For this measurement only the energy signals were required. The integral of the energy signal was used as an indicator for the light yield of the crystal sample. While it was not possible to determine the actual number of detected photons, it was possible to compare relative performance of different samples.

The resulting integrals of the energy signals were represented in histograms, each of which was then fitted with a Gaussian function to determine the position of the photopeak from the median value of the fitted function and that median was the resulting measure of light yield. An example is shown in figure 3.5.

A different set of measurements was also done to compare the performance of different optical coupling agents. Additionally the measurements were done over a longer period of time (around 1 day) in order to determine the stability of each agent. The analysis method remained the same.

3.6.3 Coincidence Time Resolution Measurements

To determine the CTR of the setup, data was acquired by saving all four waveforms for each triggered event (that being two time and two energy channels). Each event was then analysed separately. For the time signal, the first step was to evaluate the pedestal of the signal and perform baseline correction. The former was done by taking a fixed interval of the waveform before the arrival of the signal and calculating the mean value of all those points in the waveform. The later was done by shifting the entire waveform by the mean value, effectively setting the pedestal part of the waveform to zero. To evaluate the noise present in the waveform, for the same

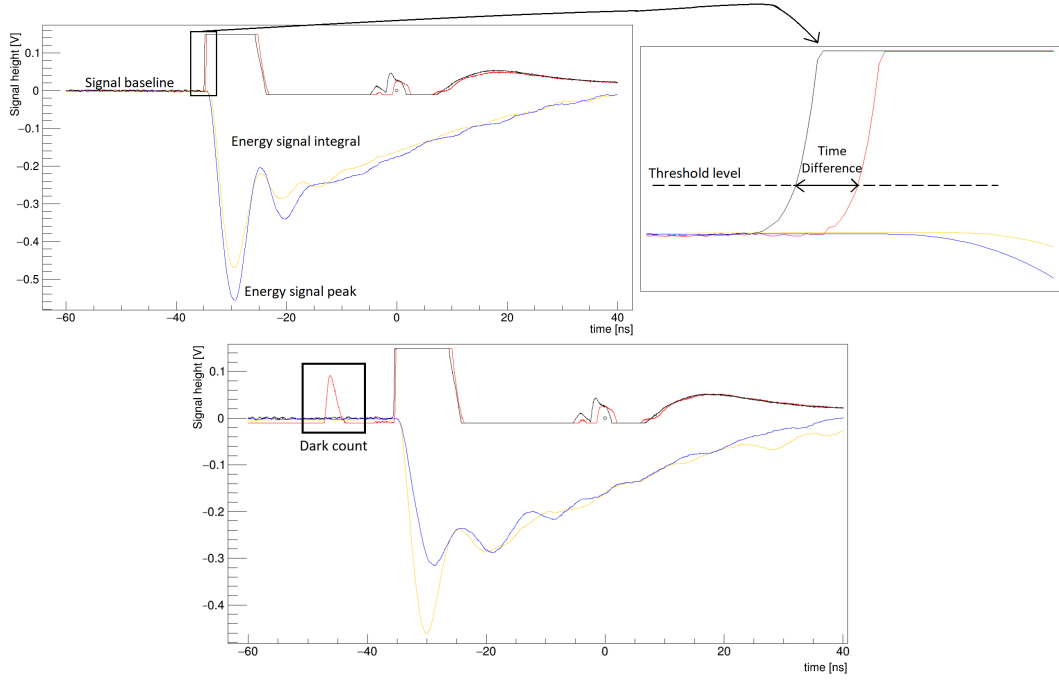


Figure 3.6: Acquired waveforms for a single triggered coincidence event. The time signals are positive and clipped due the scale settings on the oscilloscope. Energy signal waveforms are negative with the scale set so that the signal is not clipped in order to correctly calculate the peak and integral values of the signals (top). Another example of waveforms, where a single photon event is recorded on one of the waveforms before the coincidence event (bottom). The incorrect baseline correction due to a dark count is also visible for the same waveform.

interval of the pedestal, the root mean square (RMS) value of the waveform was also calculated. The timing of the signal was calculated using the leading edge by determining the time value of the waveform at a specific threshold. To get this value, linear interpolation between closest two points was used. The process was repeated for multiple values of threshold. To get the time difference, the two values from the two timing channels were subtracted from each other.

The energy signal served for discrimination between event types. In this case the analysis consisted of taking the peak value of the signal and the integral of the signal pulse. All of the calculated quantities were filled into histograms. The cuts on the data were performed by filling histograms only for events that fell within the photopeak of the energy channels. The photopeak location and width was determined by fitting the histograms of either the peak value or integral of the energy signal with a Gaussian function. The energy cut was set to encompass the interval $[\mu - 0.5\sigma, \mu + 0.7\sigma]$, where μ is the location of the peak of the function and σ the standard deviation of the function. The interval is not symmetrical and is biased towards higher energies, as those tended to give better results both because of the greater amount of detected light and lower probability of a scattered event being registered within the photopeak. Besides the photopeak cut, events were also cut based on the noise RMS histogram, with events that exhibited higher noise being cut. This techniques was also used in order to cut events, where a random SiPM dark count arrived in the interval just before the leading edge of the pulse, as those

could affect the timing due to signal pile-up as well as disturb the baseline correction algorithm. All four waveforms of an example coincidence event are shown in figure 3.6 along with a separate acquired event where a dark count arrives before the main part of the time signal.

The CTR of the setup was determined by fitting the time difference histogram (after all the cuts were applied) with a Gaussian function and calculating the FWHM from the standard deviation.

Since the experiment required a high degree of precision in order to measure CTR values below 100 ps, it was also important to determine the optimal parameters of the oscilloscope. For that reason, the time and energy signals from a single detector were split in two using a passive analogue signal splitter and the CTR analysis was performed between two copies of the same signal. In an ideal setting that would result in no observable differences but in practice this provided a baseline hard limit imposed by the acquisition hardware and the analysis methods.

Testing was focused on the performance of different crystal scintillators. This includes measurements using crystals with the same dimensions produced by different companies, and measurements with crystals with different dimensions created by the same company, for example testing how the length of the crystal affects the CTR measurement.

4. Results

4.1 Simulation Studies

4.1.1 Spatial Resolution

Effects of Background Activity

Results of a reconstruction of a point source in the centre of the FOV, obtained by 10, 30 and 50 iterations, are shown in the top part of figure 4.1. Data was simulated and reconstructed using the CS3_L10_CTR75 scanner geometry, and the voxel size was 0.8 mm. The number of iterations was chosen in order to clearly illustrate that a smaller number of iterations may reconstruct the source without apparent artefacts, while too many iterations, in this case 30 and, more apparently 50, introduce edge artefacts to the reconstructed image, and this effect grows further with the number of iterations. As the number of iterations increases, reconstructions tend to exhibit multiple apparent peaks, degrading the resolution measure. This issue does not only affect the method of estimating spatial resolution presented in this work but also the NEMA standard method. The smaller the voxel size, the more apparent this effect is, which also limits the choice of voxel size.

A way to reduce this issue is to simulate not only a point source but also an additional background. The simulation was thus repeated with the source surrounded

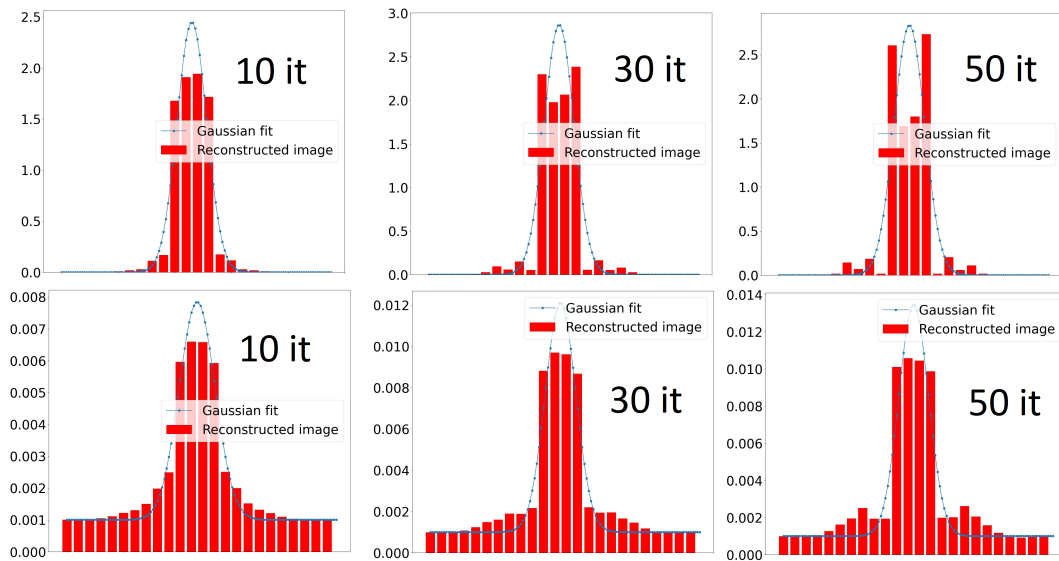


Figure 4.1: Reconstruction of a point source in the centre of the FOV, obtained with 10, 30, and 50 iterations, for a source with (bottom) and without (top) background activity for the CS3_L10_CTR75 scanner.

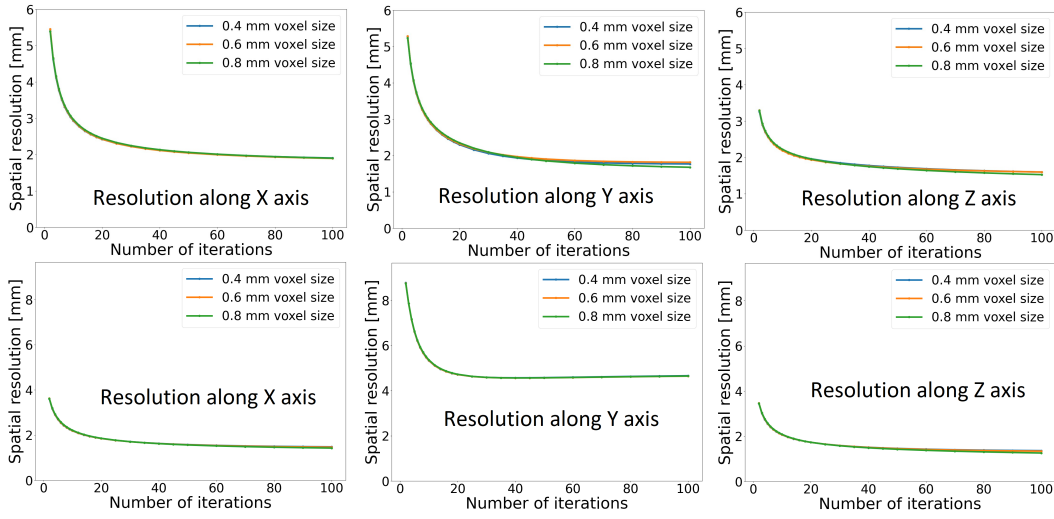


Figure 4.2: Spatial resolution dependence on the number of iterations at different voxel sizes for the CS3_L10_CTR75 scanner (top) and the CS3_L10_CTR75_panel2 scanner (bottom). Source position is 10 mm from centre of FOV in Y direction.

by a cube of activity with an edge length of 4 cm. The results of the reconstructions with 10, 30 and 50 iterations are shown in the bottom of figure 4.1. The addition of the background is taken into account as an additional constant C in the fitting function 3.1. In this case, the dip at the centre of the reconstructed source doesn't appear and the fit function better describes the reconstructed source, though the image is not completely free of artefacts.

As introducing background does improve the reconstructed image by reducing artefacts, it was used for every subsequent simulation of point sources for the evaluation of spatial resolution. 30 iterations were chosen for the reconstruction of these sources since, at that point, no edge artefacts can be seen.

Effects of Number of Iterations and Voxel Size

Analysing the single point source in background with a 10 mm offset from the centre of the FOV in the Y direction, the relationship between the number of iterations and spatial resolution was quantified. The resolution in each axis was examined separately and repeated for different voxel sizes. The results are shown in the top of figure 4.2. The figure shows the largest impact for the first 10 iterations, which then gradually tapers off and then stays fairly stable to the full 100 iterations. However, the apparent stability can be misleading, as shown in section 4.1.1, since even with the added background, the over-sharpening artefacts appear after around 30 iterations and continually increase in severity. At the same time the result may indicate a degree of robustness of the analysis.

The voxel size has a fairly negligible effect on resolution, especially along the X axis, and a minor effect above 50 iterations along the other two axes.

The simulations were repeated for a two panel system, keeping the rest of the characteristics the same. The results are shown in the bottom of figure 4.2. As before, voxel size doesn't affect the resulting resolution for most of the cases, especially for the Y axis and has a minor effect in the final 50 iterations for the other two axes.

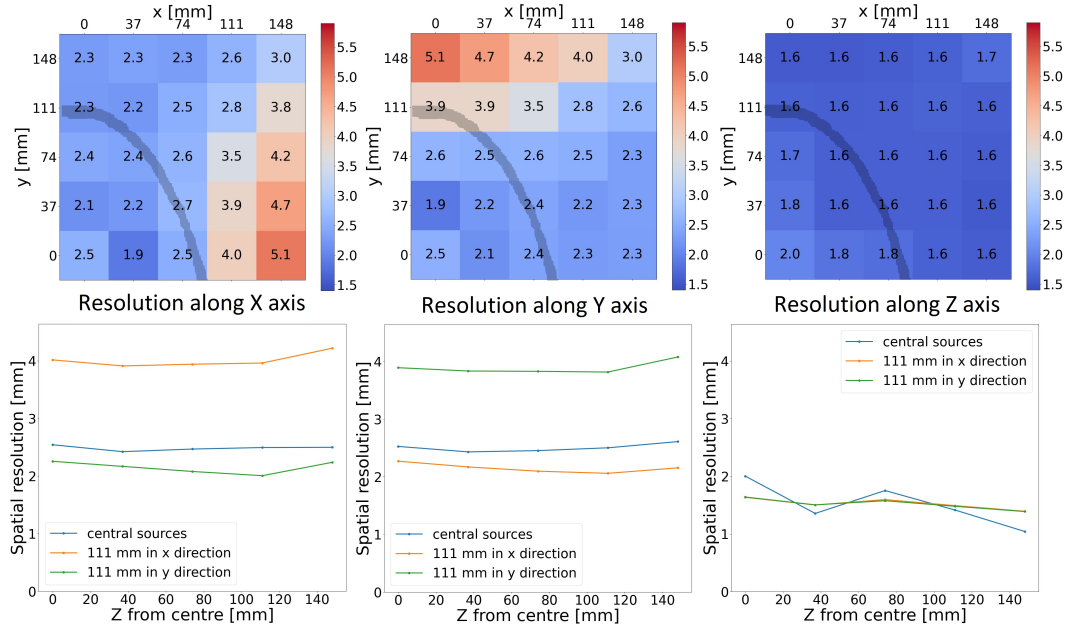


Figure 4.3: Spatial resolution for the CS3_L10_CTR75 scanner. Top: Spatial resolution in each axis for the same central slice. An outline of a skull is superimposed onto the image to show the relevant FOV for an imaging case. Bottom: Spatial resolution dependence on axial position for different X and Y positions.

The lack of the two side panels has a more obvious effect on the spatial resolution in the Y direction. The resolution is degraded by approximately a factor of 2 across all iterations owing mainly to the lack of horizontal LORs, which determine the position of the source in the Y direction. Oblique LORs and TOF information combined are the reason why the source can be localised along the Y direction at all and in principle a substantial improvement in CTR could completely remove any deterioration caused by reduced sampling of such a configuration. In the case where no oblique lines would be available, the resolution would be given by equation 2.7. On the other hand, the spatial resolution in the X and Z directions are actually slightly better than in the four panel configuration.

Spatial Resolution Across the Field of View

Spatial resolution was calculated for for each of the 125 point sources in each of the three directions. In order to simplify the presentation of the results, they are reduced and shown in two ways. First, the results are shown for the 25 sources in the central XY plane, in other words at the axial centre. For the CS3_L10_CTR75 configuration this is shown in top of figure 4.3. The bottom of the same figure shows how the spatial resolution changes across the axial direction, specifically for the central sources and also sources that are displaced from the centre for 111 mm in either X or Y directions, that being the fourth source of the grid of five.

The results in the central plane range between 1.9 mm to 5.1 mm for the resolution in the X and Y directions. The best results are obtained for the sources close but outside of the centre of the FOV. At the very centre of the FOV the resolution is degraded due to geometric effects, namely that the source is placed at the centre between eight voxels (two in each dimension) of the reconstruction matrix. The re-

sults along the X and Y directions also show a certain symmetry, as the resolution degrades towards the edges of the FOV. In essence, at the edge the four panel scanner begins to function more as a two panel configuration, with little to no LORs in either horizontal or vertical direction, as the final row or column of sources is placed 148 mm from the centre of FOV, while the edge of the panel is at 150 mm.

For the Z direction, the results range from 1.6 mm to 2.0 mm with the source at the centre of the FOV performing the worst. In general the results along this axis are also more consistent.

For the most part there is little variation in resolution at different points in the axial direction. The results in X and Y directions again show symmetry along the axial direction and are all within the range of approximately 0.3 mm. For the Z direction the largest variations are for the central sources, while there is little sensitivity to the direction of the offset from the axial centre.

The results for different tested scanner configurations are shown in figure 4.4. In these cases the 2D histograms show results for spatial resolution in the X direction for the central slice of sources. The submodule readout scheme shows deterioration of spatial resolution of about 0.2 mm compared to the same configuration with a crystal level readout. The configuration with a worse CTR also deteriorates the resolution to a similar extent of 0.2 mm, especially in the central parts of the FOV. With the reduction of crystal cross-section at constant pitch, or sparse configurations, the spatial resolution is improved, especially near the centre of the FOV, while there is a slight deterioration of spatial resolution for sources that are positioned far from the centre in the X direction. Reduced crystal pitch improved the resolution across most of the FOV even more except for the furthest sources in the X direction in both cases because of an even lower chances of vertical LORs as the sources are even closer to the edges of the scanner.

The reduction of crystal length improves the spatial resolution all across the FOV. In this case though, the results for the central source are still worse than those of the sources in the neighbouring positions. These results indicate the large effect of the DOI. Indeed, the parallax error seems to be exacerbated for the flat panel systems.

The results for the reference scanner are also presented. For this scanner, the results similarly show deterioration with the sources positioned further from the centre in the X direction. However, the results are much more uniform across the entire field of view and range between 3.2 mm and 4.5 mm. In comparison with the CS3_L10_CTR75 configuration, the mean value of spatial resolution for the central slice on the X direction is 0.8 mm worse for the reference scanner.

The results for the two panel configurations are shown in figure 4.5. As the scanner behaved differently due to its geometry, results along all three axes are shown. In the X direction the configuration seems to perform better than the four panel configuration across the entire FOV, though the reliability of the reconstruction may be called into question as the reconstructions display more edge artefacts related to having a too high number of iterations in reconstruction. In the Z direction, the results are comparable to the four panel configuration, while in the Y direction they are considerably worse across the entire FOV, as expected due to the decreased angular coverage or, in other words lower number of LORs in the X direction.

Results for long axial FOV configuration CS2.5_L10_CTR75tot are shown in figure 4.6. As another two panel configuration, the performance in the Y direction

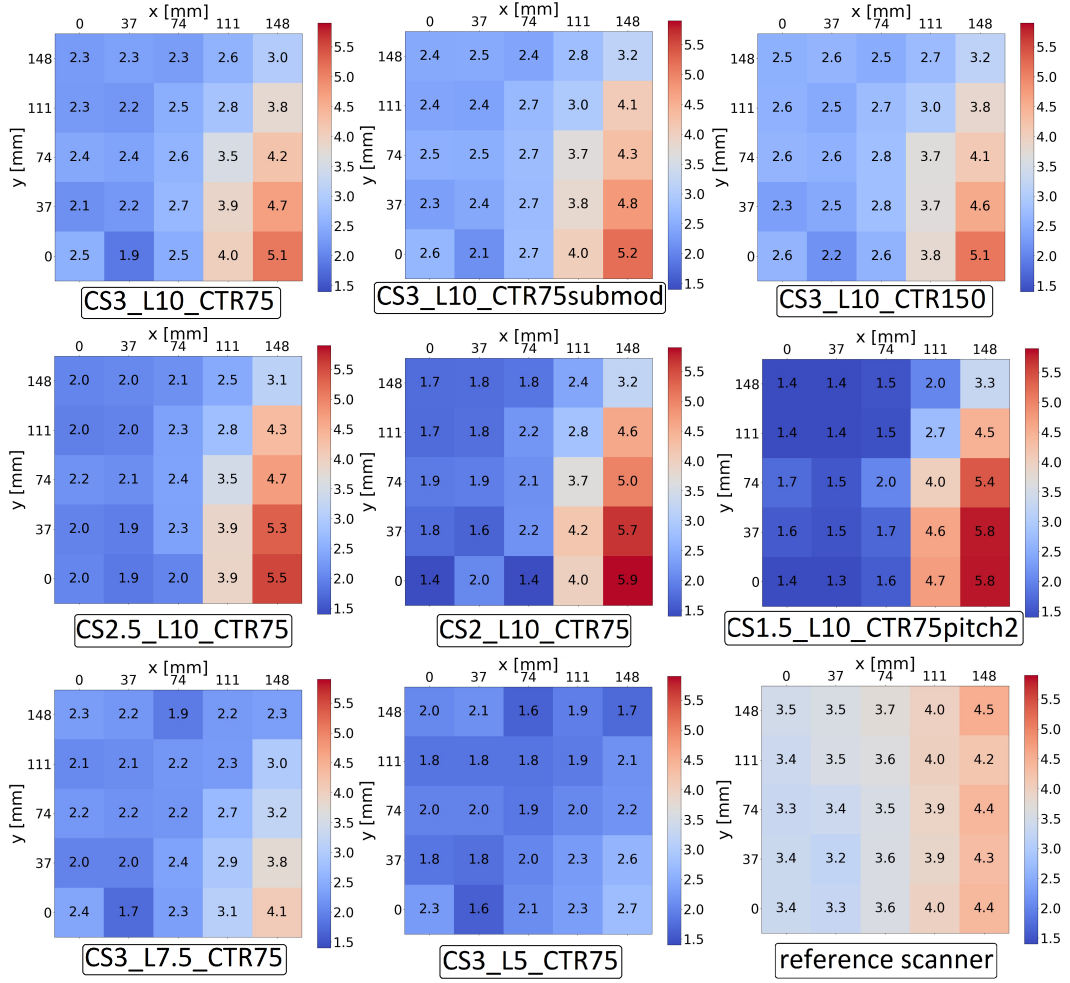


Figure 4.4: Spatial resolution along the X direction for a slice at the axial centre of the FOV for different geometries.

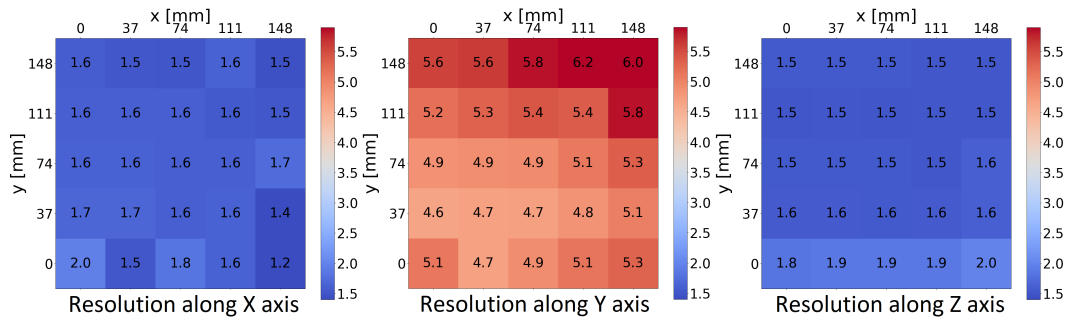


Figure 4.5: Spatial resolution for the CS3_L10_CTR75panel2 scanner along all three directions for a slice at the centre of the FOV.

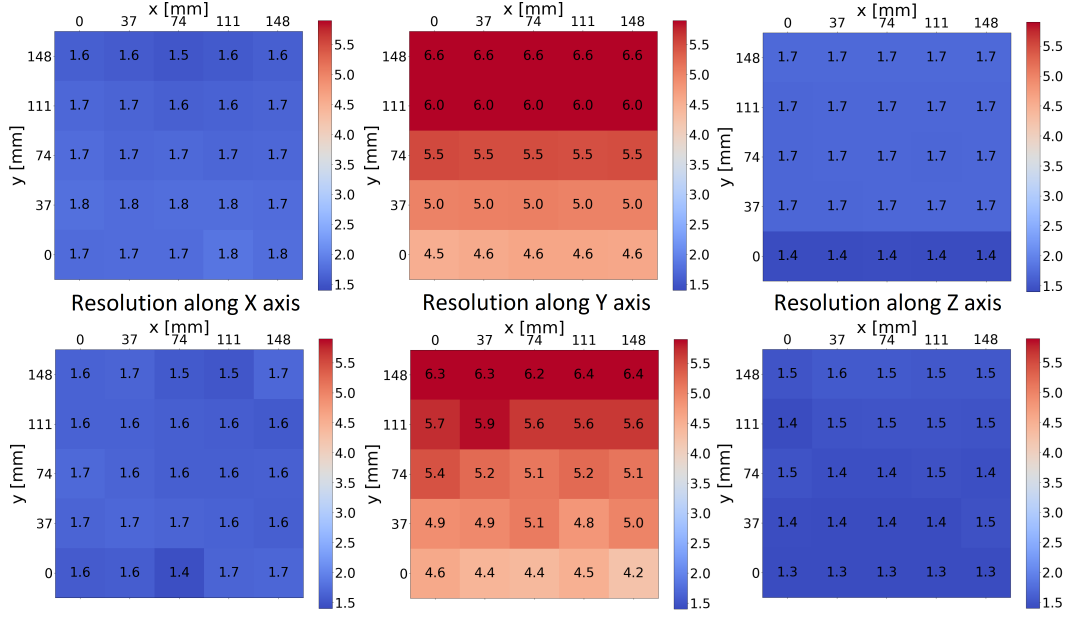


Figure 4.6: Spatial resolution for the CS2.5_L10_CTR75tot scanner along all three directions for a slice at the centre of the FOV in the case where all coincidences are accepted (top) and where the axial acceptance is limited to 25 cm (bottom).

is once more substantially worse compared to the other two directions. Limiting the axial acceptance from the whole 120 cm to 25 cm, making the acquisition more in line with standard scanners, had a minor and inconsistent effect on the spatial resolution with differences ranging up to 0.4 mm at most. Only results along the Z axis showed consistent improvement across the entire FOV. The inconsistencies could be due to two mechanisms with opposite effects in the case of all coincidences being accepted. The first being the parallax error that deteriorates the spatial resolution and the second being the increased angular coverage providing more oblique LORs that would help with the localisation of the source.

The reconstruction parameters including the voxel size and number of iterations were kept the same for all configurations to keep the comparison of results as fair as possible, though additional fine tuning of parameters might benefit individual configurations in different ways and should be considered when focusing on a single scanner.

4.1.2 Image Quality

Examples of reconstructed images of the NEMA image quality phantom are shown in image 4.7 and qualitatively show the performance of different configurations and scanner parameters, including comparing the crystal and submodule level readout, a two panel system, and the effect of CTR on the reconstructed image. The image acquired by the submodule level readout system shows a visibly lower level of noise. The two panel accordingly shows both a higher level of noise and also some artefacts, as seen most clearly in the deformation of the largest hot sphere in the Y direction. Another artefact is the higher voxel values at the left and right edges of the reconstructed phantom, where the phantom is near the edges of the scanner. Scanners with worse CTR values also show a higher level of noise, though no arte-

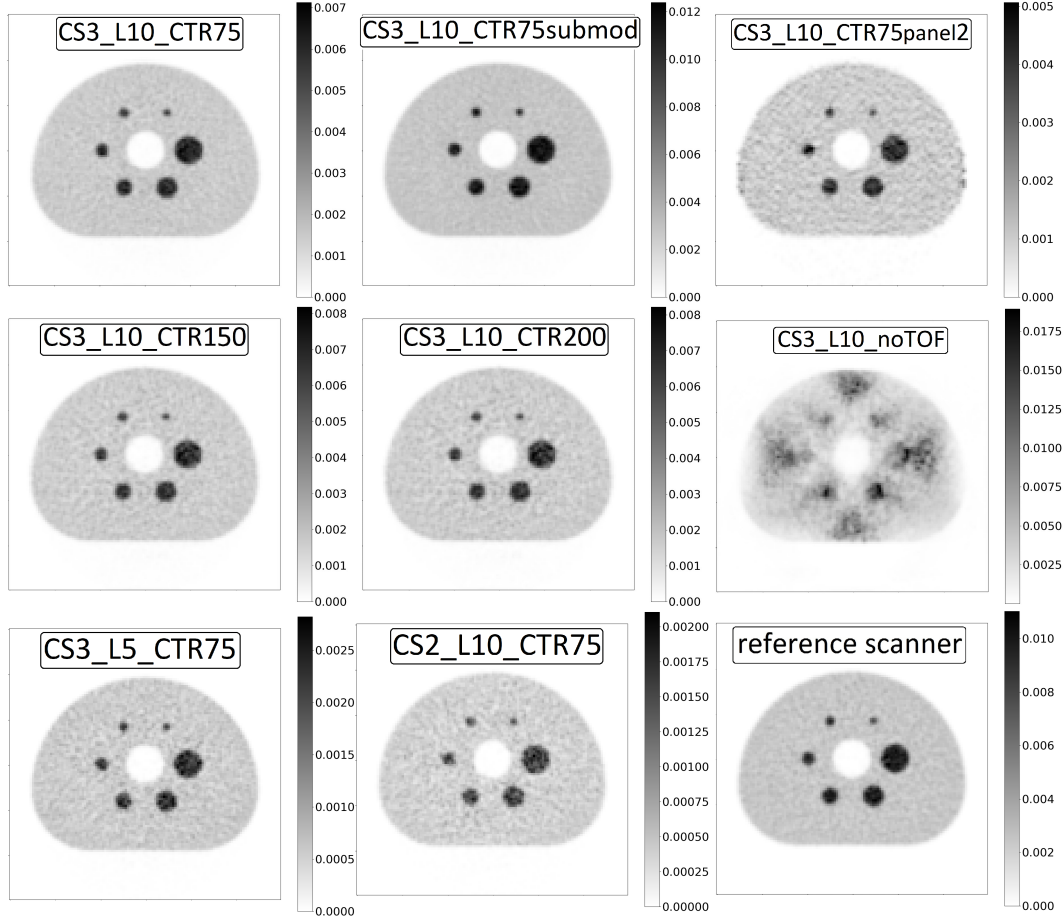


Figure 4.7: Reconstructed images of the NEMA image quality phantom for various scanner configurations and parameters. A 5 mm Gaussian filter is applied to all of the images.

facts are visible in that case. The image reconstructed without TOF information demonstrates the importance of TOF as it shows major artefacts to the point where some of the spheres cannot be visually resolved. Meaning that for a flat panel configuration TOF information is necessary even if it is only on the level of what is already available in the clinical practice. In the case of reducing either crystal length or the cross-section, the reduction of system sensitivity lead to elevated levels of noise. The reference scanner performed about on the level of the CS3_L10_CTR75 scanner.

The effect of number of iterations on both metrics was examined for the CS3_L10_CTR75 scanner configuration and the results are shown in figure 4.8. The number of iterations ranges from 2 to 100, as a single iteration was insufficient to produce the metrics or resolve the image of the phantom.

The results for image quality show only the analysis of the 13 mm, and 28 mm spheres for the sake of simplicity and brevity. They are shown in figures 4.9 and 4.10, the former comparing different scanner types and readout schemes and the latter different parameters for a four panel scanner. The results include a single point from experimental data for the reference scanner taken from [20]. The data point is represented as a grey circle on the plots along with the simulated results for the same scanner.

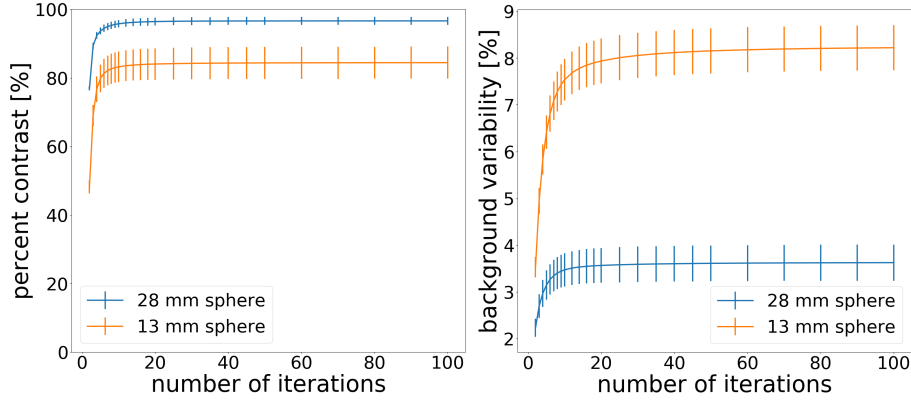


Figure 4.8: Results of percent contrast and background variability metrics as a function of number of iterations for the CS3_L10_CTR75 scanner.

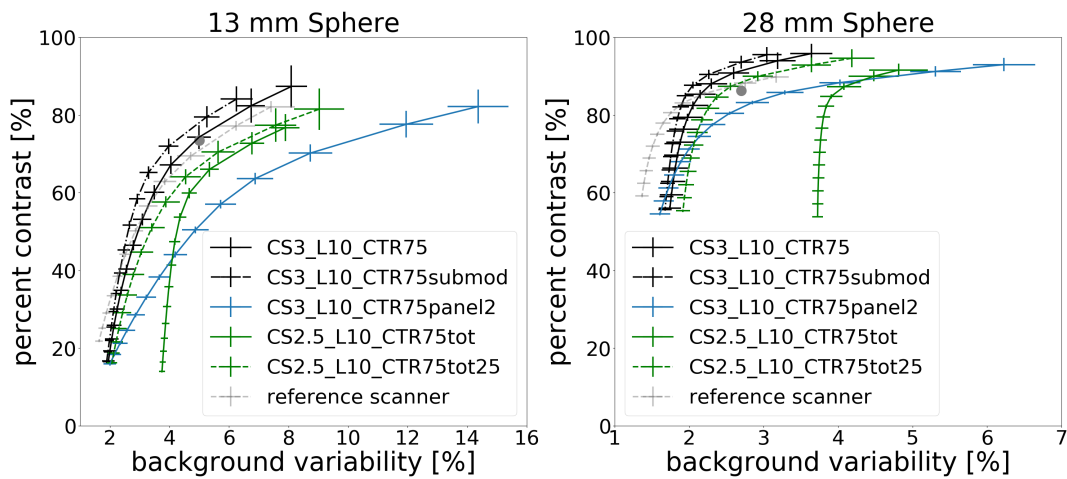


Figure 4.9: Image quality plots for the 13 mm and 28 mm spheres comparing different scanner types, including the 4 panel and 2 panel scanner, comparing different readout schemes and the long axial FOV configuration.

The results in figure 4.9 show that the submodule readout scheme, when compared at any fixed variability or contrast outperformed the crystal level readout system of the same configuration. On the other hand the submodule readout configuration was unable to reach the same highest possible contrast. In general this points to the fact that such a system has improved sensitivity, causing lower variability but also worse spatial resolution, reducing the maximum possible contrast. Both of these two configurations performed similarly to the reference scanner. The two panel configuration performance was expectedly worse as the sensitivity is far lower leading to elevated levels of noise but also a slight decrease in contrast. The performance of the extended axial FOV scanner was worse for both metrics but especially for background variability in the case of larger hot spheres. As the axial acceptance was lowered to 25 cm, the results improved for both metrics, making the performance comparable to the 4 panel configuration and the reference scanner.

The results for different scanner parameters shown in figure 4.10 are organised in three main sections. The first row of plots focuses on the effect of cross-section, or in other words the performance of sparse configurations. With the decrease in the cross-section to $2.5 \times 2.5 \text{ mm}^2$ the performance stayed relatively similar, especially for the smaller sphere. Further decrease had a more substantial effect, especially on the background variability levels, again pointing towards the lower sensitivity of such systems. The results for the configuration with the 2 mm pitch, and a two panel configuration are also shown with the performance similar to the $2 \times 2 \text{ mm}^2$ configuration.

The second row of figures shows the result for different values of CTR, ranging from 75 ps to 200 ps for the flat panel configurations and also the reference scanner, which was always simulated with 214 ps CTR. Results show improvement corresponding to the improved CTR.

The final row shows results for different crystal lengths. In this case the performance for the 10 mm and 7.5 mm systems are similar, with a more noticeable drop in performance for the 5 mm crystals, again owing to the reduced sensitivity of the system.

Extended Image Quality Phantom

The results for the extended NEMA image quality phantom acquired with the CS2.5_L10_CTR75tot scanner configuration are shown in figure 4.11. The left part of the figure shows the slices of the reconstructed image of the phantom in two views. The middle part shows the line profile through the hot cylinder both in the case when all coincidences were accepted for reconstruction and in the case when the axial acceptance was limited to 25 cm. The latter case shows a more uniform voxel value across the axial FOV while the former shows inhomogeneity with the central part of the image having lower values than the edges of the reconstructed phantom. The right part of the figure shows how the contrast changes across the FOV. As before, the reduced acceptance case shows much more consistent values as the data was more consistent with what is expected in the utilised reconstruction algorithm (that being less oblique LORs).

4.1.3 Sensitivity

The results for the sensitivity of various configurations are shown in figure 4.12. In this metric, the reference scanner outperforms most of the tested system by far. However, it should be noted that in most cases the coincidences for the flat panel

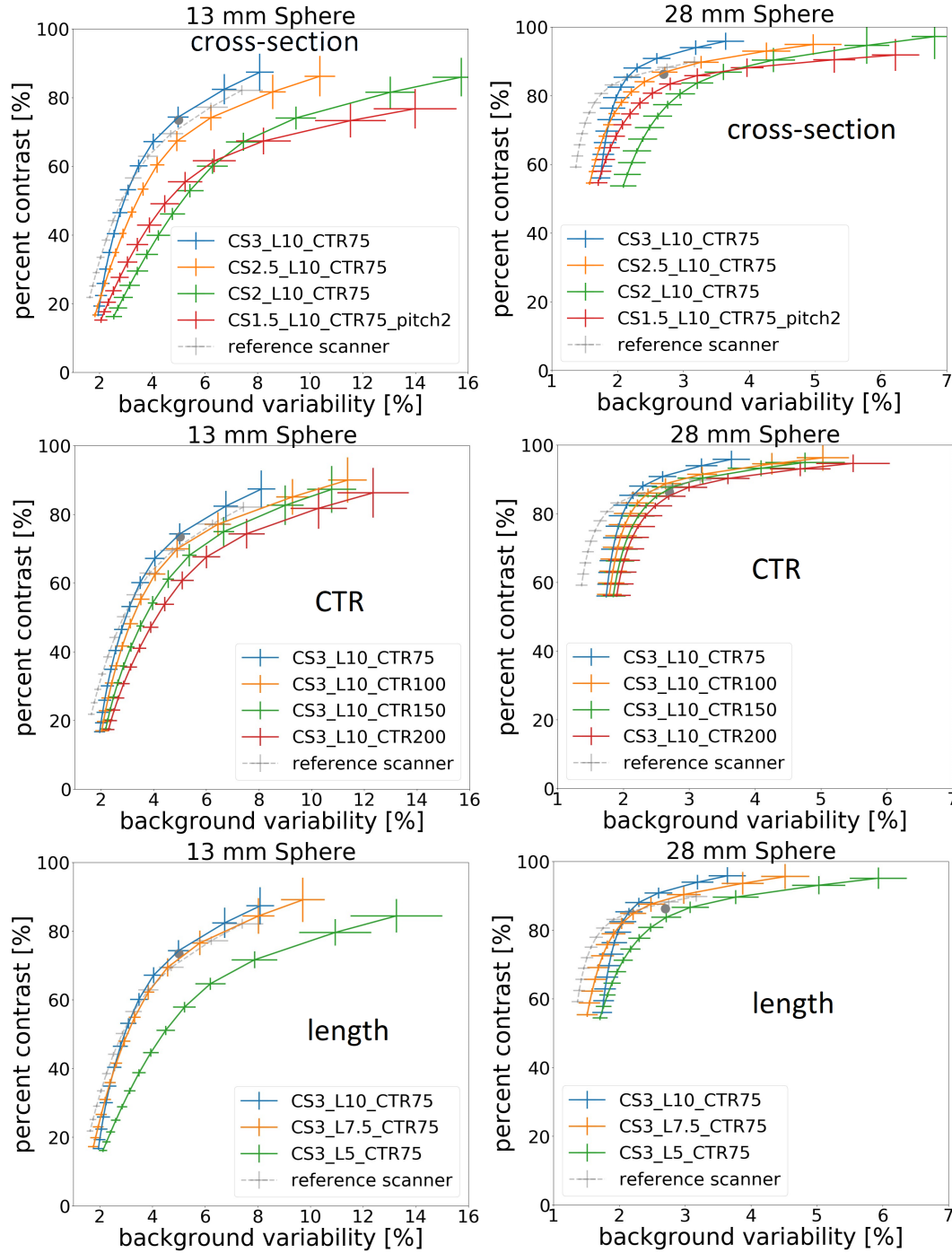


Figure 4.10: Image quality plots for the 13 mm and 28 mm spheres for different scanner parameters of the four panel configuration. The plots on the top row compare the performance of different crystal cross-sections and pitch, the middle plots compare the CTR and the bottom ones the crystal length. The grey circle represents the experimental measurement value for the reference scanner, and the grey dashed line the simulation results for the same scanner.

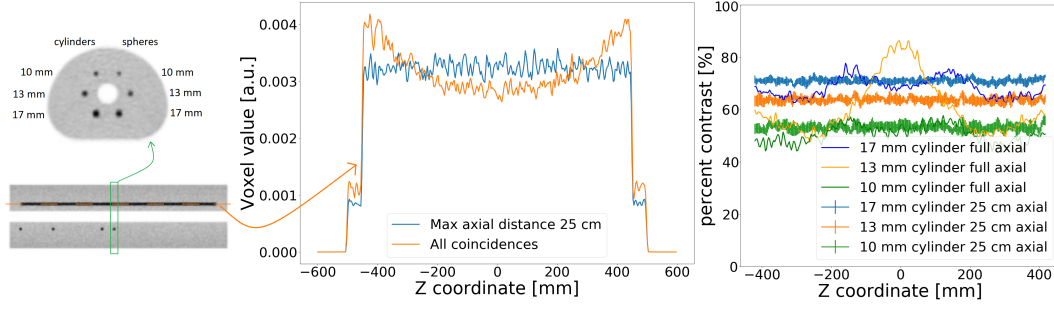


Figure 4.11: Results for the extended NEMA phantom. The reconstructed image is shown on the left, the plot in the middle shows a line profile through one of the hot cylinders, and the right plot shows the results for the contrast across the axial direction.

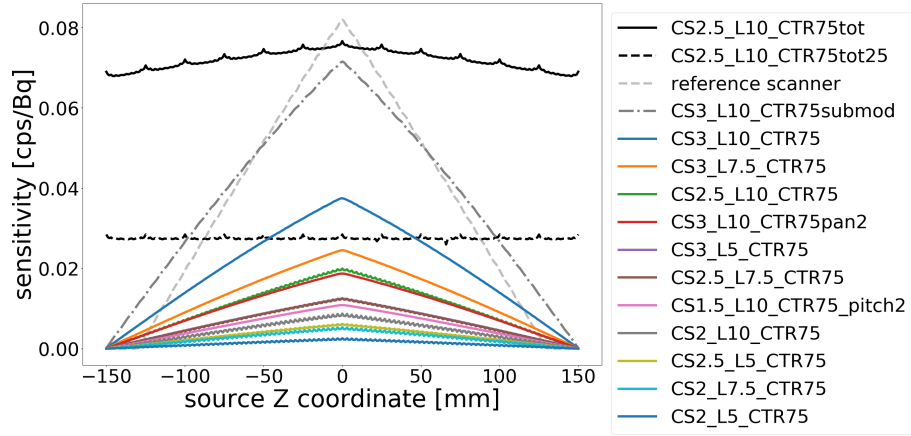


Figure 4.12: Sensitivity results for different scanner configurations.

systems are formed at the crystal level, while they are formed at the submodule level for the reference scanner. Indeed, the submodule level readout configuration CS3_L10_CTR75submod performs comparably with the reference scanner, while using less than a third of the scintillator material and also covering a larger axial FOV. Going from a crystal to a submodule level readout increases the sensitivity metric by about a factor of 2. Among the various 4 panel configurations, higher results for the sensitivity metric correspond to a higher amount of scintillator material.

The performance of the extended axial FOV configuration is shown, both allowing for all coincidences and limiting them to 25 cm in the axial direction, showing that more than a factor of 2 in sensitivity is lost, providing motivations for developing reconstruction algorithms that may be able to use all those coincidences without introducing artefacts or inhomogeneities as demonstrated in subsection 4.1.2.

4.1.4 Noise-Equivalent Count Rate

The results for $NECR_{TOF}$ are shown in figure 4.13. In this case the flat panel scanners fared better against the reference scanner, as the CTR was also taken into account for the metric, so even a scanners with the crystal level readout (CS3_L10_CTR75) was able to outperform the reference scanner. The plot only shows the results for

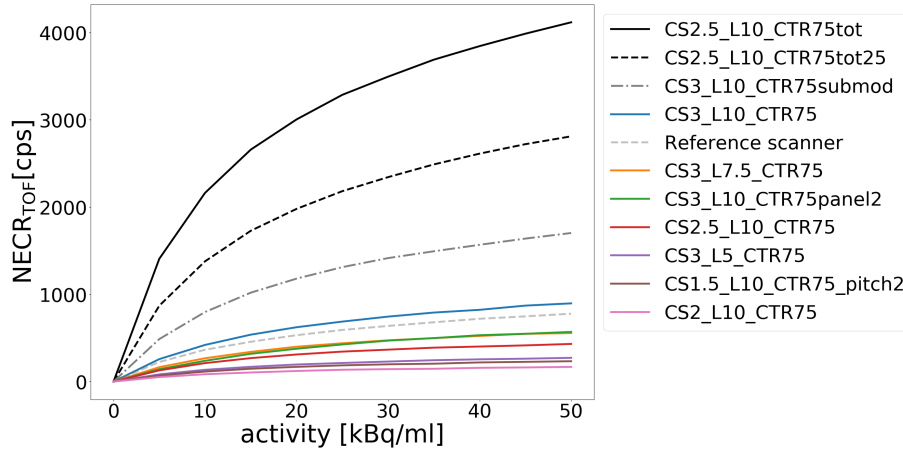


Figure 4.13: $NECR_{TOF}$ plots comparing the performance of various scanner configurations and different parameters.

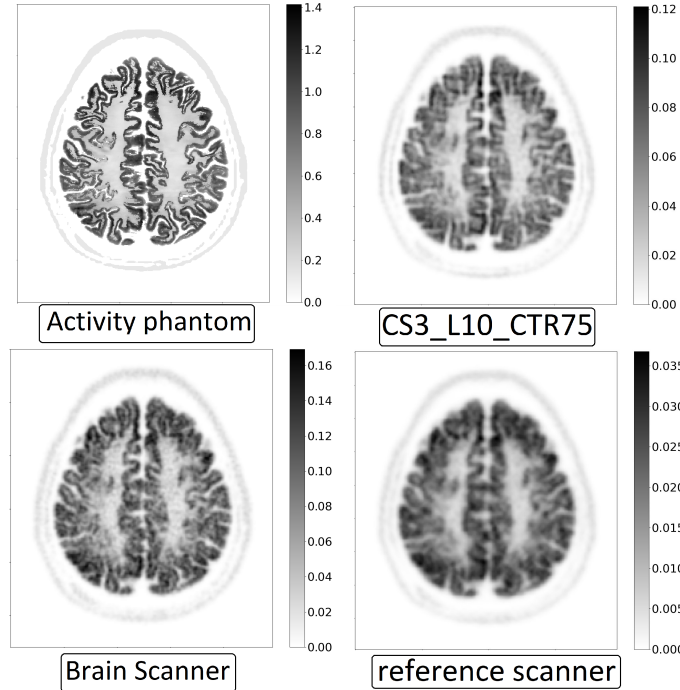


Figure 4.14: Images of the brain phantom in the transverse plane including the activity phantom and reconstructed images using different scanner configurations.

the 75 ps configurations, the best case scenario for the tested systems. Any higher value of CTR would lead to proportionate degradation of the metric, for example 150 ps CTR would halve the $NECR_{TOF}$ metric for the scanner configurations as shown in equation 3.2.

4.1.5 Brain Phantom

A slice of the activity map and corresponding reconstructed images of the brain phantom are shown in figure 4.14.

In a qualitative sense, the flat panel scanner reconstructs the image well with

many small features being visible despite the fact that the scanner itself is not specifically optimised for the brain imaging application; for example, the crystal cross-section is large for the application. Still, the images give a good representation of a possible real world imaging scenario.

The quantitative analysis using the SSIM is shown in figure 4.15, where the dependence of the metric to the width of the Gaussian filter applied to the images is plotted. In this case the crystal level readout configuration outperforms the submodule level readout configuration and both of them outperform the reference scanner on this metric, owing to the better spatial resolution in the relevant area of the FOV despite the lower sensitivity. On the other hand, the cylindrical brain scanner configuration performs worse, despite using smaller crystals, as the noise levels are higher. The results all converge as the width of the Gaussian filter exceeds 5 mm, in other words after the width of the filter is larger than the spatial resolution of all of the systems.

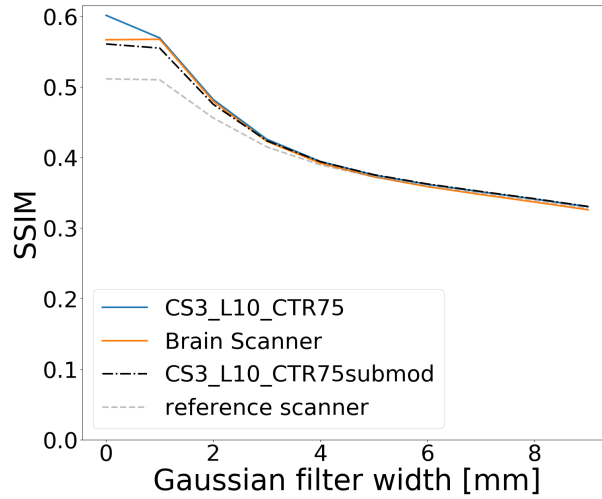


Figure 4.15: Dependence of structural similarity index on the width of the Gaussian filter applied to the brain image for different scanner configurations.

4.2 Experimental Measurements

4.2.1 Light Yield Measurements

The light yield measurements were performed using scintillator samples including LYSO and LGSO crystals from different producers summarised in table 4.1. All crystal samples had a polished surface except for the LGSO samples, which were chemically etched. The dimensions of the samples were $2.8 \times 2.8 \times 10 \text{ mm}^3$. The crystals were coupled to the photodetector with optical grease and the bias voltage of the SiPMs was set to 35 V, meaning 2.5 V overvoltage, a value far lower than what was used in subsequent CTR measurements in order to have the highest possible dynamic range and the least effect of nonlinearity that can be seen at higher operating bias voltages.

The results are shown in the left part of figure 4.16. Each measurement was repeated four times using the same crystals, but wrapped and coupled anew each time to determine the error of the measurement. The results showed a clear differ-

CHAPTER 4. RESULTS

Producer	Taiwan Applied Crystal	Hangzhou Yong Hee Photonics	Epic Crystal	EQ Photonics	OXIDE Corporation
Abbreviation	TAC	Y photonics	EPIC	EQ	LGSO
Material	LYSO	LYSO	LYSO	LYSO	LGSO

Table 4.1: Table of scintillator crystal samples used for the light yield measurements. The dimensions of all samples were $2.8 \times 2.8 \times 10 \text{ mm}^3$.

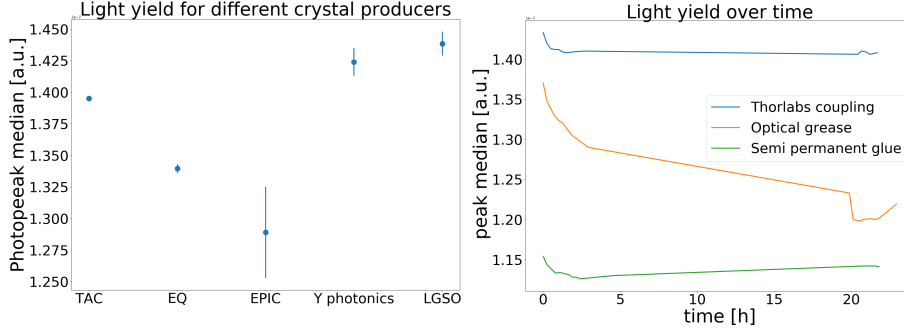


Figure 4.16: Light yield of scintillator crystal samples from different producers (left) and time dependence for different coupling agents using TAC crystal samples (right). Crystal dimensions were $2.8 \times 2.8 \times 10 \text{ mm}^3$ in all cases.

ence between the best performing LGSO and Y photonics samples, followed by TAC samples and then the other two. EPIC samples gave the worst results but were also the most inconsistent, with one of the measurements being closer to the mean value reached by the EQ sample.

Among the tested optical coupling agents were optical grease, Thorlabs index matching gel and adhesive tape. The concern with optical grease was its tendency to get absorbed into the reflective Teflon wrapping of the crystal, making the material translucent and decreasing the light collection efficiency. The results are shown in the right part of figure 4.16.

Optical grease showed deterioration in light collection efficiency throughout the measurements, confirming the suspicion. The Thorlabs gel also showed deterioration but to a lesser extent and for the most part limited to the beginning of the measurement, attributed to the initial warming up of the detector. The performance, however, was superior to that of the optical grease. The Thorlabs adhesive tape also exhibited similar deterioration at the start but then the performance increased slightly, though not to the initial levels. The improvement may be attributed to the outgassing of bubbles trapped between the tape and the crystal over time. Nevertheless, the performance was inferior to any of the other two coupling methods. It was also found to be difficult to work with, as very small pieces had to be cut without marring either surface of the tape or the crystal. The coupling itself also presented a challenge for similar reasons.

The results lead to the Thorlabs gel being the preferred coupling agent in subsequent measurements due to both superior performance and ease of use. However, even while the Thorlabs gel showed consistent results over the course of a single day, it still degraded over the course of several days or weeks, with the gel drying out and becoming opaque, thus reducing the light collection efficiency. The same effect was observed with optical grease.

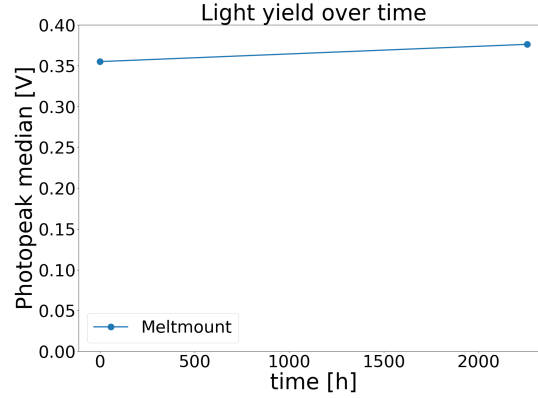


Figure 4.17: Time dependence the Meltmount coupling agent using $2 \times 2 \times 3 \text{ mm}^3$ TAC crystal samples. A much longer time elapsed between these measurements than in the case of other coupling agents.

Another tested optical coupling agent was Meltmount. This agent also presented a challenge in its application, as it is hardened at room temperature. Thus, it required heating the SiPMs, crystals and the agent itself to temperatures around 60°C . Eight layers of Teflon tape were used to wrap the crystals. The results are shown in figure 4.17, spanning an even longer period of time than the previous measurements and showing a slight improvement with time. The removal of the agent without damaging the photodetector was not possible. As the measurements were performed much later in a different experimental setup and using different scintillator samples and SiPMs, the results are not comparable to those for the other agents. Either way, the agent was not used for systematic measurements due to the difficulty it posed in application.

4.2.2 Properties and Limitations of the Data Acquisition System

The results for the intrinsic time resolution of the acquisition system obtained with the split signal are shown in figure 4.18, which shows that the scale settings of the vertical axis have a large impact on the calculated time resolution, ranging from around 20 ps to as low as 5 ps, with decreased scale settings leading to better results. A downside to the most reduced scale setting being that the threshold scan can only be performed within a very limited range. The scale setting on the horizontal axes didn't seem to have a noticeable effect on the results.

Still, the results were then used to inform the settings for the subsequent measurements, with 20 mV/div chosen for the vertical axis and 10 ns/div chosen for the horizontal axis. The higher value for the vertical axis was selected, as the split signal is half the height of the regular signal.

TAC crystal samples were used for these measurements and their dimensions were $2.8 \times 2.8 \times 3 \text{ mm}^3$.

While these settings were the most impactful for the results, additional settings were also tested. This time, however, the tests were not performed on a split signal but rather on a regular coincidence setup with a pair of detectors. The tested parameters were the oscilloscope sampling rate, bandwidth and noise filtering.

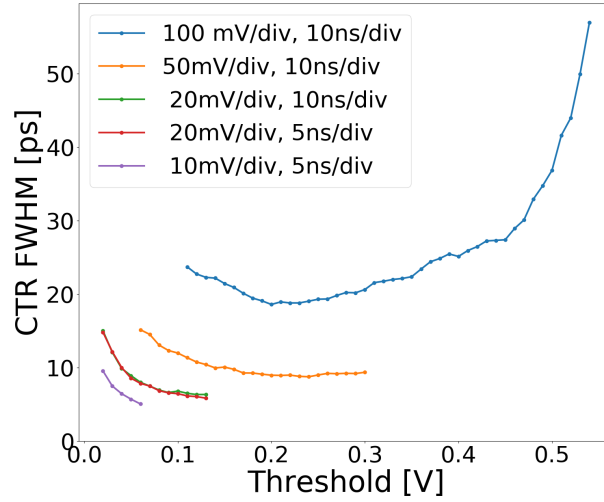


Figure 4.18: Intrinsic time resolution results for a split signal from a single detector for testing the various oscilloscope settings. In the legend, the two shown parameters in order are the scale settings for the vertical axis of the time channels, and the horizontal axis.

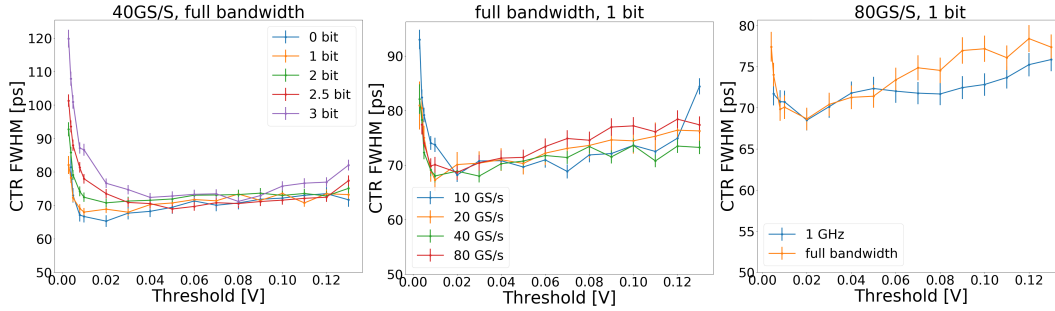


Figure 4.19: CTR results for different oscilloscope settings of noise filtering, sampling rate and bandwidth. The dimensions of the TAC crystal samples were $2.8 \times 2.8 \times 3 \text{ mm}^3$.

The threshold scans are shown in figure 4.19. In the left, the effect of noise filtering options is shown for the case with 40 GS/s sampling rate and a full bandwidth. Noise filtering seems to deteriorate the measured CTR, especially at the lowest and highest threshold values. At the central values, however, there doesn't seem to be a clear distinction in any choice of noise filtering having an impact on the CTR.

In the centre of figure 4.19, the effect of sampling rate is shown ranging from 10 GS/s to 80 GS/s for the case with full bandwidth and 1 bit noise filtering. All of the tested sampling rates seem to provide adequate sampling of the underlying signal.

The right part of figure 4.19 shows the effect of bandwidth, with bandwidth either full (36 GHz) or limited to 1 GHz. In this case, the performance for low threshold levels is comparable for both settings and only diverges for the higher values, as such the lowest bandwidth tested (which was also the lowest setting possible on the oscilloscope) was already adequate.

In the end the chosen settings for the CTR measurements were full bandwidth,

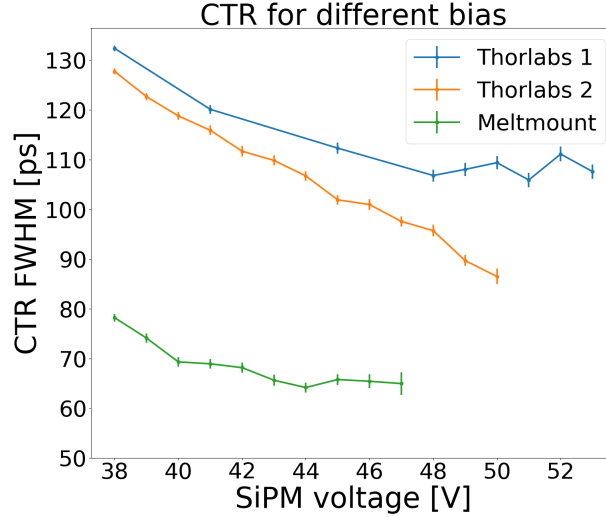


Figure 4.20: CTR dependence on bias voltage of the SiPM. The dimensions of the TAC crystal samples were $2.8 \times 2.8 \times 10 \text{ mm}^3$. Two measurements using the Thorlabs gel were performed weeks apart to evaluate the stability of the setup over a longer period of time.

40 GS/s sampling rate and no noise filtering.

The effect of bias voltage was examined by performing successive measurements for a single setup without disturbing it and only changing the bias voltage of the photodetector. The results are shown in figure 4.20. In this case a threshold scan was performed for each measurement and then the best result of each measurement was used as a data point in the graph.

The results show that the CTR in principle improved with the higher voltage. This was only to a point, as the higher voltages also increased noise levels due to dark counts and cross-talk. The photodetectors themselves were also limited in terms of highest operating voltage without damaging the detector or allowing excessive current through the SiPM. The first two measurements were performed with $2.8 \times 2.8 \times 10 \text{ mm}^3$ TAC crystal samples coupled to the SiPM with Thorlabs index matching gel. They were performed weeks apart without disturbing the setup, indicating deterioration of performance over a longer period of time.

Another measurement was performed using $2 \times 2 \times 3 \text{ mm}^3$ TAC crystal samples coupled to the SiPMs with Meltmount. For this measurement $2.8 \times 2.8 \text{ mm}^2$ SiPMs with different IV and noise characteristics were used, leading to lower maximum possible voltages for the measurements.

4.2.3 Coincidence Time Resolution Measurements

Systematic measurements of different crystal producers included various samples of scintillators crystals with dimensions of $2.8 \times 2.8 \times 10 \text{ mm}^3$. The samples are listed in table 4.2. The results of the threshold scans are shown in the left part of figure 4.21. For each sample, 200000 events were acquired and bias voltage was set to 50 V, or 17.5 V overvoltage.

The best results were obtained for the LGSO, JT, LSO, and TAC samples, all of them reaching CTR below 90 ps and were not only made by different producers but also spanned different scintillator materials altogether, specifically LSO, LYSO,

Producer	Abbreviation	Material
Taiwan Applied Crystal	TAC	LYSO
Hangzhou Yong Hee Photonics	Y photonics	LYSO
Epic Crystal	EPIC	LYSO
EQ Photonics	EQ	LYSO
HMR Technology CO.	HMR LYSO	LYSO
HMR Technology CO.	HMR LSO	LSO
OXIDE Corporation	LGSO	LGSO
JT Crystal Technology Co.	JT	LYSO

Table 4.2: Table of scintillator crystal samples used for the CTR measurements. The dimensions of all samples were $2.8 \times 2.8 \times 10 \text{ mm}^3$.

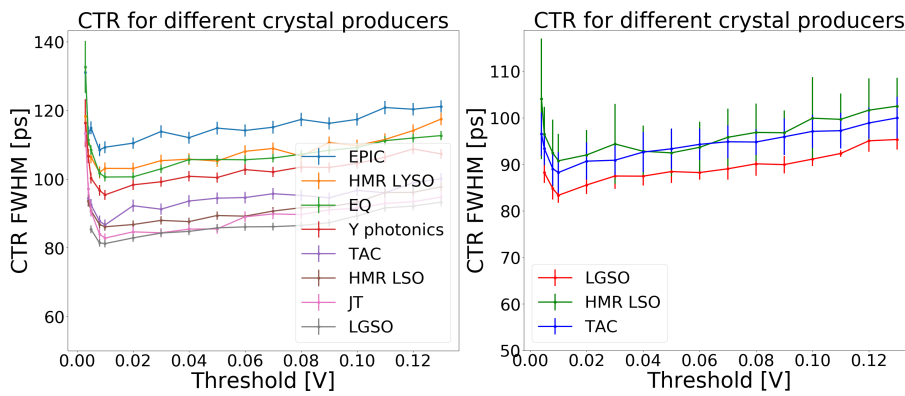


Figure 4.21: CTR results for crystal samples from different producers. Measurements for all samples are shown on the left and repeated measurements on the right. Crystal dimensions were $2.8 \times 2.8 \times 10 \text{ mm}^3$ in all cases.

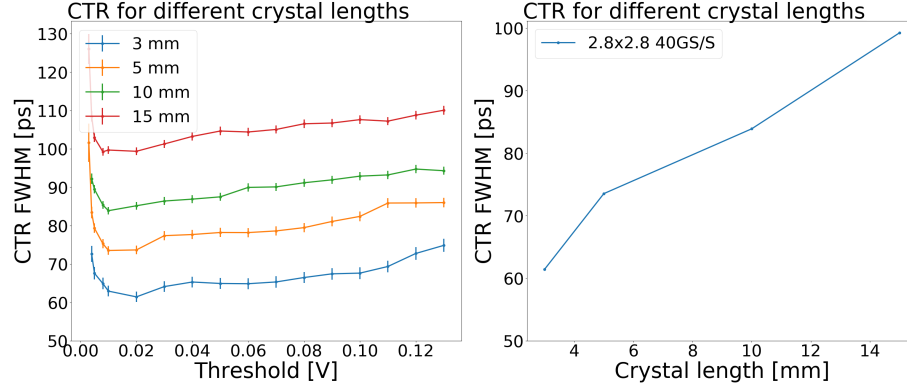


Figure 4.22: CTR results for crystal samples with different lengths. Threshold scans are shown on the left and the best CTR result dependence on crystal length on the right. TAC crystals were used and the cross section of all samples were $2.8 \times 2.8 \text{ mm}^2$.

and LGSO. As the results were obtained with a single measurement, there is a great potential for error in the results stemming from inaccuracies of the setup, particularly from wrapping the crystals, aligning the crystals to the photodetector and optical coupling between the crystal and the photodetector.

Therefore, the next step was to repeat the measurement for the three best performing crystals an additional two times. The JT sample was omitted from this measurement as the crystal was not available at the time of measurements. The results are shown in the right part of figure 4.21. For the LGSO sample all three measurements gave fairly similar results, while the other two samples gave inconsistent results. It was surmised that this was not only due to the inaccuracies of each setup, but also due to the accumulative damage caused to the SiPM as each crystal sample was coupled to it and the LGSO sample being the first tested sample. The fragile nature of the photodetector brought another layer of complexity to the measurements, since it was not possible, for a given measurement, to distinguish between an improper optical coupling of the crystal and reduced performance due to damage to the photodetector. Repetitions of measurements would then in principle also require new photodetectors for every measurement, which was impossible for the purposes of the measurements.

Effects of crystal length on CTR

Measurements were continued with the study of impact of crystal length on CTR. For these measurements TAC samples with $2.8 \times 2.8 \text{ mm}^2$ cross-sections were used. The lengths of the scintillator samples were 3 mm, 5 mm, 10 mm, and 15 mm. The results are shown in figure 4.22. All of the other parameters from voltage to oscilloscope settings and number of acquired events were kept the same as the previous measurements.

The results show that the CTR depends on the length of the crystal, conforming to the theoretical predictions. In this case the setup with 3 mm long scintillator crystals achieved 61 ps CTR, which is the best result achieved in these experimental measurements.

5. Discussion

Flat panel PET scanner configurations present a new prospective direction for the development of future devices. The main advantages of such designs include the possibility of using less scintillator material without sacrificing performance, the possibility of making the scanner more compact or even mobile, meaning that a dedicated room for the scanner would no longer be a requirement, another possibility is taking advantage of the modularity of the design in order to increase the coverage, leading to a more affordable possibility for total-body imaging. The distance between the panels could also be adjusted for each specific imaging case, leading to improvements in sensitivity and spatial resolution. The open geometry also allows the scanner to be used in new instances, for example during particle therapy or surgery. On the other hand it could also improve patient comfort.

The flat panel scanner geometry presents new challenges compared to conventional cylindrical scanners both because of the flat geometry as well as the incomplete angular sampling along the azimuthal angle. It also presents new challenges in terms of performance evaluation as the current standards make assumptions about the system that haven't been tested for these specific configurations. In fact, some of the practices required by the standard are not possible at all, for example the use of the FBP algorithm for the reconstruction.

5.1 Simulation Studies

The main simulation results are summarised in table 5.1 and confirm the potential of flat panel PET scanner designs. For example, a four panel scanner with a CTR of 75 ps and submodule readout (CS3_L10_CTR75submod) uses less than a third of scintillator material while achieving better spatial resolution and sensitivity metrics than the reference scanner. The contrast image quality metrics also support this conclusion.

Of all the simulations for the image quality metrics, spatial resolution required the most effort. As the standard methods were not applicable with the use of the novel scanner geometry, the entire approach was reconsidered. Using an iterative reconstruction algorithm, also meant, for example, having to decide on the number of iterations and voxel size of the reconstructed image, thus every parameter required testing. It was also important to not blindly trust the resulting metrics. For example, figure 4.2 might suggest that even going up to 100 iterations for the reconstruction is a perfectly valid choice, even if not optimal. A qualitative analysis of the resulting reconstructed images was required to assess the quality of the reconstruction, from the edge artefacts to over-sharpening. In fact, this holds true even more for the sources further from the centre of the FOV. This also led to the choice of the simulation of the entire grid of point sources, evaluating the performance in every part of the first octant of the FOV, even close to the edges, where the perfor-

CHAPTER 5. DISCUSSION

Geometry	Relative LSO volume	Spatial resolution [mm]	Sensitivity [kcps/MBq]	NECR _{TOF} [cps]	Percent contrast
Reference scanner	100 %	3.3	15.4 (100 %)	365 (100 %)	71 %
CS3_L10_CTR75	28.9 %	1.9	8.53 (55 %)	420 (115 %)	74 %
CS3_L10_CTR75submod	28.9 %	2.1	16.3 (106 %)	798 (219 %)	78 %
CS2.5_L10_CTR75	20.1 %	1.9	4.43 (29 %)	212 (58 %)	68 %
CS2_L10_CTR75	12.8 %	2.0	1.85 (12 %)	85 (23 %)	48 %
CS1.5_L10_CTR75_pitch2	16.3 %	1.3	2.39 (15 %)	115 (32 %)	53 %
CS3_L10_CTR100	28.9 %	2.0	8.53 (55 %)	315 (86 %)	70 %
CS3_L10_CTR150	28.9 %	2.2	8.53 (55 %)	210 (57 %)	65 %
CS3_L7.5_CTR75	21.7 %	1.7	5.55 (36 %)	268 (73 %)	72 %
CS3_L5_CTR75	14.5 %	1.6	2.81 (18 %)	135 (37 %)	56 %
CS3_L10_CTR75pan2	14.5 %	1.5	4.26 (28 %)	239 (65 %)	51 %
CS2.5_L10_CTR75tot	74.0 %	1.7	30.9 (200 %)	2160 (592 %)	63 %
CS2.5_L10_CTR75tot25	74.0 %	1.6	11.78 (76 %)	1380 (378 %)	67 %

Table 5.1: Summary of main performance metrics for different scanner parameters; the relative amount of the scintillator volume compared to the reference scanner, spatial resolution in the X direction for a source that is located 37 mm away from the centre of the FOV in the X direction, total system sensitivity, NECR_{TOF} at 10 kBq/ml activity, and percent contrast at 5 % background variability for the 13 mm sphere. Sensitivity and NECR_{TOF} columns also contain relative values compared to the reference scanner inside the parentheses.

mance was expected to be poor. Even in those cases, while the results were worse than those of the reference scanner, the difference was on the order of 1.5 mm or 25 % relative to the flat panel scanner.

The results of the spatial resolution simulations indicate that the readout scheme (crystal or submodule based) has a minor impact on the spatial resolution. Similarly, a minor deterioration due to worse CTR performance was observed as CTR value was set from 75 ps to 150 ps. The crystal cross section had the largest impact on the metric for the sources near the centre of the FOV, with the poor results due to the geometric effects disappearing as the cross-section was decreased. When the pitch was also decreased, the impact on the spatial resolution was even greater. The effect of crystal length was even more pronounced across the entire examined FOV, with shorter crystals achieving the best results in terms of spatial resolution. This indicates that the parallax error was a major contributor to the spatial resolution and that the measurement of DOI information could lead to the improvement of spatial resolution, possibly even with longer crystals, thus recovering sensitivity lost by the choice of 10 mm long and shorter crystals, or perhaps enable the use of even longer crystals than the 20 mm used for the reference scanner. The two panel configuration performed well along the X and Z directions (parallel to the panel), but the lack of sampling affected the results in the Y direction (perpendicular to the panel). Solutions for the worse performance could be a combination of all the contributing factors; that is improved CTR, increased panel size (which would improve angular coverage), and DOI measurement.

Another important matter regarding the simulations for the spatial resolution metric is the inclusion of the homogeneous background to the point sources. It was demonstrated how the iterative reconstruction method produced poor results due to the over-sharpening artefacts. In fact, the reconstructed source could in some cases resolve into two separate peaks as the number of iterations was increased and

the voxel size decreased. The added background activity ameliorated the artefacts, however, as the number of iterations was increased even further, the artefacts would show up once more, as was demonstrated in a point source and warm background reconstructed with 50 iterations. While the addition of the background improved the quality of the results, it also resulted in the deterioration of the metric itself, though that in itself may just mean it represents the real value in a more accurate manner.

The addition of the background introduced another discussion, which is the exacerbation of the computational complexity for these simulations and reconstructions. For a single source without background the simulation took on average about 2 core hours in total. When the background activity was added and nothing else changed for the same example, the simulation required 140 core hours (split into hundreds of jobs across multiple processor nodes). The sensitivity image generation took about 24 core hours and was not impacted by the inclusion of the additional background. There was, however, an impact on the reconstruction time, which was on the order of 1 core hour without the additional background and took about 23 core hours on average if the background was included. In total for each of the 125 sources, the computational cost was on the order of 27 core hours without the background and 187 core hours with the background, in other words a difference of 160 core hours per point source. For a single scanner the computational cost with the background was on the order of 23000 core hours. Such simulations would not be feasible without the heavy use of grid computing. This also limited the activity of the simulated background that was still feasible for the simulations given the available resources both in terms of the computational power and also data storage, as each set of the 125 sources ranges in hundreds of gigabytes for the simulation data and together with the reconstructed images reaches the order of a terabyte.

With the image quality phantom, it was demonstrated that the the non-sparse four panel configuration can perform on a level comparable to that of the reference scanner. The important caveat being the assumed improvement of the CTR to 75 ps (or at the very least below 100 ps). The reduction of the crystal cross-section to $2.5 \times 2.5 \text{ mm}^2$ did yield worse performance than the reference scanner, however even with the 30 % reduction in scintillator volume, the impact was not major, unlike when the cross section is reduced even further. Similarly, the reduction of the crystal length from 10 mm to 7.5 mm didn't significantly deteriorate the results despite the 25 % decrease in the scintillator volume. In order to properly reconstruct the image without any obvious artefacts the use of TOF information during reconstruction was required. While better CTR led to better results, it was demonstrated that even a CTR on the order of what modern clinical scanners are already capable of is sufficient for the reconstruction without artefacts for a four panel configuration.

With the extended image quality phantom and the long axial FOV scanner it was demonstrated that the current reconstruction software is not well adapted to such novel scanner configurations and led to inhomogeneities in the axial direction in reconstructed images. In practice that meant, that the acceptance of the events had to be limited in the axial direction, reducing the sensitivity of the scanner by over a factor of 2. This provided the motivation for the development of a new reconstruction engine YRT-PET [64] that would be able to fully take advantage of the increased coverage of the imaged subject without introducing artefacts. Nevertheless, even with the reduced axial acceptance the long axial FOV scanner matched

the performance for the image quality metrics of a 4 panel scanner with the same crystal dimensions, showing feasibility of such a configuration, providing 120 cm of axial coverage while still using less scintillator material than the reference scanner.

In terms of performance for the sensitivity metric, the reference scanner out-classes most flat panel configurations, as expected due to a much higher amount of scintillator material used. However, it is important to mention that the readout scheme for the flat panel scanners was different in most cases. Indeed, when using the submodule readout scheme for the CS3_L10_CTR75submod configuration, the metric is much more comparable. While it doesn't reach the same peak amount, it does perform better at the edges, as even with the lower amount of scintillator material, the axial FOV of the flat panel scanner configurations is 30 cm compared to the 26.3 cm of the reference scanner.

On the other hand the flat panel configurations perform much better for the NECR_{TOF} metric. This is, however only due to the assumed improvement in the CTR in the flat panel scanners.

In the simulations of the brain phantom, both the flat panel and the brain scanner configuration outperformed the reference scanner in the measured metric and also qualitative assessment of the reconstructed images. The difference can be attributed to the fact that the crystal size is larger for the reference scanner and the distance between the detector elements is also greater (in other words the scanner radius is larger). Both of these facts cause poorer spatial resolution. Perhaps a more surprising fact is the worse performance of the brain scanner configuration compared to the flat panel configuration with the crystal level readout. In that case despite further improvement in the spatial resolution as the crystals are both smaller and positioned at a smaller pitch, the loss in sensitivity outweighs the benefits of the spatial resolution, resulting in a noisier image, though the difference is not major. As the Gaussian filter is applied, the difference disappears as the noise is reduced and spatial resolution deteriorates. The intricacy of the voxelised phantom and its activity distribution also increased the computational complexity for these simulations compared to, for example, the NEMA image quality phantom. In this case the simulation for a single acquired image took on the order of 12000 core hours. The activity of the phantom was reduced compared to a realistic clinical case in order to avoid random coincidences as much as possible, which would add to the complexity of the simulations.

5.2 Experimental Measurements

Measuring CTR below 100 ps brought forth a very particular set of difficulties. Much of the instrumentation that had been available for the experimental measurements simply was not able to handle such precise timing measurements. For that reason the first measurements focused solely on the light output of different scintillator crystals, which in the end is an important factor for determining the CTR. Measurements showed clear differences between the performances of crystals made by different producers despite all of them being in essence the same LYSO material. The differences being the doping of the crystals and details in production not disclosed by the producers.

Other than the crystals themselves, the other important factor was the optical coupling. Both in terms of performance in transmission of scintillation photons as well as in performance differences and stability over a longer period of time. The first

5.2. EXPERIMENTAL MEASUREMENTS

Producer	Abbreviation	Material	Dimensions	Relative Light Yield	CTR
Taiwan Applied Crystal	TAC	LYSO	$2.8 \times 2.8 \times 10 \text{ mm}^3$	$100 \% \pm 0.07 \%$	$84 \text{ ps} \pm 1 \text{ ps}$
Hangzhou Yong Hee Photonics	Y photonics	LYSO	$2.8 \times 2.8 \times 10 \text{ mm}^3$	$102 \% \pm 0.8 \%$	$95 \text{ ps} \pm 1 \text{ ps}$
Epic Crystal	EPIC	LYSO	$2.8 \times 2.8 \times 10 \text{ mm}^3$	$92 \% \pm 3 \%$	$109 \text{ ps} \pm 2 \text{ ps}$
EQ Photonics	EQ	LYSO	$2.8 \times 2.8 \times 10 \text{ mm}^3$	$96 \% \pm 0.3 \%$	$101 \text{ ps} \pm 1 \text{ ps}$
HMR Technology CO.	HMR LYSO	LYSO	$2.8 \times 2.8 \times 10 \text{ mm}^3$		$102 \text{ ps} \pm 2 \text{ ps}$
HMR Technology CO.	HMR LSO	LSO	$2.8 \times 2.8 \times 10 \text{ mm}^3$		$86 \text{ ps} \pm 1 \text{ ps}$
OXIDE Corporation	LGSO	LGSO	$2.8 \times 2.8 \times 10 \text{ mm}^3$	$103 \% \pm 0.7 \%$	$81 \text{ ps} \pm 1 \text{ ps}$
JT Crystal Technology Co.	JT	LYSO	$2.8 \times 2.8 \times 10 \text{ mm}^3$		$83 \text{ ps} \pm 1 \text{ ps}$
Taiwan Applied Crystal	TAC	LYSO	$2.8 \times 2.8 \times 3 \text{ mm}^3$		$61 \text{ ps} \pm 1 \text{ ps}$
Taiwan Applied Crystal	TAC	LYSO	$2.8 \times 2.8 \times 5 \text{ mm}^3$		$74 \text{ ps} \pm 1 \text{ ps}$
Taiwan Applied Crystal	TAC	LYSO	$2.8 \times 2.8 \times 15 \text{ mm}^3$		$99 \text{ ps} \pm 1 \text{ ps}$

Table 5.2: Summary of results of the experimental measurements of relative light yield (compared to the TAC sample) and CTR for different scintillator crystal samples.

concerns arose after measurements that indicated the deterioration in performance in measurements done days apart without disturbing the setup. The problem was identified as the coupling agent both being absorbed into the reflector wrapped around the crystal and also in the drying of the coupling agent, affecting its optical properties. The final chosen coupling agent was the Thorlabs index matching gel, which indicated a consistent performance over a 24 hour period. Despite that fact, it was later shown that over an even longer period of time of weeks, even that coupling agent would deteriorate. The problem may have been exacerbated by the fact that the SiPMs had bare surfaces, which meant more heat transfer to the coupling agent and could have caused it to dry out.

With the switch to a more powerful oscilloscope, it was possible to move onto CTR measurements, summarized in Table 5.2. First it was important to determine the optimal parameters of the oscilloscope in order to minimise its contribution to the CTR. It was demonstrated that it could be reduced to about 10 ps (depending on the threshold) at very decreased vertical scale levels. These settings were the most important, while the sampling rate and bandwidth settings changed the results to a minimal degree. Only the noise filtering setting showed any real meaningful difference and was best kept turned off.

What followed was a large set of systematic measurements, comparing crystals made by different producers and selecting the best performing crystals for further measurements. The repeatability of the measurements was important to determine, as the process of wrapping and coupling crystals involved intricate human operation and was as such subject to human error. With that another difficulty arose as the SiPMs began accumulating damage from repeated cycles of the coupling with different crystals. It was hard to determine, whether the deterioration in performance was coincidental due to improper coupling (and other systemic factors) or the result of the degraded photodetector. That is until the damage accumulated to the point where the dark current of the SiPM rose to the level that it was no longer possible to operate the SiPM at such a high bias voltage.

The measurements of crystals with different dimensions clearly demonstrated the effect of length on the CTR and the need for the planned flat panel scanner to use

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shorter crystals than the conventional clinical scanners if the desired system CTR was to be achieved.

6. Conclusions

Flat panel PET scanner configurations have the potential to be flexible and adaptable to required situations, such as changing the distance between the panels to accommodate different subjects. They can be modular and more compact than the conventional cylindrical counterpart and represent an attractive development of TOF-PET technology. However, the development of PET detectors with excellent CTR requires extensive optimisation of design parameters and studies of image reconstruction in the novel geometry.

It was demonstrated that given sufficient CTR a flat panel PET scanner was able to match and in some specific cases even exceeded the performance of a conventional and modern clinical scanner despite the fact that the flat panel configuration used a much lower amount of scintillator material and also a lower amount of detector elements. The improved CTR was crucial in order to both compensate for the reduced sensitivity as well as eliminate artefacts arising from the incomplete angular sampling of the open geometry. While the simulated CTR of 75 ps eliminated artefacts for the four panel and long axial FOV configurations, the CTR was not sufficient for eliminating all artefacts or distortions in the two panel scanner configuration.

The results of the simulations may be used as a guide or input for further experimental measurements, especially when dealing with larger systems, such as arrays of detectors or even entire prototype scanners. Specifically, the results of these simulations were important for the purposes of developing the prototype scanner for the PetVision project [65], using shorter scintillator crystals and photodetectors with excellent time resolution. The results of these simulations were utilised for improving the efficiency of the experimental measurements and enabled the whole detector to reach the target performance. The extensive work in simulations also led to the development of the YRT-PET reconstruction engine, focusing on the possible improvements in the reconstructed images for the flat panel scanner geometry, requiring extensive simulations and optimisation.

Experimental measurements demonstrated the potential for the future improvement of CTR and the performance of the photodetectors that are currently in development. A CTR as low as 63 ps was measured. This, however, was done with short 3 mm crystals, much shorter than what was assumed for the final flat panel scanner. With the 10 mm crystal samples a CTR of 81 ps was measured, which while not reaching the assumed 75 ps is still quite near. However, even this result may not be so easily replicated in a full PET scanner. The first reason being the electronics. The integrated circuits may not match the performance of high-power consumption high-frequency electronics and a powerful oscilloscope. The second reason being that some loss of timing performance is expected as the system is scaled from a single pair of detectors to multiple modules per panel. Nevertheless, the results do indicate a reasonable possibility of achieving a CTR below 100 ps on system level,

especially as the involved technology continues to be improved. As such the results may serve as the baseline for the comparison with larger systems in the future.

The future research in this area includes several diverging branches including measuring with a double sided readout, which enables the possibility of using DOI information in the reconstruction and may in fact lead to an improvement in CTR in longer scintillator crystals. Another area in experimental measurements is moving from a single pair of detectors to a module. This way the effect on CTR as the system is scaled could be evaluated and even the first reconstructions could be performed. An examination of the effect of surface treatment of the scintillators on the resulting CTR could also prove interesting. There is also more work to be done in the area of simulations. For example, examining the propagation of visible light through the crystal and the effects of surface treatment and reflectors. It could also serve as a way to assess the conformity of the Monte Carlo simulations to the experimental measurements.

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Appendix A

Data management plan (DMP)

Type of data and methods used if new data was collected or produced

1. What data have you collected and/or produced?

Within the framework of the doctoral thesis simulation data of PET scanners and reconstructed images were generated, as well as experimental measurement data. Results of the simulations are in principle the same as data obtained from clinical scanners: files that contain the list-mode PET data. From these files algorithms for image reconstruction can create an estimate of real radiopharmaceutical distribution inside the body of a patient or a phantom. The data can be accessed with many established tools in the field of simulations in physics, image analysis and medical imaging. Data from experimental measurements was stored as either plain-text comma-separated value files containing histogrammed values of the energy measurements for the evaluation of light yield and as digitized waveform data sampled by an oscilloscope for the CTR measurements. In both cases the data can be accessed and analysed using standard established tools.

2. How did you collect and/or produce new data and how did you use existing data for your doctoral thesis?

Simulation data was generated using the GATE simulation toolkit and reconstructed using CASToR image reconstruction software. Both are open-source and produce data in a standard and open binary format. Data from experimental measurements was generated using photodetectors and other equipment for experimental particle physics. No existing data was used for the purposes of the doctoral thesis.

3. Have you been dealing with sensitive data? If yes, how have you ensured compliance with ethical measurements when collecting and/or producing data?

No sensitive data was used for the purposes of the doctoral thesis.

How the data was stored and protected during research for a doctoral thesis

1. How did you store the data?

Data has been stored on a cloud system of the Experimental Particle Physics Department of Jožef Stefan Institute, where data was initially transferred from

APPENDIX A. DATA MANAGEMENT PLAN (DMP)

the supercomputing network. The data was also saved and published on the Zenodo repository, an established system for publishing data, supported by the European Organization for Nuclear Research - CERN. Another copy of the data was stored on an external hard drive.

2. If you have worked with sensitive data, how have you ensured that it was kept safe and secure?

No sensitive data was used for the purposes of the doctoral thesis.

Long-term data availability and storage

1. In which data repository will you store the data for the long term after the completion of the research work and make it accessible in accordance with the requirement of Article 50 of the Regulations on Doctoral Studies of the UL?

The data has been published online on the Zenodo repository and are publicly accessible using the following link <https://doi.org/10.5281/zenodo.19681576>.

2. Do you plan to restrict access to the data for a certain period? If yes, please explain the reasons (e.g. for intellectual property or patent protection, or other reasons).

We do not plan any time restrictions regarding the accessibility of the data.

Persistent identifiers

1. Provide persistent identifiers, such as DOI, Handle, URN, that enable access to research data.

Zenodo: <https://doi.org/10.5281/zenodo.19681576>

2. If you used existing data in your research, please provide persistent identifiers or web addresses where this data is stored.

No existing data was used for the purposes of the doctoral thesis.

Razširjeni povzetek v slovenskem jeziku

Uvod

Pozitronska emisijska tomografija (PET) je slikovna tehnika v nuklearni medicini, ki omogoča slikanje fizioloških procesov z uporabo radiofarmakov, ki sevajo pozitrone in temelji na zaznavanju para visokoenergijskih fotonov, ki nastane pri anihilaciji pozitrona z elektronom.

Radiofarmaki v splošnem sestavljeni iz biološko aktivne molekule, radioizotopa in veznim členom med obema. Raztopina radiofarmaka je vbrizgana v pacienta in se nato porazdeli po njegovem telesu glede na svoje specifične farmakokinetične lastnosti. Količina radiofarmaka v telesu se zmanjšuje zaradi radioaktivnega razpada radioizotopa in tudi fiziološkega izločanja raztopine iz telesa. Relevantni radioizotopi so proizvedeni predvsem v ciklotronih, kjer so nabiti delci pospešeni v tarčna jedra atomov. En primer je (p,n) reakcija, kjer so protoni pospešeni in je tarča voda. V tem primeru se jedro ^{18}O spremeni v ^{18}F , ki ima enako število nukleonov, vendar en proton več in nevtron manj.

En izmed najbolj pogosto uporabljenih radiofarmakov je fluorodeoksiglukoza (FDG). Molekula je analogna glukozi, le da je ena izmed hidroksilnih skupin zamenjana z radioizotopom ^{18}F . Molekule FDG se po telesu razporedijo analogno glukozi, in služijo kot biomarker za metabolizem glukoze. Molekula FDG kot taka ne sodeluje pri presnovi, vendar pri razpadu radioizotopa ^{18}F nastane ion $^{18}\text{O}^-$, ki iz okolja privzame še ion vodika in tako molekula FDG postane običajna molekula glukoze, ki lahko sodeluje pri metabolizmu. FDG se najpogosteje uporablja v onkologiji za diagnostiko rakavih obolenj in nevrologiji za diagnozo različnih nevroloških bolezní in motenj, na primer demenc in epilepsije.

Pri anihilaciji pozitrona z elektronom nastaneta dva kolinearna visokoenergijska fotona, vsak z energijo 511 keV, kar ustreza mirovni masi elektrona oziroma pozitrona. Ko sta oba fotona zaznana v koincidenca, je mogoče dogodek lokalizirati vzdolž črte, ki povezuje oba detektorja in se imenuje črta odziva (LOR). Načeloma par vzporednih detektorjev lahko zazna anihilacijski dogodek, če se ta zgodi znotraj kvadrastega prostora med tema dvema detektorjema.

Detektorski element je sestavljen iz scintilatorskega kristala, ki pretvori visokoenergijski foton v mnogo fotonov v vidnem spektru. Te zazna fotodetektor in pretvori v električni signal, ki ga prebere in procesira elektronika.

Parametri v PET

V splošnem so vsi dogodki, ki se zgodijo znotraj koincidenčnega okna obravnavani kot koincidenčni dogodki. To okno je običajno široko nekaj nanosekund. Z napredki

v tehnologiji so mogoče tudi bolj natančne meritve časa detekcije fotonov s časovno resolucijo koincidenč (CTR) reda velikosti nekaj 100 ps. Ta natančnejša meritev časa se imenuje meritev časa preleta (TOF) in se lahko uporabi pri rekonstrukciji za izboljšavo rezultatov. Prav tako ta informacija lokalizira dogodek na LOR z Gaussovo porazdelitvijo, katere širina je sorazmerna s CTR.

Najbolj razširjene naprave za PET sestojijo iz detektorskih modulov v cilindrični konfiguraciji in notranjim premerom okoli 80 cm, kar omogoča zajem podatkov po celem azimutu okoli centra vidnega polja (FOV). Za zajem slike celotnega telesa pacienta se lahko le-tega premika v smeri geometrijske osi skenerja z uporabo motorizirane postelje.

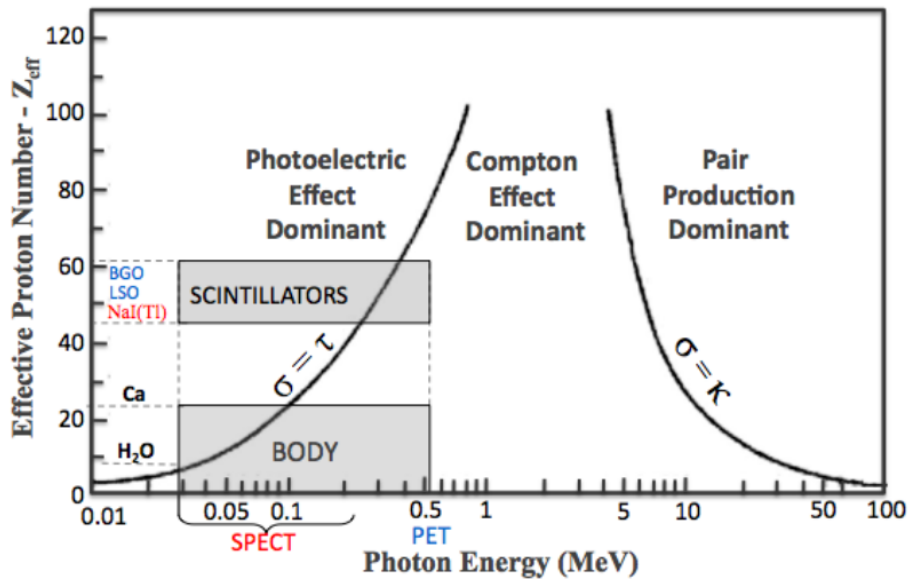
Za različne namene obstajajo specifične naprave z različnimi parametri, ki najbolj ustrezajo specifičnemu problemu. Na primer za slikanje možganov se uporabljajo naprave z manjšim premerom in tudi manjšimi detektorskimi elementi; oboje izboljša prostorsko ločljivost. Drugi primer je naprava za slikanje dojk pod kompresijo, sestavljena iz detektorjev v konfiguraciji dveh plošč. Cene takih skenerjev so dokaj nižje v primerjavi s standardnimi cilindričnimi, saj je za njih potrebnega manj materiala in ne zahtevajo motorizirane postelje. Prav tako so take naprave bolj mobilne.

Drug tip naprav je namenjen slikanju malih živali. Uporabljajo se predvsem v raziskovalne namene, kot so ocenjevanje naprav in optimizacija novih tehnik in radiofarmakov. Zaradi narave subjektov so take naprave dokaj manjše, s premerom okoli 15 cm. Predvsem je pri takih napravah problematična omejena občutljivost in prostorska ločljivost. Zahteve po slednji so strožje kot za običajne naprave, ker gre pri majhnih živalih za sorazmerno manjše strukture, ki jih je potrebno slikati. Z manjšanjem velikosti detektorskih elementov pa se zmanjšuje tudi občutljivost. Ta se delno kompenzira s tem, da lahko take naprave dosežejo večjo kotno pokritost v aksialni smeri glede na velikost subjekta v primerjavi z običajnimi napravami.

Ena izmed smeri razvoja naprav za PET je daljšanje aksialnega FOV naprav, na primer Siemens Biograph Vision Quadra z aksialnim FOV 106 cm, štirikrat več od bolj standardnega skenerja Siemens Biograph Vision 600 [1]. Še daljši pa je skener United Imaging uEXPLORER z aksialnim FOV 194 cm [2]. Oba dolga skenerja omogočata slikanje brez premikanja pacienta. Take naprave omogočajo nove pristope pri slikanju, kot je kinetično slikanje, ki spremlja časovne spremembe v razporeditvi radiofarmaka. Naprave se ponajbolj predvsem s povečano občutljivostjo, kar lahko pomeni, da se lahko doseže bolj kvalitetno sliko v istem času, ali enako kvalitetno sliko v krajšem času, ali enako kvalitetno sliko z nižjo sevalno obremenitvijo. Mogoča je kombinacija vseh treh opcij glede na optimizacijo za določen klinični problem. S povečanjem zahtev po PET bi take naprave lahko povečale število možnih obravnav, ki se jih lahko opravi v nekem časovnem obdobju [3].

Tehniko PET se lahko združuje z drugimi modalitetami slikanja v medicini. Hibridno slikanje združuje tehnike funkcionalnega in anatomskega slikanja. Primera slednjih sta računalniška tomografija (CT) in slikanje z magnetno resonanco (MRI). Oba se za razliko od PET ponajbolj z višjo prostorsko ločljivostjo in nižjim nivojem šuma. Slike CT se tudi uporabljajo pri sami rekonstrukciji slik PET za korekcijo atenuacije in sipanja.

Visokoenergijski fotoni, ki nastanejo pri anihilaciji pozitrona interagirajo z elektroni v snovi predvsem preko fotoefekta in Comptonovega pojava. Pri fotoefektu foton preda svojo celotno energijo elektronu, kjer se je del porabi za premagova-



Slika 1: Prevladujoče interakcije fotonov glede na vrstno število medija in energijo fotonov. Sivi pravokotniki označujejo tipične domene v nuklearni medicini. Specifično za PET je prevladujoča interakcija za anihilacijske fotone vedno Comptonov pojav tako v telesu pacienta kot tudi v scintilatorskih kristalih. Vzeto iz [4].

nje vezavne energije, preostanek pa postane kinetična energija elektrona. Ker gre pri pojavu predvsem za interakcije z elektroni v notranjih lupinah, se pri prehodih elektronov v nižja stanja izsevajo tudi karakteristični žarki X. Ta tip interakcije prevladuje pri nižjih energijah fotonov in pri višjih vrstnih številih atomov. Pri Comptonovem pojavu foton preda le del svoje energije elektronu, v tem primeru predvsem v zunanjih lupinah, in se siplje. Energija sipanega fotona in kot sipanja sta povezana preko enačbe

$$E'_\gamma = \frac{E_\gamma}{1 + \frac{E_\gamma}{m_e c^2} (1 - \cos \theta)}, \quad (1)$$

kjer je E'_γ energija sipanega fotona, E_γ začetna energija fotona, m_e masa elektrona, c hitrost svetlobe in θ kot sipanja fotona. Verjetnost za interakcijo je odvisna od gostote medija, njegovo povprečno vrstno število in energija fotonov določata verjetnost tipa interakcije. Prevladujoče interakcije so prikazane na sliki 1. Atenuacijo ozkega žarka opisuje enačba

$$I = I_0 (1 - e^{-\mu x}), \quad (2)$$

kjer je I število fotonov, ki je interagiralo, I_0 začetno število fotonov, x debelina medija μ linearni koeficient atenuacije, ki je različen za vsak tip interakcije in se vsak prispevek lahko seštevata linearno.

Nastali elektroni izgubljajo svojo energijo preko interakcij z okoliškimi atomi, ki se lahko obravnavajo kot trki z elektroni, kar privede do vzbujenih stanj atomov ali njihovo ionizacijo. Energijo lahko elektroni izgubljajo tudi preko interakcij z jedri atomov in nastankom zavornega sevanja. Pri potovanju elektronov skozi snov lahko nastane tudi svetloba Čerenkova, ko elektron potuje v snovi hitreje od fazne

hitrosti svetlobe. To sevanje lahko v določenih primerih postane zanimivo v konceptu detekcije.

PET skenerji zajemajo različne tipe dogodkov. Prave koincidence so dogodki, kjer sistem zazna oba anihilacijska žarka. Pri sipanem dogodku se en ali oba žarka sipata preko Comptonovega pojava preden sta zaznana, kar dogodku pripiše nepravilen LOR. Če pa se sipanje zgodi znotraj scintilatorskega kristala in temu sledi fotoefekt v enem izmed sosednjih kristalov, se lahko tak dogodek obravnava kot prava koincidenca. Diskriminacija med pravimi in sipanimi dogodki je deloma dosežena z meritvijo odložene energije v kristalu, ki je sorazmerna s svetlobnim odzivom kristala. Preostali sipani dogodki v rekonstruirano sliko dodajajo ozadje, predvsem v centralnem delu slike in s tem znižujejo kontrast slike.

Naključne koincidence so dogodki, kjer zaznana žarka izhajata iz dveh različnih anihilacijskih dogodkov, in posledično napačen LOR. Frekvenca takih dogodkov je odvisna od širine koincidenčnega okna in je približno sorazmerna kvadratu aktivnosti. V rekonstruiranih slikah se naključne koincidence odražajo kot uniformno ozadje preko celotnega FOV in nižanjem kontrasta slike.

Prostorsko ločljivost PET skenerjev določa več faktorjev in je predstavljena kot širina porazdelitve na polovici višine (FWHM). Dimenzija detektorjev določa ločljivost, ki se za dva nasprotna detektorja širine d spreminja od d pri površini detektorja do $d/2$ na sredini med obema. Pozitroni imajo pri razpadu β^+ začetno kinetično energijo, ki jo izgubijo z interakcijami z nabitimi delci. Efektivna pot, ki jo opravijo opiše parameter aritmetične sredine kvadratov (RMS), z vrednostmi med 0.1 mm in 3 mm v vodi, ki je odvisna od začetne energije pozitrona. Do anihilacije pozitrona lahko pride preden ta izgubi celotno gibalno količino in posledično zaradi ohranitve gibalne količine anihilacijska fotona nista izsevana točno pod kotom 180° . Prispevek nekolinearnosti anihilacijskih fotonov je približno $R_{180^\circ} = 0.0022 \cdot D$, kjer je D premer skenerja.

Aproksimacijo prostorske ločljivosti sistema, R_{sis} , poda enačba [5]

$$R_{sis} \approx \sqrt{R_{det}^2 + R_{doseg}^2 + R_{180^\circ}^2}, \quad (3)$$

pri čemer se lahko z zmanjšanjem dimenzij detektorjev zmanjša prispevek R_{det} , z znižanjem premera R_{180° , prispevek dosega pozitronov R_{doseg} je intrinzičen in predstavlja fizikalno mejo ločljivosti.

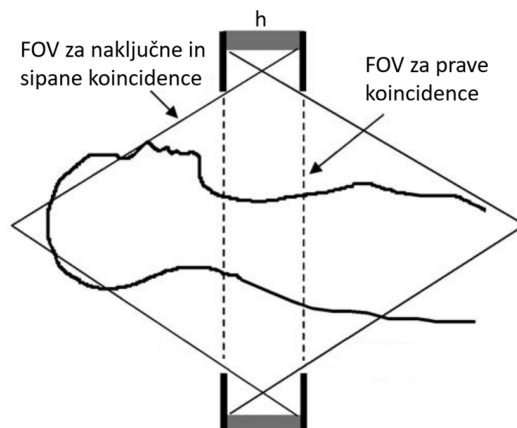
K prostorski ločljivosti prispeva tudi efekt globine interakcije (DOI). Za dogodke katerih LOR ne poteka skozi center FOV velja, da jih lahko zazna večja površina detektorja, kar efektivno poveča prispevek velikosti detektorja k prostorski ločljivosti.

Občutljivost PET skenerjev karakterizira intrinzična učinkovitost detektorjev in geometrijska pokrivnost sistema, ki jo predstavlja prostorski kot, ki ga pokrivajo detektorji. Občutljivost R_{true} opisuje enačba

$$R_{true} = E\epsilon^2 g_{ACD} e^{-\mu T}, \quad (4)$$

kjer je E frekvenca emisije, ϵ intrinzična učinkovitost detektorja, ki jo opisuje brezdimenzijska različica enačbe 2, μ atenuacijski koeficient slikanega objekta in T njegova debelina. Parameter g_{ACD} je geometrijska učinkovitost in vzpostavi delež anihilacijskih fotonov, ki potujejo v smeri detektorjev.

Primer FOV za slikanje pacienta je shematično prikazan na sliki 2.



Slika 2: Shematični prikaz pacienta med zajemom slike. Označeni so FOV za različne tipe dogodkov. Prirejeno po [6].

Detektorji

Lastnost scintilatorjev je, da del energije ionizirajočega sevanja spremenijo v fotone vidne svetlobe, katerih število je proporcionalno odloženi energiji. Delijo se na organske in anorganske. Za organske je značilno, da so scintilacije lastnost molekul iz katerih so narejeni. Zaradi relativno nizke gostote glede na anorganske scintilatorje je njihova intrinzična učinkovitost nizka in se večinoma ne uporabljajo v kliničnih napravah. Najbolj znan primer raziskovalne naprave, ki uporablja plastične scintilatorje je Jagiellonian PET [7].

Pri anorganskih scintilatorjih je mehanizem scintilacij posledica kristalne strukture. Najbolj pogosto uporabljeni scintilatorji v kontekstu PET so LSO ($\text{Lu}_2(\text{SiO}_4)$), LYSO ($\text{Lu}_{2(1-x)}\text{Y}_{2x}\text{SiO}_5$) and BGO ($\text{Bi}_4\text{Ge}_3\text{O}_{12}$).

Poleg gostote, so pomembni parametri scintilatorjev njihovo efektivno vrstno število, ki določa delež sipanih dogodkov, pridelek svetlobe, ki določa količino vidnih fotonov na enoto odložene energije, in časovne karakteristike kristalov. Slednje tri so predvsem pomembne za CTR takega detektorja. Časovno karakteristiko opisujeta parametra čas vzburjanja in razpadni čas scintilacij, ki opisujeta razvoj svetlobnega pulza znotraj kristala. Razpadni čas scintilacij za hitre anorganske kristale je tipično reda velikosti nekaj deset nanosekund, čas vzburjanja pa nekaj deset ali sto pikosekund [8]. Pomemben faktor je tudi lomni količnik kristala zaradi optične sklopitve le-tega in fotodetektorja in vpliva na delež popolnih odbojev fotonov ter produkcijo fotonov Čerenkova. Mehanične lastnosti kot so agregatno stanje, higroskopičnost in mehanična stabilnost vplivajo na stopnjo zahtevnosti pri ravnanju s scintilatorji. En izmed ključnih faktorjev je tudi cena materiala.

Drugi del verige detekcije so fotodetektorji, ki pretvorijo pulz vidne svetlobe v elektronski pulz. V PET so najbolj pogosto uporabljene fotopomnoževalke (PMT) in silicijske fotopomnoževalke (SiPM). Pri fotopomnoževalkah se vidni foton absorbira v fotokatodi, kar sprosti elektron, ki je pospešen do pozitivno nabite dinode. Ob trku z dinodo se sprosti več sekundarnih elektronov, ki so pospešeni do naslednje dinode. Po več stopnjah pomnoževanja so elektroni zbrani na anodi. Red velikosti pomnoževanja signala je okoli 10^6 . Do stohastičnih variacij prihaja predvsem v prvem delu pomnožitve, ko je število elektronov majhno [13].

SiPM sestoji iz mreže fotodiod, ki obratujejo v Geigerjevem režimu. Vsaka

celica lahko zazna po en foton. Red velikosti pomnoževanja signala je okoli 10^6 . Glavni vir šuma pri SiPM so termični nosilci naboja, ki proizvedejo enak signal kot zaznan foton. Frekvenca šuma je odvisna od temperature in je reda velikosti 100 kcps/mm².

Meritev časa preleta se nanaša na dejstvo, da je mogoče izmeriti razliko v časih detekcije obeh koincidenčnih fotonov, če je CTR sistema boljši kot širina koincidenčnega okna, ki je običajno dolg nekaj nanosekund. Brez uporabe TOF je vsak dogodek lokaliziran samo na celotni LOR, z uporabo TOF je lokaliziran z Gaussovo porazdelitvijo, katere širina ustreza CTR sistema. Razdaljo dogodka od centra med obema detektorjema poda enačba

$$\Delta d = \frac{\Delta t \cdot c}{2}, \quad (5)$$

kjer je Δd razdalja od dogodka od centra, Δt časovna razlika med detekcijo obeh dogodkov in c hitrost svetloba. Ista enačba je uporabljena tudi za oceno prostorske nedoločenosti, če časovno razliko nadomestimo s CTR.

Prva generacija TOF-PET skenerjev je bila narejena v osemdesetih letih prejšnjega stoletja. Skenerji tistega časa so dosegali CTR okoli 500 ps, kar je omogočalo izboljšavo razmerja signal šum (SNR) za faktor okoli 3 do 7, odvisno od aktivnosti [17]. Motivacija za izboljšavo CTR je bila deloma ločevanje naključnih dogodkov z oženjem koincidenčnega okna, kar je predvsem pomembno v režimu visokih aktivnosti. Ta generacija je uporabljala predvsem hitre scintilatorje kot na primer BaF₂, ki pa imajo nižjo gostoto in so posledično manj občutljivi. Z začetkom uporabe bolj občutljivih kristalov kot je BGO, je bil TOF v devetdesetih letih v zatonu dokler niso v uporabo prišli LSO in LYSO scintilatorji, ki so združevali dobro časovno karakteristiko in občutljivost. Z napredkom na vseh stopnjah detekcije lahko trenutni klinični skenerji dosežejo CTR 214 ps [20] in celo 189 ps [21]. V raziskovalnih sistemih je bil dosežen CTR 58 ps [8] in 32 ps [22]. Ti rezultati so bili doseženi z enim parom detektorjev in jih ni mogoče na lahek način prenesti v klinične sisteme, ker so bili doseženi z majhnimi kristali, kar pomeni nizko občutljivost in uporabljajo visokofrekvenčno elektroniko, ki zaradi porabe ni skalabilna oziroma so uporabljali fotodetektorje, ki niso primerni za klinične sisteme. Vseeno ti rezultati demonstrirajo potencial za izboljšavo TOF-PET skenerjev.

Vsak del detektorja prispeva k CTR in zahteva optimizacijo za doseganje najboljših rezultatov, in postavljen je bil načrt, katerega cilj se je pomikati proti teoretični meji CTR 10 ps [23].

Prispevek scintilatorja k CTR aproksimira enačba [24]:

$$\text{CTR} = 2.18 \sqrt{\frac{\tau_r \tau_d c}{n}}, \quad (6)$$

kjer je τ_r čas vzbujanja, τ_d razpadni čas scintilacij, c hitrost svetlobe in n število zaznanih fotonov. Z uporabo enega izmed trenutnih najboljših scintilatorjev (LSO:Ce:Ca), bi bil ta prispevek okoli 12 ps. Poleg materialnih karakteristik scintilatorja na CTR vpliva tudi dimenzija kristala. Daljši kristali izboljšajo občutljivost, ampak poslabšajo CTR, poleg tega pa so tudi dražji.

Tudi elektronika [25] in fotodetektorji [26] prispevajo k CTR sistema.

Izboljšavo SNR zaradi uporabe TOF aproksimira enačba [27]:

$$\text{SNR}_{\text{TOF}} = \sqrt{\frac{D}{\Delta d}} \text{SNR}, \quad (7)$$

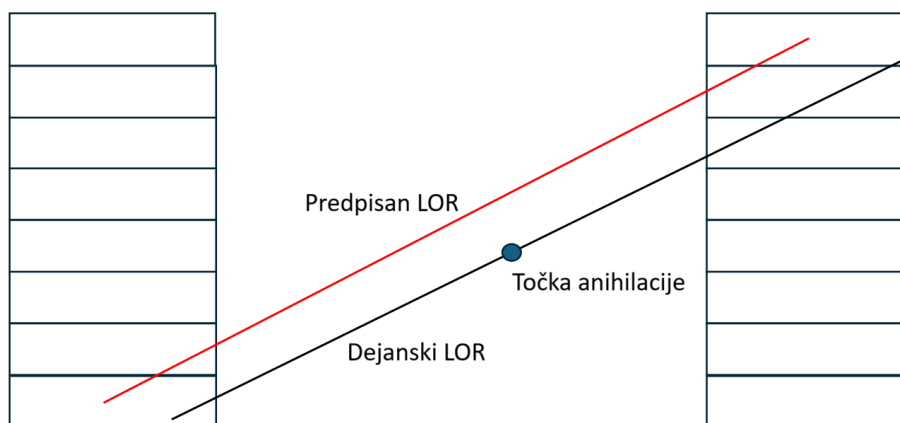
kjer je SNR_{TOF} izboljššan SNR , D širina slikanega objekta in Δd prostorska nedoločenost, ki jo poda enačba 5. Enačba velja samo v zelo specifičnih pogojih, vendar lahko služi kot aproksimacija. Izboljšava SNR zaradi TOF lahko pomeni izboljšavo slik, krajše čase slikanj (in posledično večje število slikanj na napravo) ali znižanje sevalne obremenitve za paciente.

V PET skenerjih, ki uporabljajo PMT se pogosto uporablja zasnova blok detektorja [29]. To pomeni, da ni vsak kristal sklopljen na svoj fotodetektor, ampak je večji blok scintilatorja, ki je delno ločen na na primer 64 elementov, sklopljen na samo 4 PMT. S tem se lahko izboljša prostorska ločljivost detektorja brez povečanja cene zaradi fotodetektorjev. Lokacija interakcije znotraj kristala je preračunana glede na odziv vseh sklopljenih fotodetektorjev. V sistemih, ki uporabljajo SiPM fotodetektorje, je bolj običajna sklopitev enega kristala na en fotodetektor.

Obstaja več načinov meritve globine interakcije. Diskretni načini vključujejo sisteme z več zaporednimi sloji detektorjev. Diskriminacija med plastmi lahko poteka na primer preko različnih časovnih odzivov plasti, ki uporabljajo različne materiale scintilatorjev ali ima vsak sloj scintilatorjev svoj fotodetektor. Zvezni način meritve DOI poteka preko kristalov, ki imajo fotodetektorje na obeh straneh. Meritev DOI omogočajo tudi monolitni detektorji, kjer je modul sestavljen iz enega večjega kristala in mnogih fotodetektorjev [32].

Ena izmed smeri raziskav v kontekstu PET naprav so redke geometrije. V takih sistemih niso več vsi detektorski elementi postavljeni v tesni konfiguraciji, ampak so razmaknjeni na različne načine. Pokazano je bilo, da se kvaliteta slike ohrani do neke mere tudi če bi manjkal ali vsak drugi obroč ali vsaka druga vrsta detektorjev, zaradi česar se občutljivost sistema zmanjša na 25 % prvotne vrednosti [33]. Po drugi strani redka geometrija lahko pomeni večjo pokritost v aksialni smeri brez povečanja števila detektorskih elementov, oziroma cene skenerja, kar je bilo preizkušeno z razmikom obročev detektorjev in porazdelitvijo detektorjev v šahovnico [34]. Še en pristop k redki geometriji je uporaba kristalov z manjšim presekom od fotodetektorja. S tem se cena sistema zniža zaradi manjše zahteve po scintilatorju kljub temu, da se samo število detektorskih elementov ne spremeni. Taka konfiguracija lahko potencialno izboljša CTR sistema, ker se izboljša učinkovitost zbiranja vidne svetlobe.

Še en primer nestandardne geometrije je odprta geometrija, pri kateri gre za omejeno kotno pokritost po azimutu naprave. Take naprave so uporabne v zelo specifičnih kliničnih situacijah, predvsem ko je pomemben dostop do pacienta. Ne-popolno vzorčenje po azimutu privede do artefaktov v rekonstruirani sliki. Te je možno omiliti ali z rotacijo skenerja ali pa z uporabo TOF informacije med rekonstrukcijo. Bolj pomanjkljivo vzorčenje zahteva izboljšavo v CTR skenerja [35]. Odprta geometrija naravno privede tudi do opcije nove geometrije skenerjev, in sicer z uporabo ploščate geometrije namesto cilindrične. Odprta geometrija je zanimiva tudi iz pogleda zmanjševanja cene sistema zaradi manjšega števila detektorskih elementov. Ploščata geometrija načeloma omogoča modularno zasnovo sistema, kar pomeni, da bi se paneli detektorjev lahko postavljali v različnih konfiguracijah in se prilagodili specifičnim kliničnim situacijam. Primeri postavitve vključujejo po 2 ali 4 panele okoli pacienta in več zaporednih panelov, za večjo pokritost v aksialni smeri. Prav tako bi bilo mogoče spreminjati razdaljo med paneli detektorjev, kar vpliva



Slika 3: Ilustracija paralakse za poševne LOR v ploščati geometriji PET skenerja. Rdeča črta prikazuje predpisan LOR in črna črta dejanski LOR za nek specifičen dogodek.



Slika 4: Ilustracija efekta DOI na par detektorskih elementov. V tem primeru DOI ne pripomore k pripisovanju napačne LOR, ampak vpliva na CTR, ker bi bili vidni fotoni zaznani bolj zgodaj na levem detektorju.

tako na občutljivost kot tudi prostorsko ločljivost sistema. Tak sistem bi bil lahko tudi narejen lažji ali celo mobilni in ne bi zahteval namenske sobe za skener, čeprav bi tudi tak sistem načeloma zahteval CT sliko za popravke atenuacije in sipanja pri rekonstrukciji slike.

Pri ploščati geometriji v primerjavi s cilindrično pride še bolj do izraza paralaksa zaradi efekta DOI. Pri takih geometrijah vse poševne LOR privedejo do teh napak, kar pomeni, da dejanska LOR ne ustreza pripisani LOR, kar je prikazano na sliki 3. Težave predstavljajo predvsem sistemi z daljšimi scintilatorskimi kristali. Meritve DOI bi bile koristne za take sisteme, saj bi se tako izboljšala tako prostorska ločljivost kot tudi občutljivost zaradi možnosti uporabe daljših kristalov. Poleg tega bi meritev DOI lahko pripomogla k izboljšanju CTR sistema. Pri tem gre za dejstvo, da vidni fotonu po scintilatorju potuje počasneje kot visokoenergijski fotoni. Njihovo hitrost določa lomni količnik snovi. Na sliki 4 je prikazana ilustracija primera, kjer eden izmed anihilacijskih fotonov interagira blizu fotodetektorja in drugi na nasprotni strani. DOI ima učinek na CTR tako pri poševnih kot tudi vodoravnih LOR.

Tomografska rekonstrukcija

Meritev pri PET je število zaznanih dogodkov na vsaki LOR, ki povezuje vsak par detektorskih elementov. Te podatke je potrebno rekonstruirati v 3D matriko, ki predstavlja razporeditev radiofarmaka v telesu subjekta oziroma fantoma.

Parametrizacija LOR je lahko narejena z uporabo 4 parametrov. Prvi je najkrajša razdalja LOR projicirana na ravnino XY iz centra FOV p , kot LOR ϕ , aksialna pozicija $z = 0.5 \cdot (z_1 + z_2)$ kjer je z_i aksialna pozicija vsakega izmed detektorjev

in aksialni kot θ , ki ga določa razlika med obroči detektorjev za nek dogodek. Histogrami, ki jih karakterizirata parametra p in ϕ , se imenujejo sinogrami. Dogodke je moč shranjevati tudi kot podatke v načinu seznama, kjer se za vsak dogodek shranijo relevantni podatki, kot so energija, čas in identifikacija detektorja.

Dva izmed najbolj pogosto uporabljenih rekonstrukcijskih algoritmov sta filtrirana povratna projekcija (FBP) in iterativni rekonstrukcijski algoritmi. Pri FBP je najprej potrebno opraviti Fourierovo transformacijo (FT) meritve, jo pomnožiti s filtrom še enkrat opraviti FT in nato povratno projicirati. Problem pri FBP je predvsem, da zahteva popolno vzorčenje po azimutu, torej algoritem ni primeren za odprte geometrije.

Iterativni algoritmi delujejo preko postopne aproksimacije resnične porazdelitve vira sevanja. Začnejo lahko z uniformno sliko, ki je nato projicirana in primerjana z dejanskimi meritvami slikanega objekta. Razlika med obema je uporabljena za naslednjo iteracijo aproksimacije slike.

Popravki pri rekonstrukciji

Normalizacijo je pri rekonstrukciji potrebno opraviti zaradi variacij v zbranih podatkih zaradi razlik med individualnimi detektorskimi elementi in zaradi efekta DOI, ki ima vpliv na dogodke s poševnim LOR. V osnovi gre pri popravku za izpostavljanje elementov uniformnemu viru sevanja. Normalizacijski faktor se lahko preračuna iz števila zaznanih dogodkov za vsak detektorski element.

Frekvenco naključnih koincidenč se lahko oceni z uporabo zamaknjenega koincidenčnega okna. To pomeni, da se za nek zaznan dogodek išče koincidenčne pare z nekimi dogodki po nekem arbitrarnem času, kar pomeni, da so vse tvorjene koincidence samo naključne in se predpostavi, da je frekvenca neodvisna od izbire tega časovnega zamika. Popravek se izvede z odštevanjem izmerjenih naključnih koincidenč od vseh pri običajnem koincidenčnem oknu.

Sipani dogodki so deloma filtrirani z energijsko diskriminacijo, vendar to ni zadostno. Popravki se lahko izvajajo na različne načine od Monte Carlo simulacij do statističnih modelov in uporabe mnogih energijskih oken. Prav tako se za popravke lahko uporabljajo slike CT ali transmisijske slike.

Anihilacijski fotoni, ki potujejo skozi slikani subjekt so atenuirani zaradi prepotovane poti skozi material. Popravek se izvaja predvsem z uporabo slik CT ali transmisijskih slik, kjer se palica aktivnosti rotira po obodu skenerja. Zaradi potrebe po slikah CT je mnogo skenerjev hibridnega tipa in združuje skener PET s skenerjem CT, manj pogosto tudi skener MRI.

Meritve zmogljivosti pri PET

Za standardizacijo meritev na različnih PET skenerjih je National Electrical Manufacturers Association (NEMA) izdala standarde za postopke ocene zmogljivosti [55].

Ocena prostorske ločljivosti je opravljena s slikanjem in rekonstrukcijo točkastega vira sevanja na različnih pozicijah. Predpostavlja uporabo FBP in oceno FWHM linearnega profila rekonstruirane slike s parabolično prilagoditvijo za iskanje maksimuma in linearno interpolacijo za določitev širine.

Meritve frekvence različnih tipov dogodkov je opravljeno s cilindričnim fantomom in linearnim virom. Uporablja se metrika hitrost štetja, ekvivalentna šumu (NECR), ki jo določa enačba

$$\text{NECR} = \frac{T^2}{T + S + R}, \quad (8)$$

kjer je T frekvenca resničnih dogodkov, R frekvenca naključnih dogodkov in S frekvenca sipanih dogodkov.

Meritev občutljivosti se izvaja z uporabo plastičnega cilindričnega fantoma napolnjenega z mešanico vode in radioizotopa. Zaradi atenuacije anihilacijskih fotonov je meritev ponovljena z dodajanjem vedno večjih železnih okvirov okoli fantoma, ki povzročajo dodatno atenuacijo. Preko ekstrapolacije se potem lahko določi vrednost občutljivosti brez atenuacije.

Za kvaliteto slike se uporabljata metriki kontrast in variabilnost ozadja. V tem primeru se uporablja fantom, ki je oblikovan podobno prečnemu preseku človeka v trebušnem delu telesa. Fantom je napolnjen z raztopino s specifično aktivnostjo 5.3 kBq/ml, kar služi za ozadje pri meritvi. Fantom vsebuje 6 sfer različnih premerov, ki vsebujejo raztopino s štirikrat višjo specifično aktivnostjo. Centralni del fantoma ne vsebuje aktivnosti in je napolnjen z materialom z nižjo gostoto, ki simulira pljučno tkivo. Kontrast Q določa enačba:

$$Q = \frac{\frac{C_h}{C_b} - 1}{\frac{a_h}{a_b} - 1} \cdot 100\%, \quad (9)$$

kjer je C_h povprečno število dogodkov v regiji interesa (ROI) v vroči sferi, C_b povprečno število dogodkov v ROI ozadja, kjer se uporablja sfere enake velikosti na 60 različnih pozicijah znotraj fantoma, a_h specifična aktivnost v vročih sferah in a_b specifična aktivnost v ozadju. Variabilnost ozadja BV določa enačba

$$BV = \frac{\sigma_b}{C_b} \cdot 100\%, \quad (10)$$

kjer je σ_b standardna deviacija dogodkov v ROI ozadja.

Metodologija

Simulacije

Monte Carlo simulacije so bile izvedene z odprtokodnim orodjem GATE v8.2 [56]. V splošnem je potek dela vključeval definicijo geometrije detektorja, materiala scintilatorjev, energijsko in časovno karakteristiko detektorja in shemo branja podatkov. Nato je bila definirana geometrija in porazdelitev aktivnosti slikanega fantoma. Generirani so bili dogodki parov anihilacijskih fotonov, katerih lokacija in usmerjenost je bila naključno določena glede na porazdelitev aktivnosti. Pri potovanju skozi snov lahko fotoni interagirajo z verjetnostjo glede na svojo energijo in na medij. Sledi se jim dokler se ali ne absorbirajo preko fotoefekta ali zapustijo vnaprej definirano območje, v tem primeru kocka s stranjo 4 m. Fizikalni procesi scintilacije in kasnejših korakov niso bili simulirani, zaradi računskih zahtev teh procesov. Odziv detektorjev je bil simuliran znotraj orodja GATE z modulom digitizer. Vsak par anihilacijskih fotonov je popolnoma neodvisen, kar pomeni možnosti paralelizacije problema, in sicer so bile simulacije razdeljene med mnogo procesorjev.

Uporabljena sta bila dva sistema za PET znotraj GATE *ecat* in *cylindricalPET*. Za simulacijo fizikalnih sistemov je bil uporabljen seznam procesov *emstandard_opt4*.

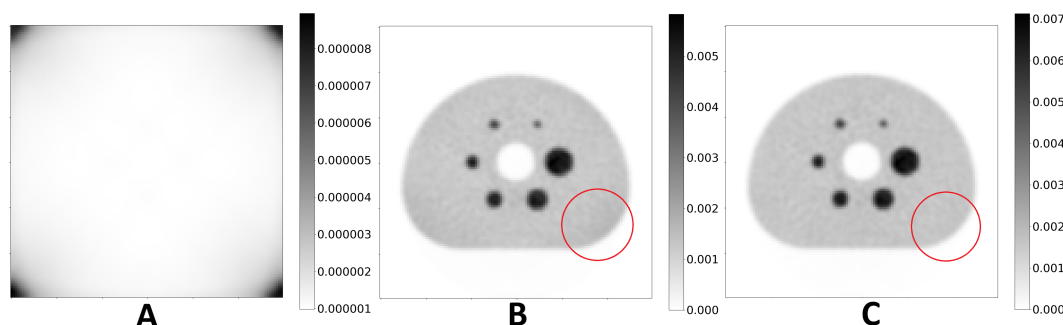
Modul digitizer je bil sestavljen iz več členov. Prvi je *adder*, ki mu je sledil *readout*, kjer je bil parameter *depth* nastavljen ali na 2 za *ecat* sisteme, ali na 3 za *cylindricalPET* sisteme. Politika branja energy-centroid je bila uporabljena za referenčni skener in winner-takes-all politika za ostale. Naslednji člen je bil *energy blurring*, kjer je bila nastavljena energijska ločljivost. Temu sta sledila *thresholder* in *upholder*, ki sta definirala energijsko okno. Zadnji člen modula je služil časovni karakteristiki, ki je dodal Gaussov filter v časovni domeni. Modul digitizer je tako sestavil posamezne zaznane dogodke, ki so bili nato razvrščeni v koincidence preko politike *takeAllGoods*.

Rekonstrukcije

Rekonstrukcija slik je bila izvedena z odprtokodnim orodjem CASToR v3.1.1 [58]. Orodje je bilo uporabljeno, da je pretvorilo geometrijo iz GATE formata v uporabnega za rekonstrukcijo, nato da je pretvorilo zbrane podatke iz formata CERN ROOT v način seznama v skladu z geometrijo in ostalimi parametri skenerja. Pri simulacijah so tipi dogodkov poznani, zato so bili za poenostavitev pri rekonstrukciji uporabljene samo prave koincidence.

Orodje CASToR omogoča nastavitve mnogih rekonstrukcijskih parametrov in algoritmov. V vseh primerih je bil uporabljen iterativni algoritem MLEM. Parametri velikosti vokslov, projektorji in velikosti slike so bili izbrani po potrebah specifičnih študij.

Orodje omogoča tudi popravek za normalizacijo in atenuacijo. Zaradi uporabe nestandardne ploščate geometrije, ki presega obseg validacije za uporabljena orodja, so bili v nekaterih primerih potrebni dodatni popravki. V teh primerih je bila dodatno simulirana homogena kocka aktivnosti, ki je sovpadala z izbrano velikostjo rekonstruirane slike. V idealnem primeru bi bila tudi rekonstruirana slika tako samo homogena slika (z izjemo variacij zaradi šuma). Za filtriranje šuma in glajenje slike je bil uporabljen širok Gaussov filter. Druge slike so bile deljene s to homogeno sliko in pomnožene z njeno povprečno vrednostjo, da so vrednosti vokslov ostale približno



Slika 5: Rekonstruirana slika homogene kocke aktivnosti (A). Rekonstruirana slika fantoma za kvaliteto slike s standardno normalizacijo (B) in dodatno normalizacijo (C). Rdeč krog označuje najbolj očitno razliko med obema slikama: nehomogenostjo ob robu rekonstruiranega fantoma.

enake. Primer dodatne normalizacije je prikazan na sliki 5.

Zaradi računske kompleksnosti simulacij in rekonstrukcij so bili uporabljeni viri Slovenskega nacionalnega superračunalniškega omrežja (SLING), predvsem super-računalnik HPC Vega [59].

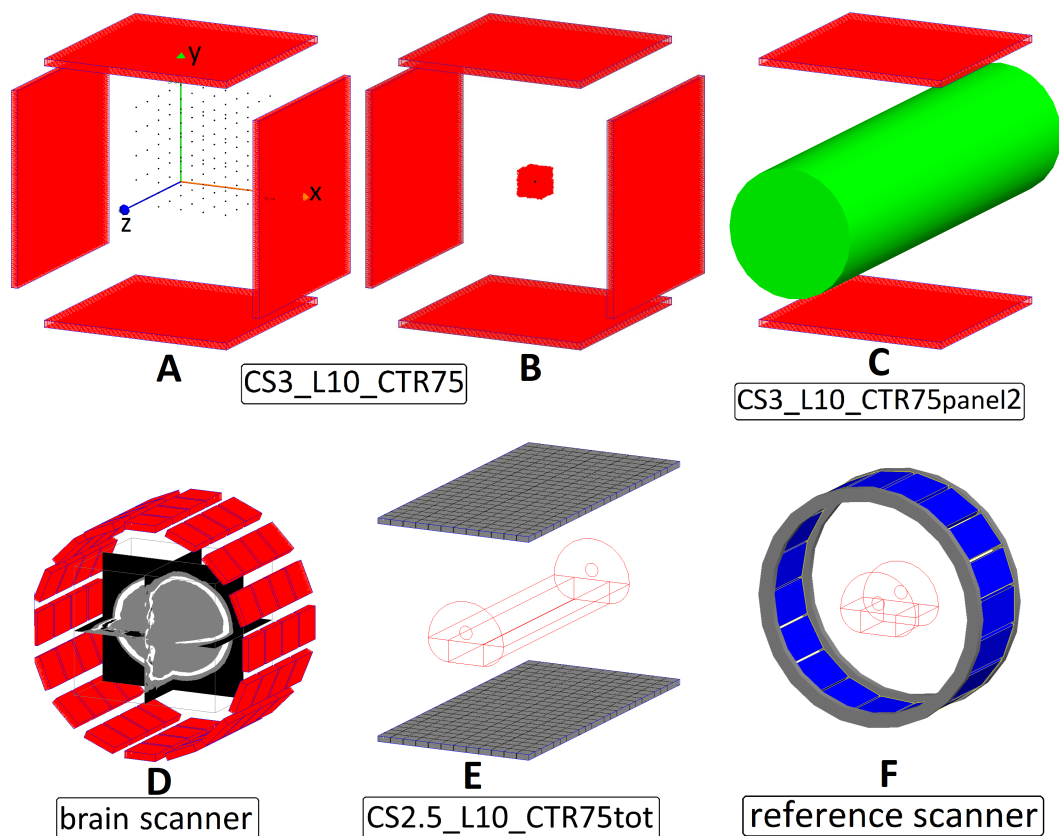
Geometrija in parametri skenerjev

Simuliranih je bilo več različnih skenerjev s ploščato geometrijo. Najbolj pogosti so bili skenerji iz 4 plošč dimenzije $30 \times 30 \text{ cm}^2$ od katerih je bila vsaka sestavljena iz 100×100 kristalov, ki pa so imeli različne dolžine in prečne preseke in razmik med kristali 3 mm. Prav tako so bile preizkušene različni CTR takih skenerjev. Preverjene so bile različne strategije branja, in sicer na nivoju kristala, kar je ekvivalentno temu, da je vsak kristal neodvisen in sklopljen s svojim fotodetektorjem in na nivoju modula, kjer je bilo po več kristalov zbranih skupaj. Ta izbira predstavlja kompromis med občutljivostjo in prostorsko ločljivostjo.

Za izboljšanje čitljivosti rezultatov je bila implementirana shema poimenovanja skenerjev. V osnovi sledi strukturi, kjer so napisani glavni parametri skenerja: **CS<prečni presek>_L<dolžina>_CTR<CTR>**. Na primer oznaka CS3_L10_CTR75 označuje skener s presekom scintilatorjev $3 \times 3 \text{ mm}^2$, dolžino 10 mm in CTR 75 ps. Parametri, ki so bili enaki za večino skenerjev so bili izpušeni (razmik med kristali 3 mm, število panelov 4, strategija branja, ki je bila na nivoju kristala) in dodani v pripono samo v primerih ko so drugačni. Pripona tot je bila dodana za podaljšani skener in v primeru omejenega aksialnega sprejemanja dogodkov je bil tej priponi dodan še ta parameter (tot25 bi pomenil, da je sprejemanje dogodkov omejeno na 25 cm).

Energijska ločljivost sistema je bila nastavljena na 10 % pri 511 keV in energijsko okno je bilo nastavljeno od 435 keV do 585 keV. Koincidenčno okno je bilo v večini primerov nastavljeno na 2 ns, razen za dolge aksialne konfiguracije, kjer je bilo nastavljeno na 4 ns.

Za primerjavo zmogljivosti skenerjev je bila uporabljena simulacija standardnega kliničnega skenerja Siemens Biograph Vision 600, ki je bil simuliran glede na specifikacije objavljene v [20] in bo imenovan referenčni skener. Velikost kristalov v tem sistemu je $3.2 \times 3.2 \times 20 \text{ mm}^3$ in so razvrščeni v modulih v obroču notranjega premera 78 cm. Aksialen FOV skenerja je 26.3 cm. Koincidenčno okno je bilo nastavljeno



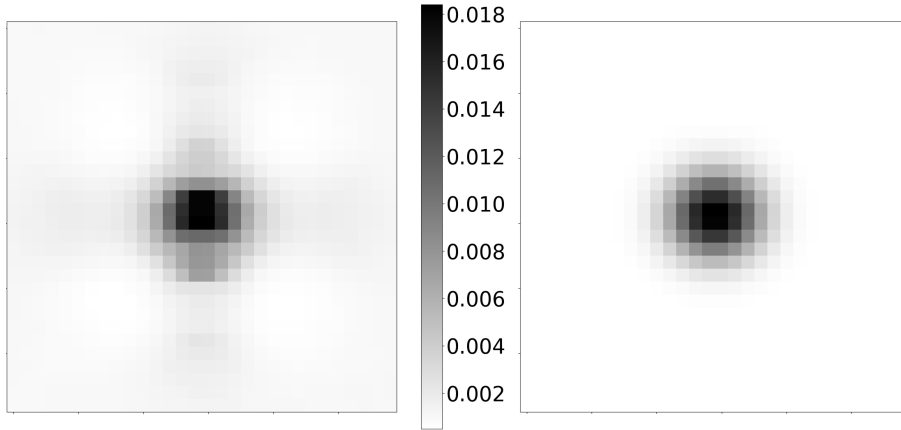
Slika 6: Vizualizacije različnih simuliranih skenerjev in fantomov. (A) skener iz 4 panelov in mrežo točkastih virov sevanja, (B) skener iz 4 panelov in enim točkastim virom sevanja obdanim s homogeno kocko aktivnosti, ki služi kot ozadje, (C) skener iz 2 panelov in fantomom za NECR, (D) skener za možgane in možganski fantom, (E) podaljšan skener in podaljšan fantom za kvaliteto slike, (F) referenčni skener in fantom za kvaliteto slike. Dodani so tudi primeri poimenovanj skenerjev.

na 4.7 ns, energijski parametri pa enako kot za skenerje v ploščati geometriji.

Različne konfiguracije skenerjev in fantomi so prikazani na sliki 6.

Simulacijske študije

Zaradi nestandardnih simuliranih sistemov je bilo potrebno spremeniti pristop za oceno prostorske ločljivosti. Najbolj očitna je bila potreba po spreminjanju rekonstrukcijskega algoritma, saj FBP ni primeren za odprte in ploščate geometrije. V vseh rekonstrukcijah je bil uporabljen algoritem MLEM, tudi za standardne cilindrične sisteme. Standardna metoda predvideva cilindrično simetrijo in predpostavlja, da je informacija o ločljivosti na nekaj pozicijah zadostna za nek skener. V ploščati in odprti geometriji to ni nujno očitno, zato je bila simulirana mreža 125 virov postavljenih v kocko $5 \times 5 \times 5$ in razmikom 37 mm. Viri so bili postavljeni v homogeno ozadje v obliki kocke s stranico 4 cm. Ker viri v taki postavitvi ne sovpadajo z osmi skenerja, je bila namesto ločljivosti v tangencialni in radialni smeri opazovana ločljivost v smereh X in Y . Aksialna oziroma smer Z je v obeh primerih enaka. Rekonstruirani viri so bili prilagojeni Gaussovi funkciji v treh dimenzijah po enačbi



Slika 7: Primer rekonstruiranega točkastega vira (levo) in prilagojena Gaussova funkcija (desno) v transverzalni ravnini. Uporabljen je bil skener z designacijo CS3_L10_CTR75.

$$f(x, y, z) = A \cdot e^{-\left(\frac{(z-z_0)^2}{2\sigma_z^2} + \frac{(y-y_0)^2}{2\sigma_y^2} + \frac{(x-x_0)^2}{2\sigma_x^2}\right)} + C, \quad (11)$$

kjer je A normalizacijska konstanta, ker so bile vrednosti podane v arbitrarnih enotah, x_0 , y_0 in z_0 določajo lokacijo centra vira, σ_i standardne deviacije v vseh treh smereh in C konstanta, ki upošteva ozadje. Ločljivost je bila izračunana kot FWHM iz standardne deviacije v vsaki smeri. Primer rekonstruiranega točkastega vira je prikazan na sliki 7. Raziskovan je bil tudi vpliv velikosti vokslov in števila iteracij v rekonstrukciji.

Za kvaliteto slike je bil simuliran NEMA fantom. Simulirani so bili zajemi dolgi 1 min (t.j. ekvivalentno 1 min zajema z resničnim skenerjem). Rekonstrukcije so bile opravljene s 50 iteracijam in velikost vokslov je bila $3 \times 3 \times 3 \text{ mm}^3$. Pri tej študiji je bila opravljena dodatna normalizacija prikazana na sliki 5.

Za podaljšani skener je bila uporabljena modificirana različica NEMA fantoma (slika 6 E). Glavni razliki sta bili podaljšanje fantoma iz 18 cm na 100 cm in da so bili ohranjene samo manjše 3 vroče sfere, ki so bile tudi replicirane na več mestih. Namesto večjih treh sfer so bili simulirani cilindri enakih premerov in specifičnih aktivnosti kot vroče sfere. Pri tem fantomu je bil namen predvsem določiti spremembe kontrasta vzdolž aksialne smeri. Zaradi nestandardne geometrije je bilo potrebno tudi omejiti sprejemanje dogodkov, v tem primeru na 25 cm.

Meritev občutljivosti je bila poenostavljena, ker so pri simulacijah možni viri brez fantoma, torej brez atenuacije. Simulirani so bili posamezni točkasti viri preko celotne aksialne smeri, v središču FOV v inkrementih 1 mm. Za to metriko niso potrebne rekonstrukcije, ampak le štetje dogodkov.

Za metriko NECR je bil uporabljen cilindričen fantom z linearnim virom. Tudi pri tej metriki niso potrebne rekonstrukcije. Da bi metrika upoštevala tudi izboljšavo do katere pride zaradi CTR sistema, je bila modificirana z enačbo

$$\text{NECR}_{\text{TOF}} = \frac{2D}{c\Delta t} \text{NECR}, \quad (12)$$

kjer je D premer slikanega objekta, Δt CTR sistema in c hitrost svetlobe.

Za primer realističnega kliničnega problema je bil uporabljen visokoločljivostni digitalni možganski fantom [62]. Fantom je bil uporabljen predvsem za neposredno kvalitativno oceno zmogljivosti skenerjev. Za kvantitativno oceno je bila uporabljena metrika strukturne podobnosti (SSIM) [63]. Slike so bile rekonstruirane s 50 iteracijam in velikostjo vokslov $1 \times 1 \times 1 \text{ mm}^3$.

Eksperimentalne meritve

Eksperimentalne meritve so bile izvedene na najbolj poenostavljeni postavitvi za PET. Uporabljen je bil en par detektorskih elementov in točkast vir sevanja ^{22}Na . Postavitev je prikazana na sliki 8. Vsak detektorski element je bil sestavljen iz scintilatorskega kristala zavitega v politetrafluoretilen (Teflon), ki je bil optično sklopljen na fotodetektor, vklopljen na ojačevalnik na tiskanem vezju in nazadnje na osciloskop. Za optično sklopitev so bili uporabljeni sledeči mediji:

- Silikonska mast (Rexon Components Inc. RX-688)
- Gel za sklopitev optičnih vlaken (Thorlabs G608N3)
- Prosojni lepilni trak (Thorlabs OCA8146-3)
- Cargille MeltmountTM 1.582

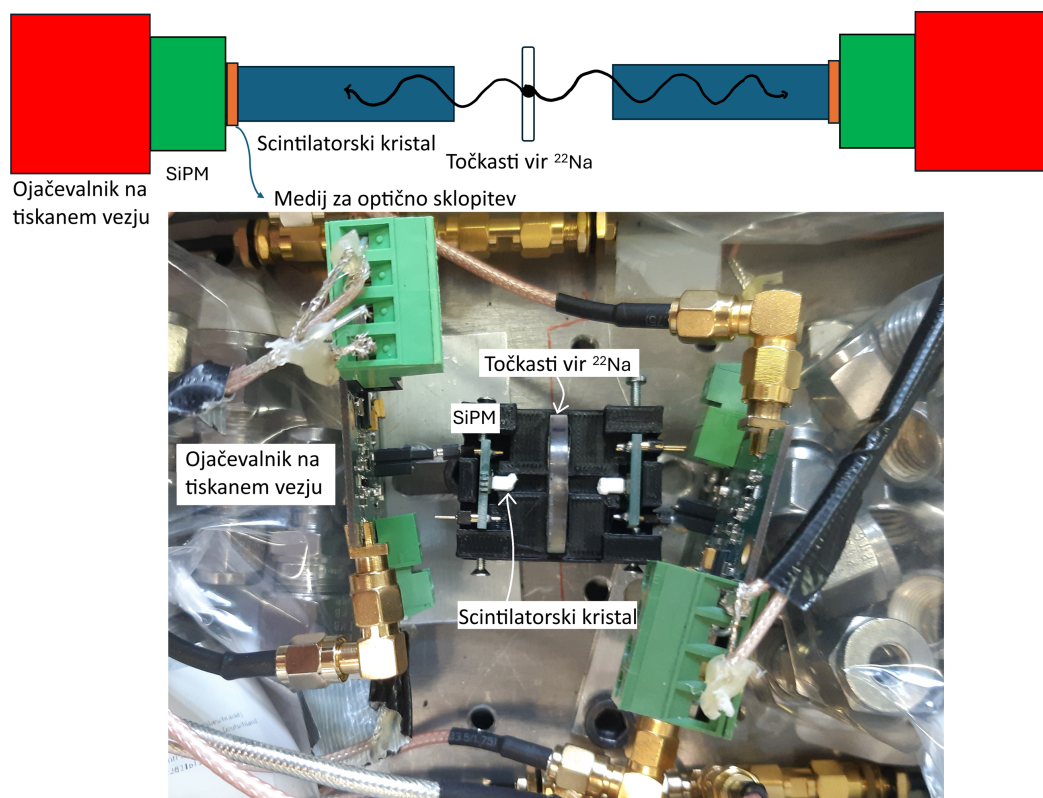
Za detekcijo vidnih fotonov so bili uporabljeni SiPM, ki jih je naredil raziskovalni inštitut Fondazione Bruno Kessler (FBK). V večini primerov je bil uporabljen model z nezaščiteno aktivno površino velikosti $3 \times 3 \text{ mm}^2$. Nepokritost je omogočila boljši CTR, vendar je tudi vodila v poškodbe aktivne površine po večkratnem sklapanju kristalov. Model fotodetektorjev je bil FBK NUV-HD-MT low field, $3 \text{ mm} \times 3 \text{ mm}$, $40 \text{ }\mu\text{m}$ LF-M0.

Elektroniko so zasnovali raziskovalcu iz Institut de Ciències del Cosmos, Univerze v Barceloni. Ta je signal razdelila na dva dela in vsakega ojačila do različne mere. Bolj ojačani signal je služil za določanje časa, manj ojačani za določanje energije dogodka.

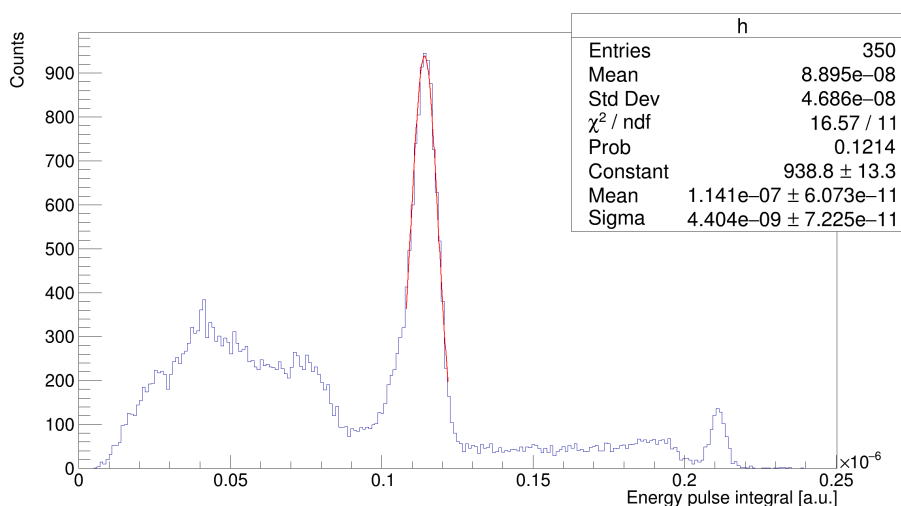
Signal je bil shranjen z osciloskopom in nato analiziran na računalniku. Za meritve CTR je bil uporabljen osciloskop Teledyne LeCroy LabMaster 10 Zi-A 36 GHz. Tekom meritev so bile uporabljene tudi DRS4 evalvacijska plošča, LeCroy WAVE-PRO 7300A in celo modularna elektronika, vendar so se ti inštrumenti izkazali za nezadostne kar se tiče časovne zmogljivosti, predvsem za CTR pod 100 ps. Uporabljeni so bili za študijo svetlobnih pulzov scintilatorjev.

Postavitev je bila najprej uporabljena za meritve pridelka svetlobe različnih scintilatorjev različnih proizvajalcev. Priderek svetlobe je eden izmed faktorjev, ki določa CTR detektorja (enačba 6). Za indikator pridelka svetlobe je bil uporabljen integral energijskega pulza. Iz tega brez kalibracije ni mogoče ugotoviti dejanskega števila zaznanih fotonov, ampak le relativne razlike med posameznimi meritvami. Rezultati integralov so bili zbrani v histogramih, kjer je bila s prilagajanjem Gaussove funkcije ugotovljena pozicija fotovrha iz spektra. Primer histograma je prikazan na sliki 9. Drugi sklop meritev je bil opravljen za testiranje časovne stabilnosti medijev za optično sklopitev.

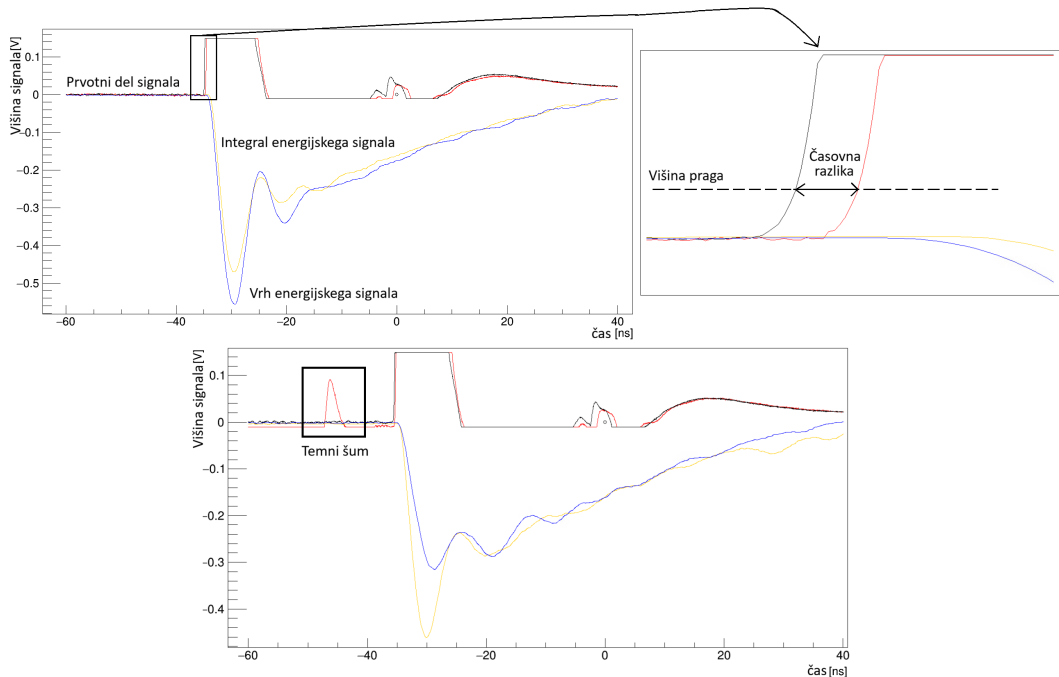
Meritve CTR so potekale preko analize posameznih signalov za vsak dogodek posebej. Pri časovnem signalu je bil prvi korak oceniti in popraviti prvotno vrednost signala pred prihodom scintilacijskih fotonov. Izračunana sta aritmetična sredina



Slika 8: Shema (zgoraj) in slika (spodaj) eksperimentalne postavitve para koincidenčnih detektorjev in vira sevanja.



Slika 9: Histogram integralov energijskih signalov, ki kaže spekter anihilacijskih fotonov. V rdeči barvi je prikazana prilagojena Gaussova funkcija. Pri višjih energijah je opazen tudi dodaten fotovrh pri 1274.5 keV zaradi fotona, ki tudi nastane pri razpadu izotopa ^{22}Na .



Slika 10: Zajeti signal iz obeh detektorjev. Prikazani so pozitivni časovni signali in negativni energijski. V spodnjem delu je prikazan primer temnega šuma in posledično nepravilen popravek signala (celoten signal je rahlo zamaknjen navzdol).

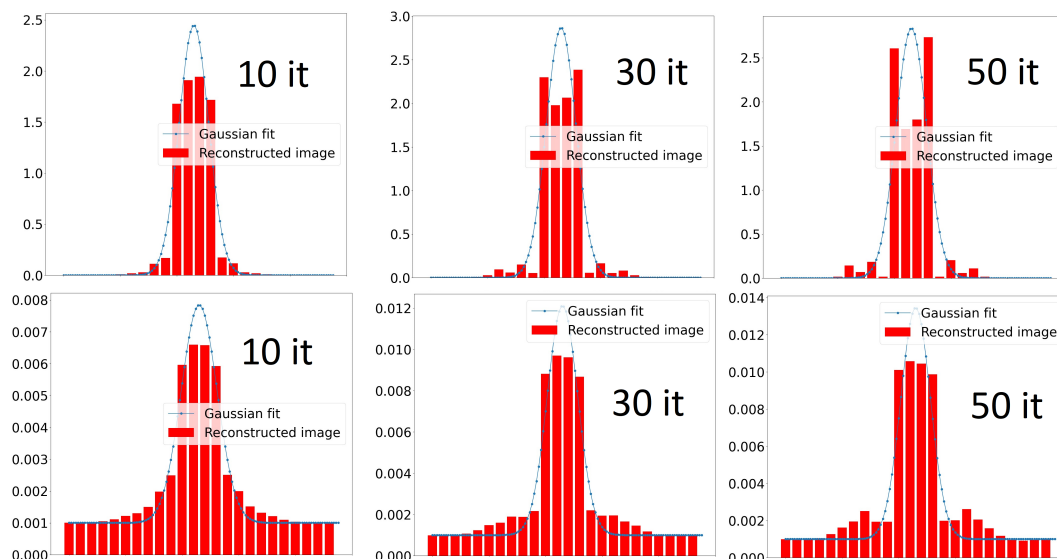
prvotnega dela, za katerega se nato zamakne celotni signal in RMS, ki opiše nivo šuma. Časovna vrednost signala je bila izračunana na različnih višinah praga z uporabo linearne interpolacije. Vrednosti časov obeh časovnih signalov sta bili nato odšteti in dodani v histogram.

Energijski signal je služil za ločevanje dogodkov. S histogramiranjem višine energijskega signala je bil narejen spekter, podobno meritvam svetlobnega pridelka. Fotovrh je bil določen preko prilagajanja z Gaussovo funkcijo. Rez na energiji je vseboval interval $[\mu - 0.5\sigma, \mu + 0.7\sigma]$, kjer je μ lokacija fotovrha in σ njegova standardna deviacija. Interval ni simetričen in je pristranski k višjim energijam, kar zniža verjetnost sipanih dogodkov in izboljša CTR. Poleg reza na energiji, je bil narejen še rez na šumu iz meritve RMS začetnega dela časovnega signala. S tem so bili odrezani dogodki, kjer je bil prisoten višji nivo šuma ali pa celo termično sprožen dogodek.

Vsi signali in primer koincidence so prikazani na sliki 10. Poleg tega je prikazan tudi primer temnega šuma.

CTR sistema je bil določen preko prilagoditve Gaussove funkcije histogramu časovnih razlik po opravljenih rezih na energiji in šumu in je bil določen kot FWHM preračunan iz standardne deviacije funkcije. Meritve so bile osredotočene na zmožljivosti kristalov različnih proizvajalcev in vpliva dimenzije kristala na CTR.

Zaradi potrebe po natančnosti so bile tudi preiskovan tudi vpliv različnih nastavitev osciloskopa. Tako je bil tudi uporabljen razdeljen signal iz enega samega detektorja in na njem opravljena analiza. Tako je bila določena meja natančnosti pri uporabljeni opremi in analizi.



Slika 11: Rekonstrukcija točkastega vira v centru FOV brez ozadja (zgoraj) in z ozadjem (spodaj) za skener CS3_L10_CTR75.

Rezultati

Simulacije

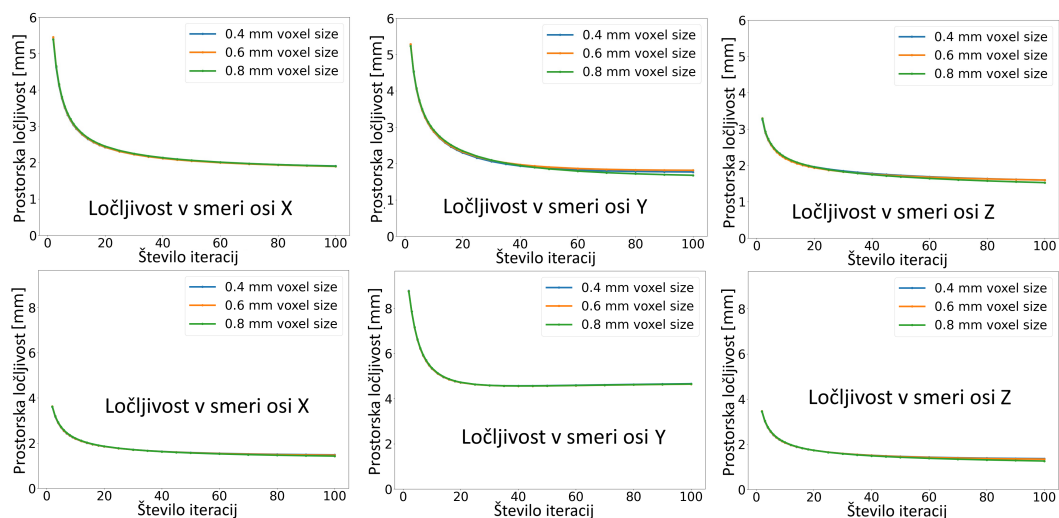
Za oceno prostorske ločljivosti so bile uporabljene analize rekonstrukcije točkastih virov. Rekonstrukcije enega takega vira za geometrijo CS3_L10_CTR75 v središču FOV so prikazane v zgornjem delu slike 11. Velikost voksla je bila 0.8 mm. Prikazan je vpliv števila iteracij in artefakti, ki se posledično pojavijo.

Za znižanje artefaktov je bilo točkastim virom dodano ozadje, prikazano v spodnjem delu slike 11. V tem primeru se artefakti začnejo pojavljati šele pri 50 iteracijah. Za nadaljnjo študijo prostorske ločljivosti so bile rekonstrukcije opravljene s 30 iteracijami (razen pri študiji vpliva števila iteracij) in v vseh primerih je bilo točkastim virom dodano ozadje.

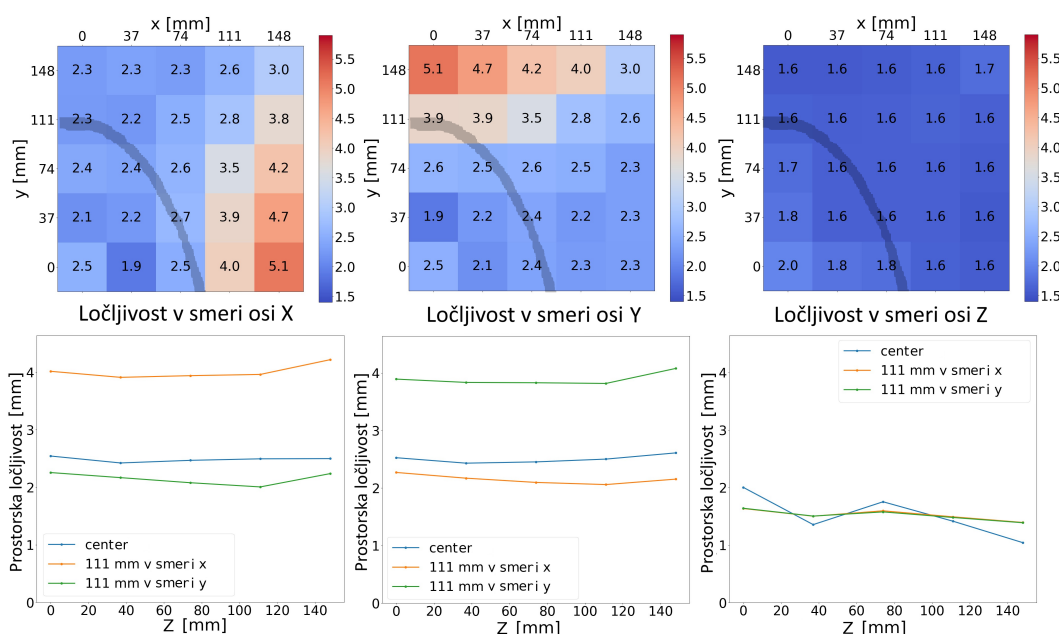
Analiza vpliva števila iteracij in velikosti vokslov je bila opravljena na točkastem viru z ozadjem, izmaknjenim 10 mm v smeri Y iz centra FOV. Rezultati so prikazani na sliki 12 za skener s 4 paneli in 2 paneloma. Vpliv velikosti vokslov je bil v večini primerov zanemarljiv. Število iteracij je imelo velik vpliv na rezultate do okoli 20 iteracij, nato se je vpliv postopno zmanjševal. Kljub očitni robustnosti rezultatov pri visokem številu iteracij je potrebno razumeti, da se z večanjem števila iteracij pojavljajo vedno večji artefakti na rekonstruiranih slikah. Očiten je tudi vpliv dveh manjkajočih panelov predvsem na ločljivost v smeri Y .

Za izračun prostorske ločljivosti čez večji obseg FOV je bilo simuliranih 125 točkastih virov razporejenih v mrežo. Za poenostavitev so na vrhu slike 13 prikazani rezultati za 25 virov v aksialnem centru FOV za skener CS3_L10_CTR75. Prikazane so ločljivosti v vseh treh smereh. Na spodnjem delu iste slike je prikazana sprememba ločljivosti na različnih aksialnih pozicijah. Razpon ločljivosti v smereh X in Y je od 1.9 mm do 5.1 mm. V smeri Z je razpon med 1.6 mm in 2.0 mm. Variacije po aksialni smeri so bile v večini primerov dokaj majhne.

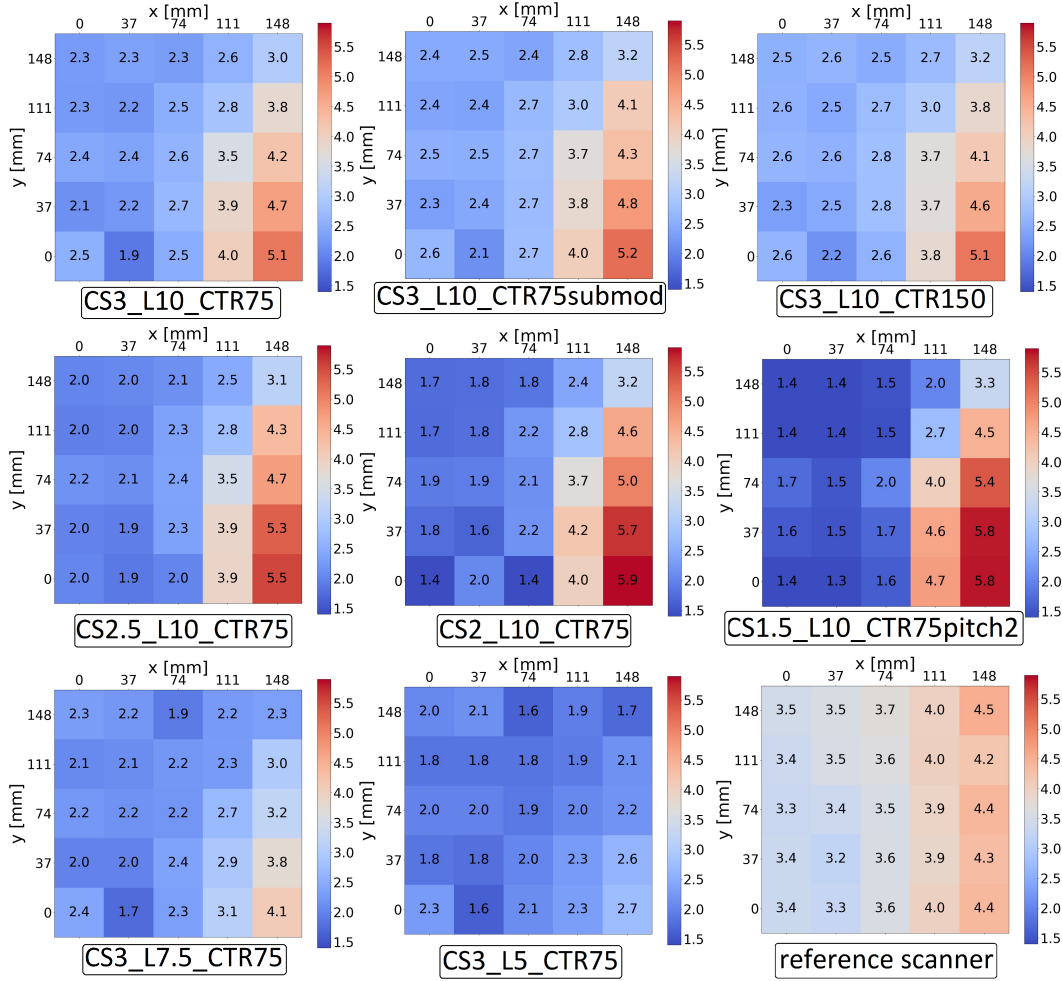
Za poenostavitev predstavitev rezultatov za ostale skenerje so na sliki 14 prika-



Slika 12: Odvisnost prostorske ločljivosti od števila iteracij in velikosti vokslov za konfiguracijo CS3_L10_CTR75 (zgoraj) in CS3_L10_CTR75_panel2 (spodaj). Točkasti vir se je nahajal 10 mm iz centra FOV v smeri Y.



Slika 13: Rezultati za prostorsko ločljivost za skener CS3_L10_CTR75. Zgoraj: prostorska ločljivost za centralne točkaste vire. Obris glave je dodan za ilustracijo relevantnega dela FOV. Spodaj: odvisnost prostorske ločljivosti od aksialne pozicije za različne pozicije na oseh X in Y.



Slika 14: Prostorska ločljivost v smeri X za vire v aksialnem centru za različne geometrije in parametre skenerjev.

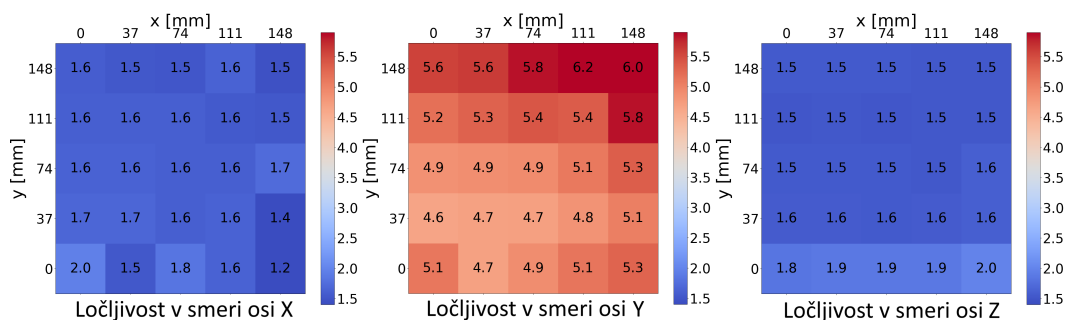
zani samo rezultati za centralne vire in ločljivost v smeri X .

Prikazan je vpliv strategije branja, kjer so rezultati pri branju na nivoju submodula slabši za okoli 0.2 mm. Slabši CTR prav tako prispeva k slabši prostorski ločljivosti. Bolj očitni vplivi imata prečni presek kristalov in njihova dolžina. V obeh primerih je ločljivost boljša za manjše kristale. Prikazani so tudi rezultati za referenčni skener. Tu so rezultati bolj uniformni po vsem FOV, ampak v povprečju slabši kot pri na primer skenerju CS3_L10_CTR75.

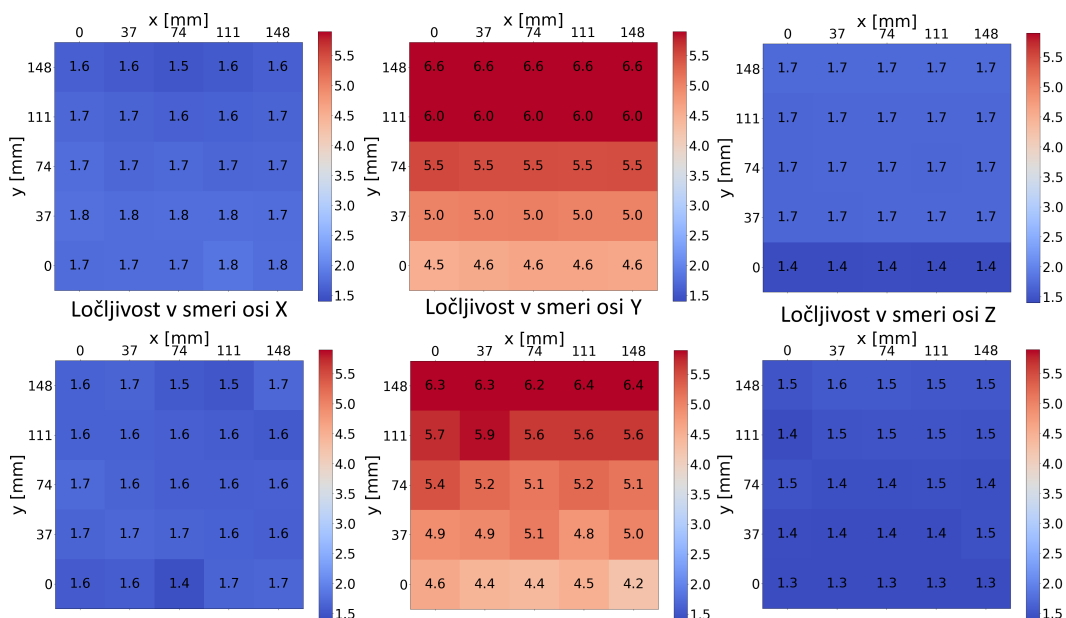
Rezultati za skener iz dveh panelov so prikazani na sliki 15. Zaradi drugačne simetrije skenerja so v tem primeru prikazani rezultati za ločljivost v vseh treh smereh. V tem primeru je najbolj očitna razlika za ločljivost v smeri Y zaradi pomanjkanja LOR v smeri X .

Rezultati za podaljšani skener iz dveh panelov CS2.5_L10_CTR75_{tot} so prikazani na sliki 16. V tem primeru so tudi prikazani rezultati v vseh treh smereh. Prikazan je tudi vpliv omejenega aksialnega sprejemanja dogodkov na 25 cm v spodnjem delu iste slike.

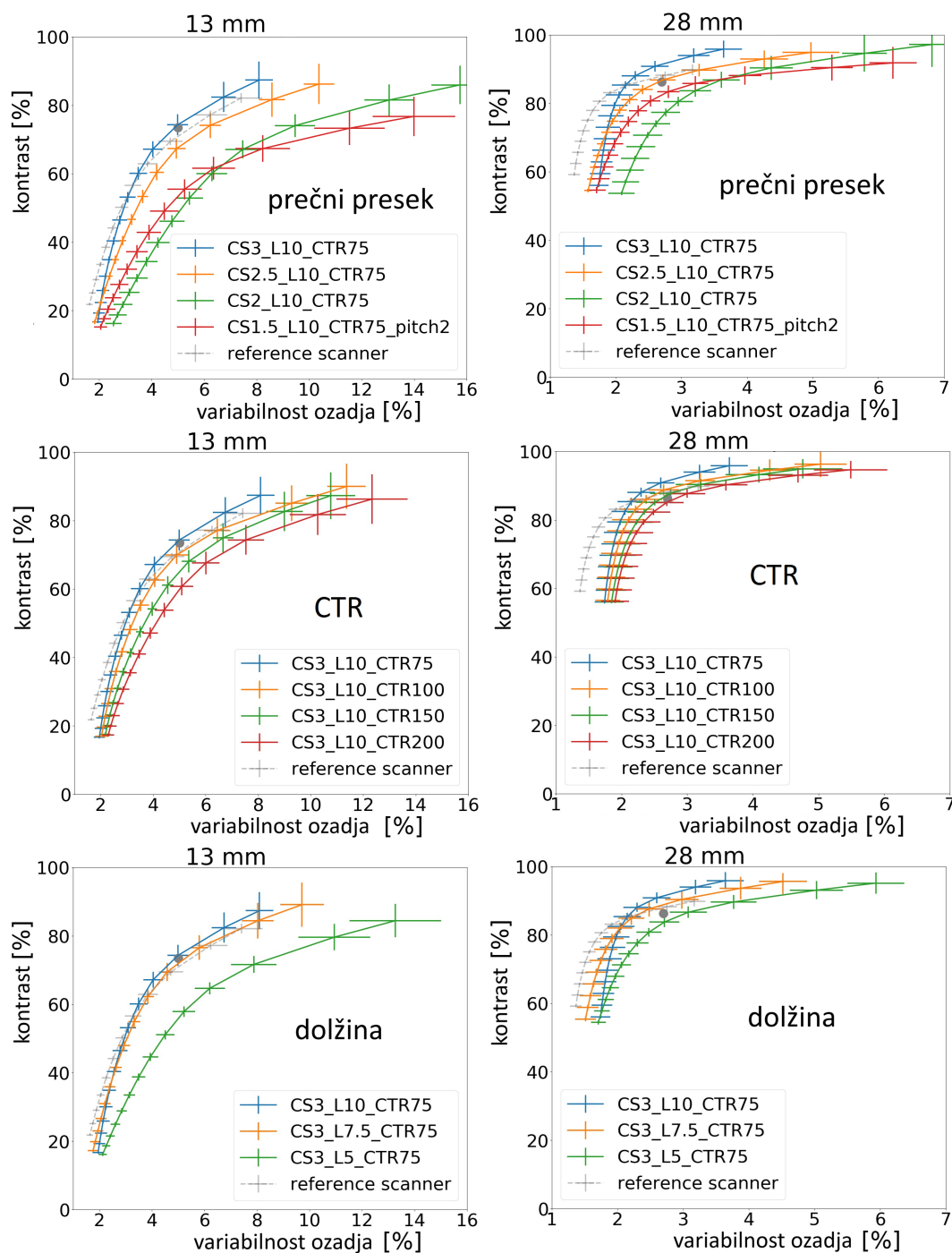
Rezultati za kvaliteto slike vsebujejo metriki kontrast in variabilnost ozadja. Na sliki 17 so prikazani rezultati za vroče sfere s premerom 13 mm in 28 mm. Primerjani so različni parametri skenerjev, specifično prečni presek kristalov, njihova dolžina in



Slika 15: Prostorska ločljivost za skener CS3_L10_CTR75panel2 v vseh treh smereh za vire v aksialnem centru FOV.



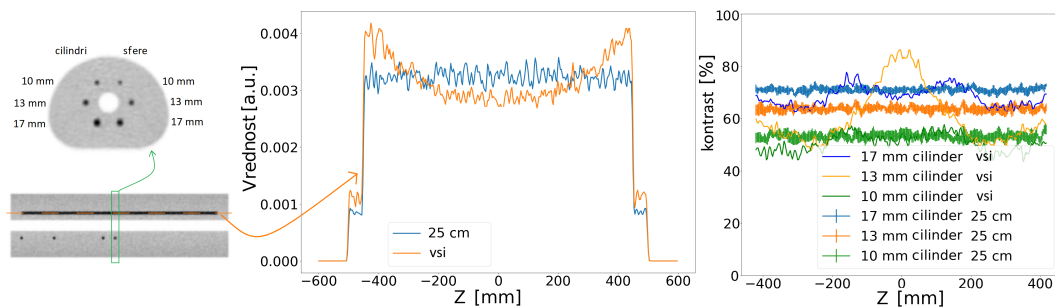
Slika 16: Prostorska ločljivost za skener CS2.5_L10_CTR75tot v vseh treh smereh za vire v aksialnem centru FOV v primeru sprejetja vseh koincidencah (zgoraj) in v primeru omejenega aksialnega sprejemanja dogodkov na 25 cm (spodaj).



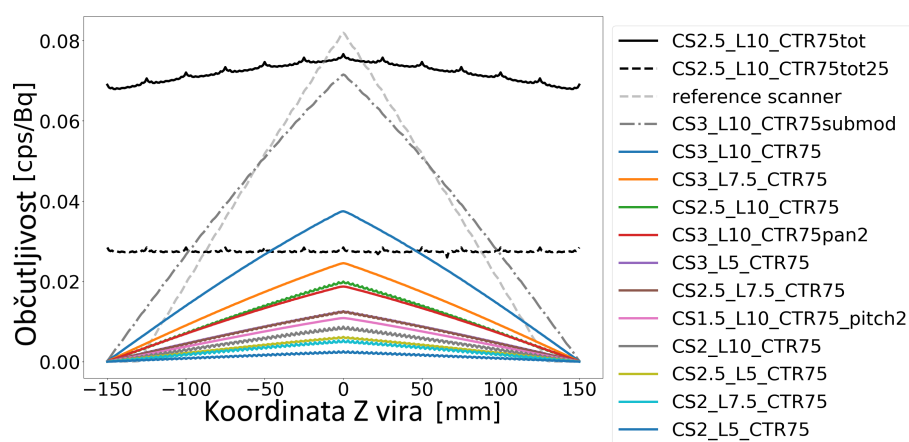
Slika 17: Diagrami za kakovost slike za sfere s premerom 13 mm and 28 mm za različne parametre skenerjev. Zgornja vrsta primerja vpliv prečnega preseka kristalov, srednja vrsta vpliv CTR in spodnja vrsta vpliv dolžine kristalov. Siv krog predstavlja eksperimentalno meritev za referenčni skener.

CTR sistema. Prav tako je vključena simulacija z referenčnim skenerjem in siv krog, ki prikazuje rezultat eksperimentalne meritve vzet iz [20].

Rezultati za podaljšani NEMA fantom in skener CS2.5_L10_CTR75tot so prikazani na sliki 18. Levi del prikazuje rekonstruirano sliko iz dveh perspektiv. Srednji del prikazuje linearni profil skozi vroči cylinder v primeru vseh sprejetih dogodkov in



Slika 18: Rezultati za podaljšani NEMA fantom. Na levi strani je rekonstruirana slika, na sredini linearni profil skozi vroč cylinder in na desni kontrast na različnih aksialnih pozicijah.



Slika 19: Rezultati za občutljivost za različne konfiguracije skenerjev.

omejitve aksialnega sprejemanja dogodkov na 25 cm, kjer je opazna bolj uniformna vrednost vokslov. Desni del prikazuje spremembo metrike kontrasta pri različnih aksialnih pozicijah, tudi v tem primeru so za omejeni skener rezultati bolj uniformni.

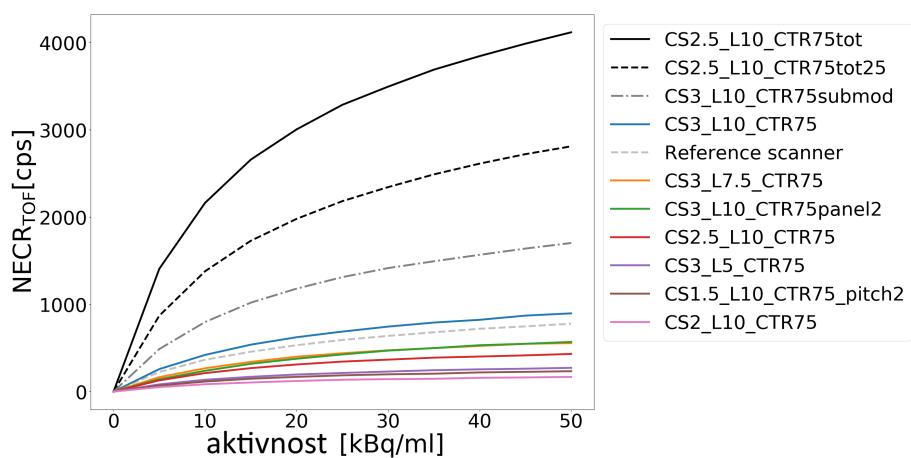
Rezultati za občutljivost so prikazani na sliki 19. Pri tej metriki je prikazan pomen strategije branja, ki spremeni rezultate za približno faktor 2. Na primer CS3_L10_CTR75submod je primerljiv z referenčnim skenerjem, čeprav uporablja precej manj scintilacijskega materiala. Rezultati za CS3_L10_CTR75 so dokaj slabši.

Za podaljšani skener CS2.5_L10_CTR75tot je tudi prikazano kako omejitev sprejemanja CS2.5_L10_CTR75tot25 zmanjša občutljivost za več kot faktor 2.

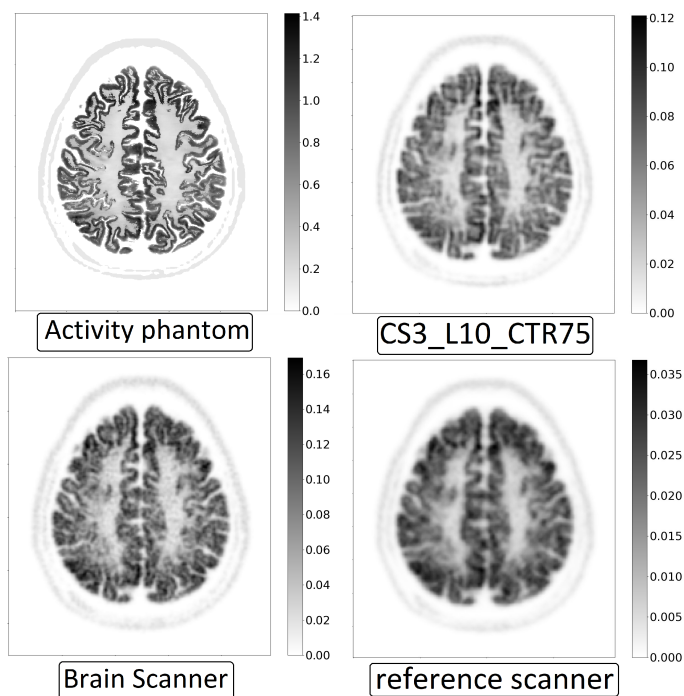
Rezultati za $NECR_{TOF}$ so prikazani na sliki 20. Pri tej metriki je bil upoštevan tudi CTR, zato so bili tudi skenerji s strategijo branja na nivoju kristala (CS3_L10_CTR75) primerljivi z referenčnim skenerjem.

Prečni prerez možganskega fantoma in rekonstruiranih slik je prikazan na sliki 21.

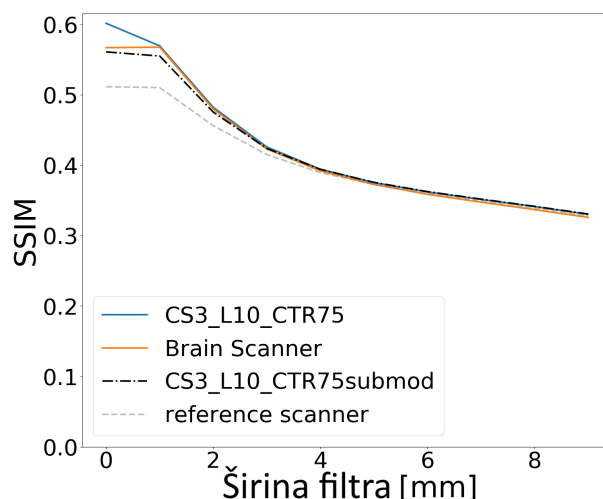
Slike lahko služijo za kvalitativno oceno zmogljivosti. Kvantitativni rezultati z metriko SSIM so prikazani na sliki 22, kjer so na slikah uporabljeni vedno širši Gaussovi filtri.



Slika 20: NECR_{TOF} diagrami, ki primerjajo zmogljivosti različnih konfiguracij in parametrov skenerjev.



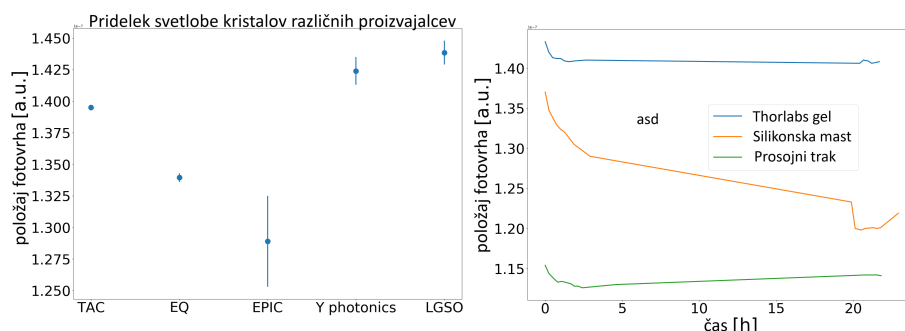
Slika 21: Slike možganskega fantoma v transverzalni ravnini in rekonstruirane slike z različnimi skenerji.



Slika 22: Odvisnost metrike SSIM od širine Gaussovega filtra za različne konfiguracije skenerjev.

Proizvajalec	Taiwan Applied Crystal	Hangzhou Yong Hee Photonics	Epic Crystal	EQ Photonics	OXIDE Corporation
Označba	TAC	Y photonics	EPIC	EQ	LGSO
Material	LYSO	LYSO	LYSO	LYSO	LGSO

Tabela 1: Tabela scintilatorskih kristalov uporabljenih za meritev pridelka svetlobe. Dimenzije vseh kristalov so bile $2.8 \times 2.8 \times 10 \text{ mm}^3$.



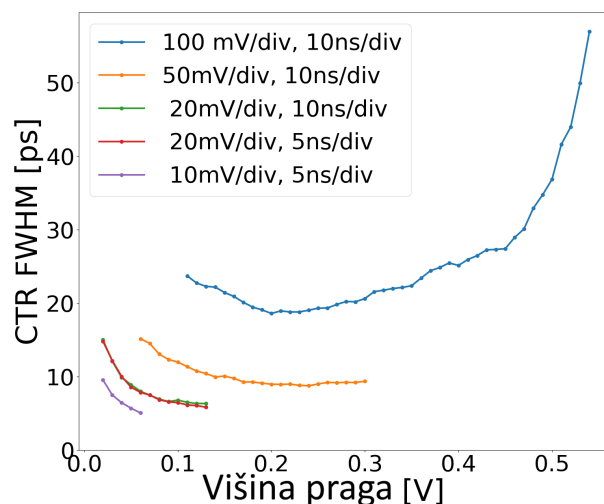
Slika 23: Svetlobni pridelek scintilatorskih kristalov različnih proizvajalcev (levo) in časovna odvisnost pridelka za različne optične sklopitve (desno). Dimenzije kristalov so bile v vseh primerih $2.8 \times 2.8 \times 10 \text{ mm}^3$.

Eksperimentalne meritve

Za meritve pridelka svetlobe kristalov so bili uporabljeni kristali različnih proizvajalcev in materialov, povzeto v tabeli 1. Dimenzije kristalov so bile $2.8 \times 2.8 \times 10 \text{ mm}^3$. Kristali so bili sklopljeni s fotodetektorji s silikonsko mastjo in napetost na SiPM je bila nastavljena 35 V oziroma 2.5 V nad prebojno napetostjo, dokaj manj, kot v prihodnjih meritvah CTR za najboljši dinamični razpon in linearnost odziva.

Rezultati so prikazani v levem delu slike 23. Vsaka meritev je bila ponovljena štirikrat. Vsakič so bili kristali ponovno zaviti v Teflon in sklopljeni. Pri tem se je LGSO kristal izkazal za najboljšega.

V desnem delu slike 23 je prikazana časovna odvisnost svetlobnega pridelka za



Slika 24: Intrinzična časovna ločljivost sistema za razdeljen signal in različne nastavitve skale osciloscopa.

različne sklopitvene medije. Zaradi absorpcije v Teflon in sušenja silikonske masti, le ta ni primerna za meritve ali uporabo preko daljšega obdobja. Zato je bil v meritvah CTR uporabljen večinoma Thorlabsov gel za sklopitev optičnih vlaken. Prosojni lepilni trak se je izkazal za neprimerne za sistematične meritve. Sklopitveni medij meltmount se je tudi izkazal za stabilnega na daljše časovno obdobje, vendar ni bil primeren za pogosto sklapljanje detektorjev in sistematične meritve.

Vpliv različnih nastavitev osciloscopa je prikazan na sliki 24. V tem primeru je bil signal enega fotodetektorja razdeljen na dva dela in analiziran. Zaradi omejene ločljivosti osciloscopa je bilo potrebno spremeniti vertikalno skalo časovnega signala, oziroma približati signal. S tem je bilo mogoče doseči intrinzično časovno ločljivost sistema in analize pod 10 ps. Vertikalna skala energijskega signala in horizontalna skala nista imeli vidnega vpliva. Izbrana je bila vertikalna skala 20 mV/div.

Sistematične meritve CTR so vključevale kristale velikosti $2.8 \times 2.8 \times 10 \text{ mm}^3$ različnih proizvajalcev, prikazanih v tabeli 2. Rezultati so prikazani na levi strani slike 25. Na desni strani so prikazane trikratne ponovitve meritev za tri primere kristalov. V vseh primerih je bilo zbranih 200000 dogodkov. Napetost na SiPM je bila 50 V, oziroma 17.5 V nad prebojno napetostjo.

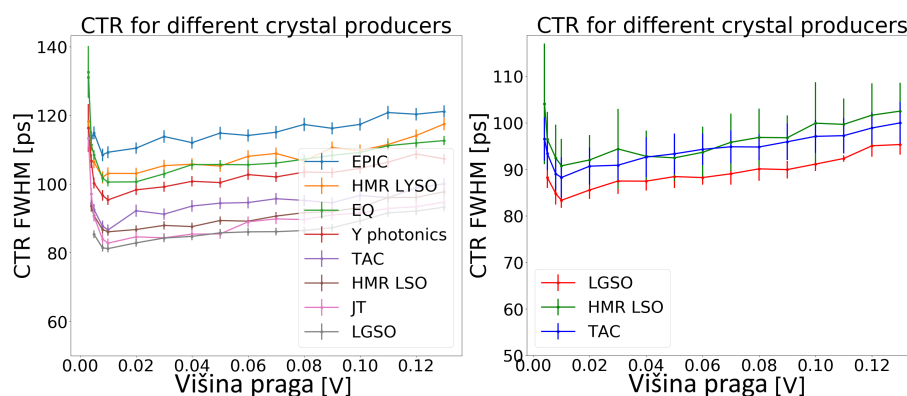
Najboljši rezultati so bili doseženi s kristali LGSO, JT, LSO in TAC, od katerih so vsi dosegli CTR pod 90 ps.

Meritve so se nadaljevale s študijo vpliva dolžine kristala na CTR. Uporabljeni so bili TAC kristali s prečnim presekom $2.8 \times 2.8 \text{ mm}^2$. Dolžine kristalov so bile 3 mm, 5 mm, 10 mm in 15 mm. Rezultati so prikazani na sliki 26.

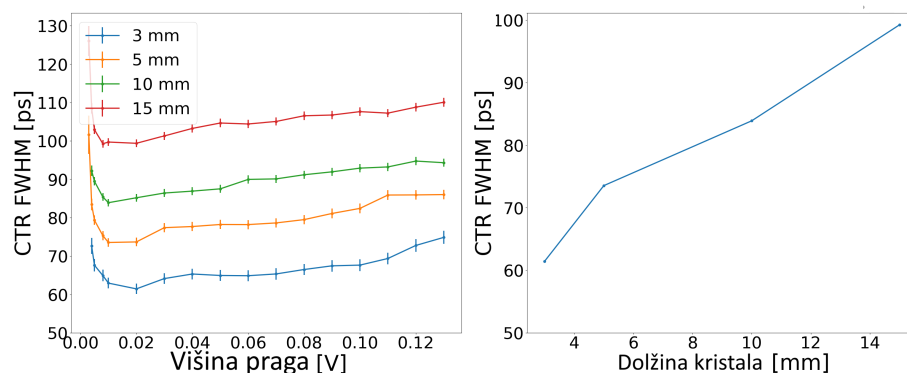
Vpliv dolžine se sklada s teoretično napovedjo. Najboljši rezultat je bil 61 ps, dosežen s 3 mm dolgimi kristali.

Proizvajalec	Oznaka	Material
Taiwan Applied Crystal	TAC	LYSO
Hangzhou Yong Hee Photonics	Y photonics	LYSO
Epic Crystal	EPIC	LYSO
EQ Photonics	EQ	LYSO
HMR Technology CO.	HMR LYSO	LYSO
HMR Technology CO.	HMR LSO	LSO
OXIDE Corporation	LGSO	LGSO
JT Crystal Technology Co.	JT	LYSO

Tabela 2: Tabela scintilatorjev za meritve CTR. Dimenzije so bile vedno $2.8 \times 2.8 \times 10 \text{ mm}^3$.



Slika 25: Rezultati CTR meritev za kristale različnih proizvajalcev. Meritve za vse primerke so prikazane na levi in ponovitve na desni. Dimenzije kristalov so bile vedno $2.8 \times 2.8 \times 10 \text{ mm}^3$.



Slika 26: Rezultati CTR meritev za kristale različnih dolžin.

Geometrija	Relativni volumen kristalov	Prostorska ločljivost [mm]	Občutljivost [kcps/MBq]	NECR _{TOF} [cps]	Kontrast
Referenčni skener	100 %	3.3	15.4 (100 %)	365 (100 %)	71 %
CS3_L10_CTR75	28.9 %	1.9	8.53 (55 %)	420 (115 %)	74 %
CS3_L10_CTR75submod	28.9 %	2.1	16.3 (106 %)	798 (219 %)	78 %
CS2.5_L10_CTR75	20.1 %	1.9	4.43 (29 %)	212 (58 %)	68 %
CS2_L10_CTR75	12.8 %	2.0	1.85 (12 %)	85 (23 %)	48 %
CS1.5_L10_CTR75_pitch2	16.3 %	1.3	2.39 (15 %)	115 (32 %)	53 %
CS3_L10_CTR100	28.9 %	2.0	8.53 (55 %)	315 (86 %)	70 %
CS3_L10_CTR150	28.9 %	2.2	8.53 (55 %)	210 (57 %)	65 %
CS3_L7.5_CTR75	21.7 %	1.7	5.55 (36 %)	268 (73 %)	72 %
CS3_L5_CTR75	14.5 %	1.6	2.81 (18 %)	135 (37 %)	56 %
CS3_L10_CTR75pan2	14.5 %	1.5	4.26 (28 %)	239 (65 %)	51 %
CS2.5_L10_CTR75tot	74.0 %	1.7	30.9 (200 %)	2160 (592 %)	63 %
CS2.5_L10_CTR75tot25	74.0 %	1.6	11.78 (76 %)	1380 (378 %)	67 %

Tabela 3: Povzetek glavnih metrik za različne geometrije in parametre skenerjev; relativna količina scintilatorskih kristalov v primerjavi z referenčnim skenerjem, prostorska ločljivost v smeri X za vir, ki je izmaknjen iz centra FOV za 37 mm v smeri X , celotna občutljivost sistema, NECR_{TOF} pri aktivnosti 10 kBq/ml in kontrast pri variabilnosti ozadja 5 % za sfero s premerom 13 mm. Občutljivost in NECR_{TOF} vsebujeta tudi relativne vrednosti glede na referenčni skener.

Diskusija

Detektorji za PET v ploščati geometriji predstavljajo nove perspektive in smeri razvoja naprav. Glavne prednosti vključujejo znižanje porabe scintilatorskega materiala brez znižanja zmogljivosti, možnost izdelave bolj kompaktnih naprav, modularnost in možnost povečanja pokritosti. Odprta geometrija bi omogočila nove uporabe v PET, predvsem med hadronsko terapijo in kirurgijo.

Nova geometrija predstavlja tudi nove izzive, predvsem zaradi nepopolnega vzorčenja vzdolž azimuta. Prav tako standardi za evalvacijo niso bili razviti za takšne naprave in tako niso zadostni za te primere.

Simulacije

Glavni rezultati simulacij so povzeti v tabeli 3 in potrjujejo potencial detektorjev za PET v ploščati geometriji. Na primer skener CS3_L10_CTR75submod uporablja manj kot tretjino scintilatorskega materiala, vendar dosega ali celo presega zmogljivost referenčnega skenerja v različnih metrikah.

Rezultati za prostorsko ločljivost indicirajo, da ima strategija branj majhen vpliv na ločljivost. Podobno ima majhen vpliv tudi CTR. Večji vpliv sta imela razmik med kristali in prečni presek kristalov. Slednji predvsem v centralnem delu FOV. Prav tako je imela velik vpliv po celotnem FOV dolžina kristalov. Ta vpliv je bil predpisan predvsem paralaksi zaradi DOI pri poševnih LOR. Tako bi meritve DOI omogočale izboljšavo ločljivosti in ohranitev občutljivosti z daljšimi kristali.

Pomemben dejavnik pri simulacijah za prostorsko ločljivost je bilo dodajanje homogenega ozadja, ki je omililo artefakte zaradi prevelikega ostrenja rekonstruirane slike in drugih omejitev iterativnega rekonstrukcijskega algoritma. To ozadje je povečalo računsko zahtevnost simulacij. Za simulacijo in rekonstrukcijo enega točkastega vira (od 125) brez ozadja je bilo potrebnih okoli 27 procesorskih ur, za vir z ozadjem pa okoli 187 procesorskih ur. Prav tako so se z dodajanjem ozadja povečale zahteve po prostoru za shranjevanje podatkov, ki je bil za set 125 simulacij

Proizvajalec	Oznaka	Material	Dimenzije	Relativni pridelek svetlobe	CTR
Taiwan Applied Crystal	TAC	LYSO	$2.8 \times 2.8 \times 10 \text{ mm}^3$	$100 \% \pm 0.07 \%$	$84 \text{ ps} \pm 1 \text{ ps}$
Hangzhou Yong Hee Photonics	Y photonics	LYSO	$2.8 \times 2.8 \times 10 \text{ mm}^3$	$102 \% \pm 0.8 \%$	$95 \text{ ps} \pm 1 \text{ ps}$
Epic Crystal	EPIC	LYSO	$2.8 \times 2.8 \times 10 \text{ mm}^3$	$92 \% \pm 3 \%$	$109 \text{ ps} \pm 2 \text{ ps}$
EQ Photonics	EQ	LYSO	$2.8 \times 2.8 \times 10 \text{ mm}^3$	$96 \% \pm 0.3 \%$	$101 \text{ ps} \pm 1 \text{ ps}$
HMR Technology CO.	HMR LYSO	LYSO	$2.8 \times 2.8 \times 10 \text{ mm}^3$		$102 \text{ ps} \pm 2 \text{ ps}$
HMR Technology CO.	HMR LSO	LSO	$2.8 \times 2.8 \times 10 \text{ mm}^3$		$86 \text{ ps} \pm 1 \text{ ps}$
OXIDE Corporation	LGSO	LGSO	$2.8 \times 2.8 \times 10 \text{ mm}^3$	$103 \% \pm 0.7 \%$	$81 \text{ ps} \pm 1 \text{ ps}$
JT Crystal Technology Co.	JT	LYSO	$2.8 \times 2.8 \times 10 \text{ mm}^3$		$83 \text{ ps} \pm 1 \text{ ps}$
Taiwan Applied Crystal	TAC	LYSO	$2.8 \times 2.8 \times 3 \text{ mm}^3$		$61 \text{ ps} \pm 1 \text{ ps}$
Taiwan Applied Crystal	TAC	LYSO	$2.8 \times 2.8 \times 5 \text{ mm}^3$		$74 \text{ ps} \pm 1 \text{ ps}$
Taiwan Applied Crystal	TAC	LYSO	$2.8 \times 2.8 \times 15 \text{ mm}^3$		$99 \text{ ps} \pm 1 \text{ ps}$

Tabela 4: Povzetek rezultatov eksperimentalnih meritev relativnega pridelka svetlobe (v primerjavi s primerkom TAC) in CTR različnih kristalov.

na redu velikosti nekaj 100 GB.

Pri simulacijah NEMA fantoma za kvaliteto slik je bilo demonstrirano, da lahko skenerji s 4 paneli ob zadostni izboljšavi CTR (pod 100 ps) dosežejo rezultate primerljive z referenčnim skenerjem. V primeru redke geometrije in zmanjševanja dolžine kristalov so rezultati do neke mere ostali konsistentni, z dodatnim zmanjševanjem količine scintilatorskega materiala so se metrike poslabšale.

S podaljšanim fantomom za kvaliteto slike je bilo prikazano, da trenutna orodja za rekonstrukcijo niso optimalna za tako geometrijo in je bilo potrebno omejiti aksialno sprejemanje dogodkov, kar je znižalo občutljivost konfiguracije za več kot faktor 2 in pripomoglo k motivaciji za razvoj novega orodja za rekonstrukcijo slik, ki bi lahko izkoristilo povečano aksialno pokritost brez uvažanja artefaktov [64]. Tudi z omejitvami trenutnih orodij je bil po zmogljivosti podaljšani skener primerljiv s 4 panelnim skenerjem istih dimenzij.

Pri metriki občutljivosti so bili rezultati za referenčni skener boljši od večine ploščatih. En izmed razlogov je bil predvsem strategija branja, saj je pri konfiguraciji CS3_L10_CTR75submod metrika postala bolj primerljiva kljub manjši količini scintilatorskega materiala. Vse ploščate konfiguracije so tudi imele večji aksialni FOV kot referenčni skener. Po drugi strani je bila zmogljivost ploščatih konfiguracij pri metriki NECR_{TOF} dokaj boljša, predvsem zaradi vključitve CTR v metriko.

Pri simulacijah možganskega fantoma so tako ploščate konfiguracije kot tudi specializiran možganski skener dosegli boljše rezultate od referenčnega skenerja, predvsem zaradi boljše prostorske ločljivosti, ki je bila posledica uporabe manjših kristalov v vseh dimenzijah in tudi manjšega razmika med kristali.

Eksperimentalne meritve

Meritve CTR pod 100 ps so pripeljale do zelo partikularnih izzivov. Večina instrumentacije, ki je bila na voljo, ni bila dovolj zmogljiva za tako natančne meritve časa. Zato so prvotne meritve vključevale samo energijski odziv fotodetektorjev oziroma meritev količine zaznane svetlobe. Že te same so pokazale očitne razlike v zmogljivosti različnih kristalov. Prav tako je bil preverjen vpliv medijev za optične sklopitve.

Meritve CTR so postale mogoče z uporabo zmogljivejšega osciloskopa. Oboji eksperimentalni rezultati so povzeti v tabeli 4. Potrebno je bilo določiti optimalne

parametre osciloskopa in minimizirati vpliv opreme na izmerjen CTR. Slednji je bil ocenjen na okoli 10 ps.

V sistematičnih meritvah so bili primerjani različni kristali različnih proizvajalcev, materialov in dimenzij. Ponovljivost meritev je bila deloma okrnjena zaradi nedoločenosti, ki so nastale pri sklapljanju in zavijanju kristalov. Prav tako je sklapljanje kristalov akumuliralo poškodbe na fotodetektorjih, kar je omejilo možnost ponavljanja meritev in slabšalo rezultate z vsako novo meritvijo.

Zaključek

Detektorji za PET v ploščati geometriji imajo potencial fleksibilne aplikacije, na primer s spreminjanjem razdalje med detektorji za določene klinične primere. Lahko so modularni in bolj kompaktni od konvencionalnih cilindričnih naprav in predstavljajo privlačno možnost napredka na področju TOF-PET tehnologije. Razvoj detektorjev z odličnim CTR zahteva obsežno optimizacijo parametrov in zasnovanja ter študijo rekonstrukcijskih pristopov v novi geometriji.

Pri zadostni izboljšavi CTR je bilo pokazano, da lahko skener v ploščati konfiguraciji doseže ali celo preseže zmogljivost referenčnega kliničnega skenerja kljub uporabi manjše količine scintilatorskega materiala in manjšega števila detektorskih elementov. Izboljšan CTR je bil nujen za kompenzacijo zmanjšane občutljivosti sistema in za eliminacijo artefaktov v rekonstruiranih slikah zaradi nepopolnega vzorčenja po azimutu oziroma odprte geometrije.

Eksperimentalne meritve so demonstrirale potencial za izboljšavo CTR. Izmerjen je bil CTR 63 ps, vendar le s 3 mm dolgimi kristali. Pri 10 mm dolgih kristalih je bil najboljši dosežen CTR 81 ps. Čeprav ni bil dosežen CTR 75 ps, ki je bil predpostavljen v simulacijah, je rezultat vseeno dokaj blizu. Po drugi strani tudi dosežen rezultat ne bo nujno lahko dosežen na večjem sistemu, kjer bodo namesto osciloskopa uporabljena integrirana vezja. Prav tako se pri samem skaliranju sistema pričakuje izguba pri časovni zmogljivosti. Kakorkoli že, pri doseženih rezultatih obstaja razumna možnost doseganja CTR 100 ps na navoju sistema, predvsem s stalnim napredkom tehnologije na tem področju.

Prihodnje raziskave na tem področju zajemajo več divergentnih vej, na primer meritve DOI, dosežene z obojestransko pokritostjo kristala s fotodetektorji, kar bi potencialno lahko tudi vodilo v izboljšanje CTR ali uporabe daljših kristalov. Drugo področje je skaliranje iz enega para detektorjev v modul, kjer bi se lahko preveril vpliv skaliranja sistema na CTR. Več raziskovalnega dela je tudi mogočega na področju simulacij. Predvsem propagacija vidne svetlobe skozi kristal in učinek površine kristala ter reflektorskih prevlek in ovojev. Prav tako bi simulacije lahko služile kot način preverjanja konformnosti simulacijskih orodij z eksperimentalnimi meritvami.

List of publications related to this doctoral thesis

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2. Razdevšek, G., Fakhri, G. E., Marin, T., Dolenec, R., Orehar, M., Chemli, Y., Gola, A. G., Gascon, D., Majewski, S., & Pestotnik, R. (2025). Flexible and modular PET: Evaluating the potential of TOF-DOI panel detectors. *Medical Physics*, 52(5), 2845–2860. <https://doi.org/10.1002/mp.17741>
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