Simulation and evaluation of a high resolution VIP PEM system with a dedicated LM-OSEM algorithm

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ABSTRACT: Over the last two decades there have been a growing number of designs for positron emission tomography (PET) cameras optimized to image the breast. These devices, commonly known as positron emission mammography (PEM) cameras allow much more spatial resolution by putting the photon detectors directly on the breast. PEM cameras have a compact geometry with a restricted field of view (FOV) thus exhibiting higher performance and lower cost than large whole body PET scanners. Typical PEM designs are based on scintillators such as bismuth germanate (BGO), lutetium oxorthosilicate (LSO) or lutetium yttrium orthosicilate (LYSO), and characterized by large parallax error due to deficiency of the depth of interaction (DOI) information from crystals. In the case of parallel geometry PEM, large parallax error results in poor image resolution along the vertical axis. In the framework of the Voxel Imaging PET (VIP) pathfinder project, we propose a high resolution PEM scanner based on pixelated solid-state CdTe detectors. The pixel PEM device with a millimeter-size pixel pitch provides an excellent spatial resolution in all directions 8 times better than standard commercial devices with a point spread function (PSF) of 1 mm full width at half maximum (FWHM) and excellent energy resolution of down to 1.6% FWHM at 511 keV photons at room temperature. The system is capable to detect down to 1 mm diameter hot spheres in warm background.

KEYWORDS: Solid state detectors; Image reconstruction in medical imaging; Medical-image reconstruction methods and algorithms, computer-aided software

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1 Introduction

Breast cancer is the most common cause of cancer death among women [1]. PEM is an organ dedicated PET scanner for breast screening [2]. PEM devices have a restrict FOV to a single breast thus increasing the performance of a conventional whole-body PET scanner for the specific exam, together with considerable reducing the costs [3]. Additional advantages are lower necessary dose and enhanced device portability. The coplanar detector geometry based on scintillator is the most commonly used since it provides best in-plane\(^1\) spatial resolution down to 2 mm full width at half maximum (FWHM) [4] and high contrast images with 4 mm detectable lesion size for 10:1 tumor to normal tissue ratio (TNR) [5]. However, designs based on scintillator crystals have many intrinsic limitations including a relatively poor energy resolution (5–10% for commonly used crystals [6]), the incompatibility with strong magnetic fields when coupled with photo-multipliers (PMT), and relatively large parallax error due to the uncertainty of the depth of interaction information (DOI) (> 5 mm FWHM) [7]. All these intrinsic limitations affect the detector sensitivity, and the image quality, and limit the minimum detectable tumor size and the correct assessment of the malignancy of small lesions [7]. In the framework of the VIP pathfinder project [8], we propose a high resolution PEM design [9] based on finely segmented room temperature CdTe detectors to overcome the intrinsic limitations of state-of-the-art commercial PEMs based on scintillating crystals. In this study, the high resolution VIP-PEM design is simulated and evaluated in terms of detector performance, and imaging performance according to the NEMA NU-4 2008 protocol [10] and by using the LM-OSEM algorithm [11] for image reconstruction.

\(^1\)Parallel to the paddle surface.
2 Detector specifications and simulation setup

The VIP-PEM conceptual design scanner is based on the VIP unit detector module (figure 1A) made of four CdTe pixelated detectors. The CdTe detectors have a parallelepiped shape with 2 cm × 1 cm section and 2 mm thickness. CdTe detectors provide excellent energy resolution as low as 1.6% FWHM for 511 keV photons at room temperature [12]. This allows to reject most of the scattered events thus reducing noise in the reconstructed image and increasing the image contrast. Each of the CdTe detector is pixelated into 200 voxels of 1 mm × 1 mm × 2 mm pitch and is bonded to a thinned read out chip (ROC) and then mounted on a kapton printed circuit board (PCB). The ROC and the PCB are 50 µm thick each to minimize the amount of passive material within the detector active region, and a 15 µm additional thickness is considered to take into account of the conductive glue between ROC, PCB and CdTe detectors. The combined attenuation coefficient of the passive material accounts for less than 2% compared to 2 mm CdTe. Each read-out channel is bonded to a microchip hosting a fully integrated front-end electronic as designed and developed by the VIP project. In this approach, the microchip transforms each channel in a virtually independent detector. Finally, one side of the module hosts an electronic connector to the external bus. The resulting detector has a 3-D segmentation with a density of ∼ 450 channels per cm³. The positioning of the module with respect to the incident radiation, with photons entering from the opposite side with respect to the electronic connector to maximize the stopping power and minimize the amount of passive material of the final scanner. In the VIP-PEM design, incident radiation is facing a minimum of 4 cm CdTe.

Mimicking the typical coplanar design, the VIP-PEM scanner consists of two parallel heads including detector modules. Each head is made of 80 modules arranged along two lines for a total 128000 channels per head. The coordinate system is chosen as in figure 1B and centered in the center of the FOV. The distance between the two paddles can be varied between 40 mm and 80 mm. The head section is 170 mm wide along the x-axis and 40 mm wide along the z-axis, and the two detector heads must slide axially for a complete scan of the 170 mm × 60 mm × 240 mm FOV.
3 Analysis method

3.1 System simulation

In order to evaluate the VIP-PEM system performance and assess its image quality, the design is simulated with the GEANT4-based Architecture for Medicine-Oriented Simulations (GAMOS) [13]. Given the huge number of channels in the detector (> \(10^5\)), the energy, position and trigger time stamp of each hit is recorded in list-mode with each channel triggering and collecting information independently from the others. GAMOS provides the simulation of particle interactions with the defined materials and the detector. The smart-pixel slow shaper integrates the deposited energy with 20 \(\mu\)s peak time. After digitizing the peak value, the time needed to reset the pixel electronic before the next event is 130 \(\mu\)s. To simulate the effect of the electronic measuring time and dead time, all energy depositions within the same voxel and within the first 20 \(\mu\)s window time contribute to the total energy of a single hit; energies deposited right after and within the 130 \(\mu\)s dead time, are lost. A channel activates if the energy deposited exceeds the 20 keV trigger threshold. The coincidence searching algorithm processes the list mode data to group consecutive hits laying inside a coincidence time window of 20 ns [12]. Within a group of coincident hits, energies of hits whose reciprocal distance is below 2 mm are added together and the new position assigned to the E-weighted centroid. After merging, only coincidences with two hits are considered with both the corresponding collected energies equal to 511 keV with ±1.6% tolerance.

3.2 Image reconstruction

The VIP PEM scanner has already been tested with the most well-known analytic algorithm Filtered Background (FBP) [14]. This method works very fast, but the main problem with FBP is that it requires a detector with an angular coverage of at least 180 degrees and thus can not be used for the VIP PEM scanner without producing artifacts in the final image [9].

3.2.1 List mode ordered subset expectation maximization

Ordered Subset Expectation Maximization (OSEM) [15] is an iterative image reconstruction algorithm which has been developed to overcome the problems of FBP. To reduce the running time of the OSEM algorithm, it first computes an initial guess of the reconstructed image, such as a blank uniform image, this image is then forward-projected and estimated projections are compared to measured projections. The “difference” between measured and estimated projections leads to the correction of the estimated image, and a new iteration is performed to assess the convergence between the estimated and measured projections. Iterations are continued until a reasonable agreement between the two sets of projections is achieved [14]. In the OSEM algorithm, the projection views are grouped in different sets (called subsets), the algorithm goes through the subsets in a specified order, and the image is updated after processing each subset [14]. The OSEM algorithm gives more precise results than FBP, but it requires a considerable amount of CPU time and computer memory. This is because OSEM uses a system matrix with a size that depends on the number of voxels in the detector. Since the OSEM algorithm is not practical to use for such detectors, a list mode implementation of the OSEM (LM-OSEM) may significantly reduce the required CPU memory and time because, since the data is presented in list mode, the sum over all detector bins...
would be replaced by a sum over all detected events in the iterative update function [16]. In the present study, all the images are reconstructed with a LM-OSEM algorithm optimized for the VIP-PEM design with no correction applied. The simulation results show that the LM-OSEM has a great potential for highly pixelated detectors with limited angular coverage.

4 Simulation results

4.1 Spatial resolution

Spatial resolution test is performed in order to measure the ability of the system to distinguish two points. It is characterized by FWHM of the reconstructed PSF obtained from the measurement of the activity distribution of compact radioactive point sources. For this measurement a radius of 0.15 mm point like source embedded in an acrylic cube of 10 mm extend on all sides is used. The test is performed by placing the point like source in the x direction at 0 (center of FOV), 10, 20, 30, 40 and 50 mm as NEMA NU4-2008 [10] standards requires. Detector separation is 60 mm. PSF is measured at each position. Simulation results indicate a spatial resolution around 1 mm FWHM regardless of the three spatial directions [9] (8 times better volumetric resolution with respect to conventional scanner [4]).

4.2 Image quality evaluation performance

For the image quality evaluation, an image quality phantom, corresponding to NEMA NU4-2008 [10] standards are simulated for two different alignments of the phantom, along the Z and Y axis, in order to compare the quality of the in-plane and cross-plane images. The phantom has central uniform region, cold regions in a hot background in the upper part and hot regions in a cold background in the lower part. The phantom is made of polymethacrylate. The hot region has 1, 2, 3, 4, and 5 mm in diameter, respectively. Their length is 20 mm. The cold region have two cylindric chambers of 14 mm in length and 8 mm in diameter. One of the chamber is filled with air and the other one is filled with nonradioactive water. The starting activity is about 3.7 MBq. The phantom is placed in the center of the FOV with the cylinder axis aligned both of the in plane and cross plane. And, it has been performed both results. A total of 10 million coincidences are collected for each scan as NEMA NU4-2008 [10] requires. The detector separation is 60 mm. The VIP-PEM scanner NEMA NU4-2008 [10] image quality phantom and the corresponding activity line profiles of the in-plane results are shown in figure 2, the cross-plane results are shown in figure 3. The calculations of the recovery coefficient (RC) and the image uniformity are done with the phantom aligned with the Z axis (in-plane) and Y axis (cross-plane), with a paddle distance of 60 mm, the uniform region shows good uniformity with 6.51%, 6.58%, respectively. Due to the partial volume effect [17] the RC increases with bigger diameter rods and the standard deviation (STD) of the RC decreases as it has been shown in table 1, and table 2. According to simulation results the VIP PEM scanner can achieve excellent image contrast both in the cross-plane and in-plane when it is compared with real measurements of commercial PEM scanner [4].

2 Perpendicular to the paddle surfaces.
Figure 2. NEMA NU4-2008 phantom is aligned along the vertical axis, reconstructed using LM-OSEM algorithm with five iterations and twenty subsets. Top-left: cold inserts region; top-middle: uniform region; top-right: hot rods. Bottom-left: activity line profiles of cold inserts region; bottom-middle: activity line profiles of uniform region; bottom-right: activity line profiles along the 1 mm and 2 mm hot rods.

Table 1. VIP-PEM Image Quality parameters after placing the phantom of the in-plane.

| Rod Diameter | 1 mm | 2 mm | 3 mm | 4 mm | 5 mm |
|--------------|------|------|------|------|------|
| RC           | 0.22 | 0.47 | 0.72 | 0.98 | 0.99 |
| (% STD)      | 6.51 | 6.33 | 5.12 | 4.49 | 4.50 |

| Uniformity | Air | Water |
|------------|-----|-------|
| Max.       | 11.0| 0.10  |
| Mean       | 9.58| 6.51  |

Figure 3. NEMA NU4-2008 phantom is aligned along the horizontal axis, reconstructed using LM-OSEM algorithm with five iterations and twenty subsets. Top-left: cold inserts region; top-middle: uniform region; top-right: hot rods. Bottom-left: activity line profiles of cold inserts region; bottom-middle: activity line profiles of uniform region; bottom-right: activity line profiles along the 1 mm and 2 mm hot rods.
Table 2. VIP-PEM Image Quality parameters after placing the phantom of the cross-plane.

| Rod Diameter | 1 mm | 2 mm | 3 mm | 4 mm | 5 mm |
|--------------|------|------|------|------|------|
| RC (%) STD   | 0.19 | 0.44 | 0.71 | 0.95 | 0.98 |
| Uniformity   |      |      |      |      |      |
| Air          | Max. | 11.5 | Min. | 0.11 | 0.11 |
| Water        | Mean | 9.39 | (%)STD | 6.58 | 13.1 | 13.2 |

Figure 4. Derenzo phantom is aligned along the Y axis. Left: hot rods with diameter 1 mm, 1.5 mm, 2 mm, 2.5 mm; right: activity line profile of 1 mm rods.

Figure 5. Derenzo phantom is aligned along the Z axis. Left: hot rods with diameter 1 mm, 1.5 mm, 2 mm, 2.5 mm; right: activity line profile of 1 mm rods.

4.3 Derenzo phantom

A Derenzo phantom is simulated for the phantom aligned along the Z and Y axis with a paddle distance of 60 mm. The phantom has different rods size with diameter 1 mm, 1.5 mm, 2 mm, 2.5 mm, and 3 mm. The height of rods are 12 mm. The outside diameter of cylinder is 36 mm and the inside diameter is 15 mm. The distance between rods is 1.4 mm, 1.5 mm, 2 mm, 2.5 mm and 3 mm, respectively. Results in figures 4 and 5 show that hot rods down to 1 mm diameter are clearly visible. The phantom reconstructed with LM-OSEM algorithm after five iterations and twenty subsets. A total of 10 million coincidences are collected for each scan.
4.4 Breast phantom

The breast phantom consists of four hot spot spheres of 1mm, 1 mm, 3 mm and 4 mm diameter, respectively and embedded in a warm background with tumor to normal tissue ratio (TNR) of 10:1. The detector separation is 55 mm. A total of 5M coincidences are collected for each scan for a total integrated activity of 5 kBq/mL in the FOV. According to the simulation results the VIP-PEM scanner is expected to detect lesions down to 1 mm diameter as shown in figure 6. The VIP PEM scanner is clearly outperforming the reported results of the commercial devices [5].

5 Conclusion

The proposed high resolution PEM design is developed within the Voxel Imaging PET (VIP) Pathfinder project and evaluated via Monte Carlo simulation. Several tests are performed to assess the imaging performance of the VIP PEM scanner with the accurate modeling of the required experimental conditions. The image quality performance of the simulated VIP PEM system has been characterized using NEMA NU 4-2008 [10]. Images have been reconstructed with a LM-OSEM algorithm with no correction applied. Even though it is slower than FBP, it gives more precise results with less CPU memory. Simulation results show the feasibility and potential for providing metabolic images with a sensitivity 2.2 cps/kBq [9], comparable with the published values for the state-of-the-art commercial scanners [4, 5]. The measured scatter fraction is 0.038 [9]. This is due to the fact that pixelated CdTe detectors are able to provide excellent energy resolution (1.6% FWHM at 511 keV). The measured random fraction is negligible up to $10^6$ Bq and peaks at around $10^8$ Bq. Saturation effects become evident for activity bigger than $10^8$ Bq, well above the level expected in a standard positron emission mammography ($\sim 10^6$ Bq) [9]. This work shows that VIP PEM scanner can achieve an excellent image resolution as low as $\sim 1$ mm FWHM in all directions and collect virtually noise-free data with the potential of producing excellent quality images. 8
times smaller volumetric resolution with respect to conventional scanners [4, 5]. The simulation results show the potential of the novel design to provide high metabolic images for very small lesions down to 1 mm diameter hot spheres with a 10:1 TNR. A high resolution VIP PEM scanner prototype is being developed within the framework of the VIP project to confirm the simulation findings.

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