Clear-PEM: A dedicated PET camera for improved breast cancer detection

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Abstract

Positron Emission Mammography (PEM) can offer a noninvasive method for the diagnosis of breast cancer. Metabolic images from PEM using ¹⁸F-fluoro-deoxy-glucose (FDG), contain unique information not available from conventional morphologic imaging techniques like X-ray radiography. In this work the concept of Clear-PEM, the system presently developed in the frame of the Crystal Clear Collaboration at CERN, is described. Clear-PEM will be a dedicated scanner, offering better perspectives in terms of position resolution and detection sensitivity.

1. Introduction

Breast cancer is the most frequent malign neoplasm in women. According to the American Cancer Society, one in each nine women will develop invasive breast cancer the long of their life [1]. About thirty years ago the introduction of the regular breast cancer screening by X-ray mammography allowing an early detection of this illness, reduced the mortality on 29% [2] Presently, the American Cancer Society and the American College of Radiology recommend an annual screening mammography starting at 40 years old, even for women not included in any risk group. Conventional X-ray mammography has an overall sensitivity (number of true positive/total positive) of 80%, depending on the breast type. For fatty breasts a sensitivity of 95% can be achieved with a lower limit in the size of a detectable tumor of 5 mm, while for dense breasts the sensitivity drops to 70% with a lower limit in size of 10 to 20 mm. In what concerns (classical) PET, it has been shown that sensitivity does not depend on the breast density. Moreover, the localization of tumors otherwise not seen on X-ray mammography or ultrasonography, can be done with PET. In addition the specificity (number of true negatives/total negatives) of conventional X-ray mammography is rather low, typically 30%, while studies indicate a specificity over 95% for PET. In fact there is a large domain of application for a dedicated PEM. The primary task will be the diagnosing of primary malign lesion on the breast, and the control of recurrence in patients with previous morphological problems like those made by surgery or other cause. The assessment of the treatment response is also a possibility. Chemotherapy is being increasingly used in locally advanced breast cancer. The kind of response to this treatment may be assessed with PEM, avoiding unnecessary side effects to non responders [3]. The system should also be applied to inconclusive cases after an X-ray exam where it should provide information as detailed as possible. PEM also must cover both the breast and the lymph node area so the detector geometry have to fit two different anatomical constraints.

Since biopsy gives the ultimate answer when diagnosing breast cancer the PEM scanner should be coupled to a stereotactic biopsy device. Breast exams will be performed with patients in prone position. This position allows for the largest decoupling of the breast from the body and provides a more comfortable positioning for the patient. A scanner table with holes for the breast must be then foreseen. The system will also allow to exam the axilla by placing the patient axilla between the PEM plates.

2. The PEM prototype

The choice of the PEM geometry considered several factors: sensitivity, image reconstruction, cost, etc. A two parallel plate preliminary configuration have been presently favored by prototype studies (figure 1). This configuration allows for a better adaptation to the breast geometry by variable plates separation distance.
Also the axilla exam will be easier with this geometry. Due to a breast close-proximity PEM will allow a smaller injected dose in the patient, and smaller examination time. The proposed PEM camera aims a spatial resolution between 1-2 mm (compared to ~10 mm for a whole body PET) [4]. To achieve this resolutions each camera plate will be constituted by a matrix of scintillating Lu based crystals with a 2x2 mm$^2$ cross-section and the light signal will be read by Avalanche Photo-Diodes (APD). These photodetector have several advantages over position-sensitive PMT’s, like higher quantum efficiency or better lateral uniformity, and they also allow the construction of compact assemblies, which is an important feature for mammography. The data acquisition system under development aims to a maximum event rate of 1 MHz which is compatible with an examination time of ~10 min necessary to obtain clinical significant images.

3. PEM system requirements

In a PEM system the fraction of accepted two-photon events (detection sensitivity) must be as high as possible in order to reduce the injected dose in the patient and allow for a smaller examination time. In particular a PEM device should optimize the two-photon events sensitivity for photons coming from the breast. Our goal is to achieve a typical value of 10% in the center of the Field Of View (FOV) when the PEM plates are 10 cm apart.

Only a fraction of the total injected activity will be fixed in the breast. This fraction is responsible for the true coincidence rate (events originated in the FOV). Although not well known, in the present, the available literature indicates a value of about 0.5% of the injected activity. The activity fixed in other body parts will be seen as background events (random coincidences) that will affect the image quality. A good compromise would be the reduction of these background coincidences to a level below 10% of the true rate. Preliminary studies point toward a true coincidences rate between 40 and 250 kHz, for a total activity of 10 mCi, depending on the PEM plate separation and breast uptake fraction. A total single event (one photon) rate in the detector up to 3 MHz is expected, depending on the detector shielding.

Figure 1 shows a schematic representation of a possible PEM system implementation in position for breast exam. The PEM detector is shown together with an X-ray mammograph and a stereotatic biopsy system. The integration of these two devices in the system will extend the examination capabilities. The PEM detector itself, will be constituted by two parallel plates, with an adjustable separation distance between the plates. Separation distances between 6 and 40 cm are foreseen.

The two plates will be able to rotate around the PEM axis, allowing to take data in several orientations as needed for the reconstruction of tomographic images.

To exam the axilla region (or the breast in the front-back configuration) the PEM detector will be rotated 90° and an image is produced with one plate below the table and the other over the patient shoulder (or back).

4. Prototyping

The design and optimization of the PEM detector parameters are being obtained using Monte Carlo simulation techniques. Moreover the Monte Carlo simulation also provides realistic data for reconstruction purposes. A dedicated and versatile Monte Carlo simulation framework is under construction based on GEANT4 [5]. The ROOT [6] toolkit have been adopted for event data storage and analysis. In the present, the developed framework consists of three autonomous modules: PhantomFactory, PEMsim and DIGITsim.

The PhantomFactory module simulates radioactive decay in different phantoms: homogeneous, heterogeneous, mathematical-type and voxel-based phantoms. Photons reaching a scoring region are stored for later tracking. The PEMsim module then performs the detector simulation. As input PEMsim uses data from the PhantomFactory module. Each photon or photon pair that interacts with the detector defines an event. The DIGITsim module simulates the signal formation process in the crystals and the response of the associated electronics. This module converts the information from PEMsim (energy, time) per event into a
signal shape, adds electronic noise and performs the signal A/D conversion.

Detection sensitivity, system count rate (prompt + accidental events), spatial resolution and depth-of-interaction (DoI) capability of Clear-PEM device were investigated with Monte Carlo. In the PEM working region between 7-13 cm detector separation plate distances a sensitivity of 7 to 17% was found for a $^{18}$F point source placed in the center of a 270 cm$^3$ water phantom. Sensitivity was found to decrease by about a factor of two when the source was placed 4 cm off-axis. The system count rates were assessed using a mathematical phantom implemented in the simulation framework. Uptake in the considered organs represents the upper limits of tracer measured 1 hour after an injection of 10 mCi of $^{18}$F-fluoro-deoxy-glucose (FDG). Most of the accidental coincidences were found to be produced by FDG uptake in torso (92%), liver (8%) and heart (1%) essentially due to their proximity to the detector's FOV. Results for a 350-700 keV energy window, 4 ns time window with 1 ns r.m.s. single-photon time measurement and 13 cm detectors separation distance are displayed in the following table:

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<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Single-photon rate</td>
<td>1.5 MHz/plate</td>
</tr>
<tr>
<td>Accidental</td>
<td>17 kHz</td>
</tr>
<tr>
<td>coincidence rate</td>
<td></td>
</tr>
<tr>
<td>Prompt coincidence</td>
<td>36 kHz (up to 250 kHz)</td>
</tr>
<tr>
<td>rate</td>
<td></td>
</tr>
<tr>
<td>Total coincidence</td>
<td>54 kHz</td>
</tr>
<tr>
<td>rate</td>
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</table>

Table 1. Count Rates

An increase less than 5% in single-photon and accidental coincidence rates was obtained when events from $^{176}$Lu radioactive decay (300 Bq in LuAP crystals) were added to $\beta^+$ $^{18}$F decays. The Clear-PEM design significantly increases detection sensitivity in comparison with conventional PET cameras (< 0.1%). Count-rate simulation results are within operation limits for the data acquisition system, able to read 1 MHz event rates, allowing to fully profit the large detector acceptance. PEM intrinsic spatial resolution for a point source in air placed in the center of the FOV was estimated to be 1.2 mm FWHM. This result takes into account $^{18}$F positron range, non-collinear photon emission, crystal size and crystal identification algorithm for multi-hit events based on Compton kinematics. DoI

5. Tests

In order to assess PEM detector key aspects, two experimental setups have been assembled. The first system uses a single LuYAP (2×2×20 mm$^3$) crystal wrapped in Tyvek, each top face coupled to a photomultiplier. A small NaI(Tl) scintillator is used to electronically collimate the 511 keV gamma photons from a $^{22}$Na source. These configurations allows to investigate differential light collection as function of the depth of interaction in the crystal. One of the PEM scanner basic components, consisting of 32 LYSO:Ce crystals optically isolated with Tyvek and coupled with to a 4×8 pixels Hamamatsu APD S8550 array is also under the testing process. A pixel array is connected to 32-channel readout arrangement, which includes a charge sensitive preamplifier and amplifier system developed by the Crystal Clear Collaboration. The VME readout includes a peak-sensing ADC and as an alternative a custom 100 MHz sampling ADC can be used.