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Breast imaging with a dedicated PEM

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Abstract

During the last decade there was a growing interest on the application of Positron Emission Tomography, PET, techniques to Breast Imaging. More recently, preliminary results suggested the use of dedicated devices to Breast Imaging using the same technique, the so-called Positron Emission Mammography cameras, PEM. In this article we review the arguments leading to a dedicated instrument. Based on these arguments we describe the concept of a PEM camera under development within the Crystal Clear Collaboration and the first results of its expected performance in terms of sensitivity and position resolution.

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1. Introduction

For a long time, medical imaging was mainly based on the physical principles of X-ray radiography and ultrasonography. The progress on these two techniques occurred mainly at the level of image detection, software for image processing and data storing. Recently, other techniques, based on different physical mechanisms, gave to the field of medical imaging new horizons on the exploration of Human Body morphology, physiognomy and functionality. A recent example is the Tomography by Emission of Positrons, PET, mainly used on tumor detection.

For the case of Breast Imaging, the commonly used technique is the X-ray mammography, combined, or not, with ultrasonography. One compares the PET methodology with conventional

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technique for the breast cancer case. Breast cancer is the most common feminine neoplasm leading to invasive breast cancer in about 11% of the cases [1]. In the US this is the most common form of cancer among women. The incidence of breast cancer has been rising for the past two decades, while mortality has remained relatively stable since the 1950s [2]. Much of the increase in incidence over the past 15 years is associated with increased screening by physical examination and mammography.

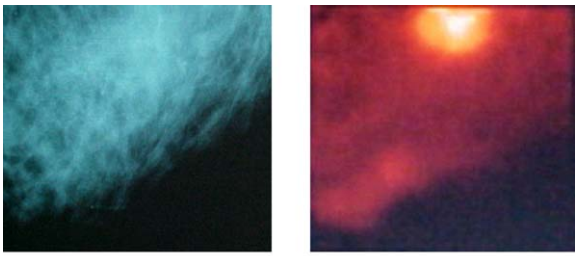


Fig. 1. Digital and PET mammographs. For PET a 4 min of acquisition time was needed with 10mCi of injected FDG [3].

2. Why do we need new imaging techniques

Although breasts have been X-rayed for more than 70 years, modern mammography has only existed since 1969 when the first X-ray machines used only for breast imaging became available. Since then, the technology has advanced a great deal producing higher quality mammograms with lower radiation dose. This technique probes the different densities of the breast tissue at the centimeter level. The appearance of the breast on a mammogram varies so much from woman to woman that it may lead to misleading interpretations.

As a result of its morphologic capabilities, X-ray mammography has an overall *sensitivity,* number of true positive over total positive, of about 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 10–20 mm. The size of the detectable tumor is important since the prognosis of cancer is related to its size. On the other hand, its *specificity,* the number of true negative over total negative, is rather low, typically around 30%. There is room for decreasing the number of unnecessary biopsies and misleading diagnosis.

3. The whole body PET

There is a clear need for an increase in sensitivity and specificity. This may be achieved with the use of PET with ^{18}F-fluoro-deoxy-glucose (FDG) as a radiotracer coupled to a PET device. Since there is an increase in glucose consumption in a cancer cell, FDG is an indirect marker of the cell proliferation. FDG-PET has been a success for the examination of the whole body tumors.

In spite of the limited statistics, the results obtained so far with a whole body FDG-PET are very positive in what concerns breast cancer diagnosis:

1. For localized breast cancer, the sensitivity found in literature varies between 77% and 100%, and the specificity between 88% and 100% [3], all independent of breast density;
2. For the axillary's lymph node invasion, sensitivity between 94% and 100%, and specificity of 83% were found in Ref. [4].

These results clearly show an improvement with respect to the actual methods. Fig. 1 shows the comparison of the result obtained on the same breast when we look at a digital X-ray mammogram and a whole body PET mammogram.

While with the *Classical* Digital X-ray image one is not able to detect any significant difference in the breast density, and thus, no conclusion can be drawn, with the whole body PET one clearly sees a *hot spot*, indicating a significant increase on the glucose metabolism of that region, a clear hint for a biopsy that, unfortunately, may still be misleading given the poor whole body PET resolution.

4. PEM

PEM (Positron Emission Mammography) is a PET device dedicated to breast cancer detection. It should cover not only the breast but also the axillary's lymph node area. Since cytology/anatomo-pathology will be the ultimate and conclusive methodology, one should be able to couple a stereotactic biopsy device to the PEM scanner.

With PEM, we aim to detect 1–2 mm tumors, faster, with a lower injected dose, with a more cost-effective device when compared to whole body PET.

4.1. Schematic layout

Given the required functionality a possible schematic layout for the breast examination configuration is shown in Fig. 2.

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).

The patient is in prone position on the scanner table with breast out of an aperture for examination purposes. The hot spot inside the breast represents the region where FDG had more uptake

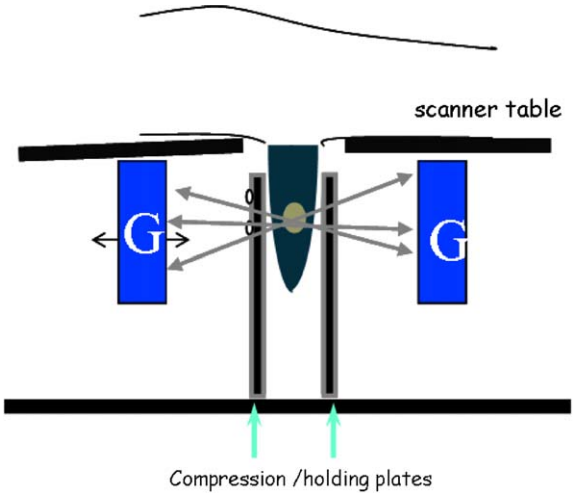


Fig. 2. Schematic layout of a PEM detector as described in the text.

(most likely the cancer area) from where two time-coincident photons are emitted back-to-back (arrows). These are detected by the two rotating planar gamma detectors (G), each consisting of a dense matrix of about 3000 scintillation crystals ($2 \times 2 \times 20\,\mathrm{mm}^3$) coupled to APD (Avalanche Photo-Diodes) light detectors on one or both sides of the crystal matrix. This high segmentation coupled to DoI (Depth of Interaction) capabilities is needed to achieve the 1–2 mm spatial resolution we require from our system.

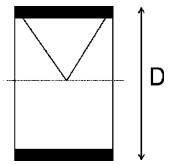
Possible crystals are the commercially available LSO, and LuAP, developed by the Crystal Clear Coll. at CERN, which is 13% denser but still with a poorer light yield. Further discussion on the influence of the crystals, their characteristics and of the readout system on the performance can be found in Refs. [3,5].

4.2. Whole body PET vs PEM

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. One should optimize the detection 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.

The detector sensitivity depends on the detector geometry through the solid angle coverage and the detector resolution, favoring the cost-effective solution of two rotating parallel plates with high crystal segmentation and DoI capability; the photon interaction probability and light yield, long and dense crystals; fast data acquisition and minimal dead time [3,5]. Let us use PEM with PET by first remembering that the signal's *significance* (σ) represents how good we can distinguish the two-photon events coming from the cancer volume (S) from the background (B) events, coming from FDG absorbed in the rest of the breast and other organs but still falling inside the FoV (1). It will increase with the number of events (n) and with the detector resolution (R):

$$\sigma = S/\sqrt{B}, \quad \sigma_n = \sqrt{n} \cdot \sigma, \quad \sigma_R = R^{-2/3} \cdot \sigma. \qquad (1)$$



For the solid angle coverage we can consider the schematic layout where a ring (PET) or two plates (PEM) are separated by a distance D. The solid angle coverage for each plate varies with D^{-2}. If we consider, as an example, that PET has a ring distance of $D = 60$ cm and PEM has the plates separated by $D = 6$ cm, the solid angle coverage of PEM is about 50 times that of PET. Meaning that for PEM, 50 times less acquisition time is required if one aims at the same significance.

PEM's spatial resolution aims at 1–2 mm compared to the typical 1 cm of PET. This requires fine granularity, or crystal segmentation of $2 \times 2\,\text{mm}^2$ and DoI capability of a few mm to minimize the parallax reconstruction errors. If one computes these two resolutions in Eq. (1) the result is about 125 times less acquisition time for PEM to obtain the same significance of a whole body PET.

Although depending on the FDG uptake in the breast, these trends were confirmed by simulation and confirm the advantages of PEM over PET.

5. Simulation results

The design and optimization of the PEM detector parameters are being obtained using a dedicated and versatile Monte Carlo simulation framework based on GEANT4 and ROOT [6] as the toolkit adopted for event data storage and analysis. At present, the developing framework consists of three autonomous modules. The *PhantomFactory* that simulates radioactive decay in different phantoms, *PEMsim* that performs the detector simulation, and *DIGITsim* that simulates the signal formation process in the crystals and the response of the associated electronics.

Detection sensitivity, system count rate (prompt + accidental events), spatial resolution and depth-of-interaction (DoI) capability of the detector are under investigation with this simulation tool. In the PEM working region, a two-plate separation between 7 and 13 cm, a detector sensitivity of 7–17% was found for a ^{18}F point source placed in the center of a 270 cm^3 water phantom. This value decreased by a factor of two when the source was placed 4 cm off-axis.

Considering that only a part of the injected FDG will be fixed in the breast and the activity fixed in other body parts will blur the images, one tries to reduce this background to a level below 10% of the true rate. Preliminary studies point towards a true coincidence rate between 40 and 250 kHz, for a total activity of 10 mCi, depending on the PEM plate separation and breast uptake percentage. A total single event (one photon) rate in the detector up to 3 MHz is expected, depending on the detector shielding.

The system count rates were assessed using a mathematical phantom implemented in the simulation framework. Uptake in the considered organs represent the upper limits of tracer measured 1 hour after an injection of 10 mCi of 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 plate distance are shown in Table 1.

Count-rate simulation results are within operation limits for the data acquisition system under construction, which is able to read 1 MHz event rates, allowing to fully profit from 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 simulation studies were performed for a single LuAP:Ce crystal with double side readout. Best configuration yields

Table 1
Count rates

Single-photon rate	1.5 MHz/plate
Accidental coincidence rate	17 kHz
Prompt coincidence rate	36 kHz (up to 250 kHz)
Total coincidence rate	54 kHz

2.4 mm FWHM DoI resolution with a light collection efficiency between 28 and 30%.

6. Summary and conclusions

Breast cancer is a widespread form of cancer, in women. The actual detection techniques that look to tissue density suffer from some lack of specificity and sensitivity. Techniques that are sensitive to the metabolism, like PET, show better sensitivity and specificity. At present these instruments are dedicated to examine the whole body. We showed that a dedicated breast device, PEM, can improve dramatically the sensitivity to small tumors (1–2 mm) at substantially lower cost and examination time. Preliminary simulation results are encouraging and show that the proposed targets can be achieved.

References

[1] Cancer Facts and Figures, American Cancer Society, Atlanta, Georgia, 1995.
[2] NCI's Surveillance, Epidemiology, and End Results (SEER) website at: http://seer.cancer.gov/
[3] P. Lecoq, J. Varela, Nucl. Instr. and Meth. A 486 (2002) 1 and references therein.
[4] Adapted from Bombardieri et al., Q. J. Nucl. Med. 45 (2001) 245.
[5] J. Varela, Nucl. Instr. and Meth. A, (2004) these Proceedings.
[6] http://geant4.web.cern.ch/geant4 and http://root.cern.ch