Molecular breast imaging: First results from Italian-National-Institute-of-Health clinical trials

F. Cusanno\textsuperscript{a,}\textsuperscript{*}, E. Cisbani\textsuperscript{a}, S. Colilli\textsuperscript{a}, R. Fratoni\textsuperscript{a}, F. Garibaldi\textsuperscript{a}, F. Giuliani\textsuperscript{a}, M. Gricia\textsuperscript{a}, M. Lucentini\textsuperscript{a}, M.L. Magliozi\textsuperscript{a}, F. Santanvenere\textsuperscript{a}, S. Torrioli\textsuperscript{a}, M.N. Cinti\textsuperscript{b}, R. Pani\textsuperscript{b}, R. Pellegrini\textsuperscript{b}, G. Simonetti\textsuperscript{c}, O. Schillaci\textsuperscript{c}, S. Del Vecchio\textsuperscript{d}, M. Salvatore\textsuperscript{d}, S. Majewski\textsuperscript{e}, G. De Vincentiis\textsuperscript{b}, F. Scopinaro\textsuperscript{b}

\textsuperscript{a}Istituto Superiore di Sanita’ and INFN gruppo Sanita, Viale Regina Elena 299, 00161 Rome, Italy
\textsuperscript{b}University La Sapienza, Rome, Italy
\textsuperscript{c}University Tor Vergata, Rome, Italy
\textsuperscript{d}CNR Napoli, Napoli, Italy
\textsuperscript{e}Jefferson Lab, Newport News, USA

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Abstract

Dedicated high resolution detectors are needed for detection of small tumors by molecular imaging with radionuclides. Absorptive collimation are typically used for imaging single photon emitters, but it results in a strong reduction in efficiency. Systems based on electronic collimation offer higher efficiency but they are complex and expensive. In case of scintimammography, dual-head detectors increase sensitivity and cancel out the dependence of the lesion depth. In the system presented here, pixellated scintillator arrays (NaI:Tl) were coupled to arrays of PSPMT's, HPK H8500 Flat Panel. A dual-head detector having field of view of \(100 \times 100\) mm\(^2\) and \(150 \times 200\) mm\(^2\) were designed and built. The electronic system allows readout of all the anode pad signals. First clinical trials, performed in the framework of the Scintimammography project of Italian National Institute of Health and University of Tor Vergata in Rome, and University of Naples, are presented.

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1. Introduction

Breast cancer is major health problem especially for women from western countries. Early detection leads to more efficient treatment, leading to better outcomes, therefore in many countries mass screening is routinely performed. The most widely used screening technique for asymptomatic women is mammography, which is typically very sensitive but not specific. In addition, it cannot detect efficiently lesions in women with dense breast or after-surgical interventions. As a result, majority of mammography-directed biopsies are performed on benign lesions and a significant number of biopsies are therefore unnecessary. Hence, additional adjunct diagnostic methods need to be applied. Among them molecular imaging with radionuclides has a central role to play. Standard gamma cameras were initially used and have shown the ability to differentiate malignant from benign lesions, but they do not offer sufficient spatial resolution to detect small lesions when used in breast imaging scintimammography procedure with \(^{99m}\text{Tc}\)-sestamibi. Several designs of dedicated gamma cameras have been implemented, tested and shown to substantially increase the detection sensitivity for sub-centimeter size lesions [1–3]. Nevertheless, there is still high level of interest in novel technologies for these compact gamma cameras to further improve their performance in the breast-imaging tasks. Key parameters for detecting

*Corresponding author. Tel.: +390649902235; fax: +390649387075.
E-mail address: francesco.cusanno@iss.infn.it (F. Cusanno).
small lesions are: spatial resolution, signal to noise Ratio (SNR) and contrast. Energy resolution plays only a secondary additional role in imaging breast under compression [4,5]. After through optimization of intrinsic detector properties, the collimation technique has to be carefully designed in order to maximize the SNR, which is critical in the detection of small lesions with low uptake. The optimization procedure of the intrinsic properties of the gamma detector includes the selection of the scintillator material and its degree of segmentation, as well as proper light sampling characteristics. Electronics, data acquisition (DAQ) system and image reconstruction techniques can also play an important role. In this paper we report about such an initial study, funded by the Italian Ministry of Health for the Italian National Institute of Health, in collaboration with the Imaging Department of Tor Vergata University in Rome and Naples University [6]. Phantom measurements, as well as pilot clinical trials in early cancer detection were performed as described below.

2. Equipments and methods

2.1. Detector

A dual-head detector, having field of view (FOV) of 100 × 100 mm² and 150 × 200 mm², was designed and built (Fig. 1).

Low-energy-high-sensitivity (LEHS) lead collimators are used. The 100 × 100 mm² head is equipped with 22 mm length, 1.9 mm exagonal holes, 0.2 mm septa collimator, the 150 × 200 mm² head is equipped with 20 mm length, 1.8 mm exagonal holes, 0.3 mm septa collimator. NaI(Tl) scintillators have been used because of high light yield and good match between scintillation emission peak and response of bialkali phoocathodes used in photomultipliers. Arrays of NaI(Tl) of different pixel sizes (down to the present technological limits for NaI(Tl) arrays fabrication) with pixel pitch of 1.5 mm for 100 × 100 mm² head and 1.2 mm for 150 × 200 mm²) were coupled to arrays of position sensitive photomultiplier tubes (PSPMT). The obvious choice for the photodetectors was the Hamamatsu H8500 (“Flat Panel”) Multi-Anode PMT’s. The H8500 is very compact, having a metal envelop of 51.7 × 51.7 × 15.4 mm³. The photocathode in these PMTs is bialkali and it has 12 stages of metal channel dynodes for electron multiplication. The PMT active area of 49.7 × 49.7 mm² (effective area of 94%) is covered by an anode array consisting of a 8 × 8 matrix in which each individual anode is 6 × 6 mm².

2.2. Electronics

The PMT anode pad channels are read out independently by a track-and-hold multiplexed system (Fig. 2) based on the VATA IDE AS system, using Front End Cards FEC 5053 equipped with VA_HDR11_TA32 chips. This solution significantly improves the quality of imaging (in particular in terms of peak-to-valley and spatial distortions of the centroid maps) with respect to resistive chains. Multiplexing permits to reduce complexity and cost of electronics, providing, in the adopted solution, a 2 kHz event rate capability of 1024 channels, limited by the write access speed of the mass storage sub-system. Higher rates can be obtained with more recent, still cost-effective, solutions (that are under evaluation) where a sparse readout logic is introduced at the track-and-hold stage or after the multiplexed ADCs.

2.3. Data processing

Higher flexibility of the independent channel readout (with respect to the conventional resistive chain) is exploited at different levels during the processing of the data: the collected charge centroid is computed on equalized channels after a proper spatial windowing (peculiar of the independent readout) that reduces distortion effects of the background and noisy channels. The centroid map of a flood calibration run defines the crystal (pixel) centers and therefore a local mapping of the PMT channels on the regular crystal grid; border and residual spatial distortions are then compensated by a projection of the centroid image from the PMT channel to the crystal grid defined by the above mapping.
3. Results

3.1. Phantom measurements

Measurements have been performed with $^{99m}$Tc-filled phantoms.

In Figs. 3 and 4 measurements with multisource phantom is showed, with spherical “lesions” of 12, 10, 9, 8, 7 and 6 mm with lesion-to-background uptake ratio of 10:1. The two images were simultaneously acquired, with the hot sources positioned closer to the 100 $\times$ 100 mm$^2$ head. The different distances could explain the different spatial resolution of the two images. Furthermore, the different intrinsic quality of the two scintillators might play a role in the images.

3.2. First clinical trials

In Figs. 5 and 6, the very first imaging result obtained from the clinical trial at the Imaging Department of University of Tor Vergata, Rome, is shown. At the present time, the final image correction and the construction of the

Fig. 2. Concept of the used electronics readout.

Fig. 3. Image of multi-source $^{99m}$Tc phantom on the 150 $\times$ 200 mm$^2$ head.

Fig. 4. Image of multi-source $^{99m}$Tc phantom on the 100 $\times$ 100 mm$^2$ head.

Fig. 5. Image of first clinical trial at Department of Imaging of University Tor Vergata, detected on the 150 $\times$ 200 mm$^2$ head.

Fig. 6. Image of first clinical trial at Department of Imaging of University Tor Vergata, detected on the 100 $\times$ 100 mm$^2$ head.
combined image is under optimization. In the presented uncorrected images, a tumor is clearly visible at the chest wall, corresponding to the top of the image. The tumor is more evident on the 150 × 200 mm² head, closer to the lesion.

4. Summary

A dual-head detector for imaging breast tumors have been designed and built in the framework of the scintimmamography study, funded by the Italian Ministry of Health for the Italian National Institute of Health, performed in collaboration with the Imaging Departments of Tor Vergata University, Rome and Naples University. Optimization has been performed in order to find the best configuration of the scintillator type, pixel dimension, photodetector pixel size, electronics readout and collimation system.

Electronics system able to read out all the individual channels, has been used.

Measurements with phantom were performed. Clinical trials have been started at the Department of Medical Imaging at Tor Vergata University in Rome, they are planned at Naples University as well.

4.1. Outlook

A new electronics is going to be designed and it will allow higher counting rate and use of smaller anode pixel size (Hamamatsu H9500) so smaller scintillator pixel size (1.0 mm) that, according to the simulations, seems to improve the SNR.

Full optimization of the dual-head detector layout is under development.

Study of an alternative collimation system (coded aperture) has been performed. It could be the key parameter for the real possibility of detecting small tumors (< 5 mm in diameter) provided better radiopharmaceuticals are available. In fact Bombesin has already shown to be a possible alternative to MIBI [7–9].

Moreover better scintillators (i.e. larger number of photons using LaBr₃:Ce) appear in the market and will be used as soon as they become available.

Simulations are underway for choosing the best layout (continuous vs. pixellated).

Photodetectors with very small anode pixel (1.6 × 1.6 mm²) are now available (Planacon Model 85021 from Burle). This would allow better light sampling and higher number of pixels in the image with possible improvements using coded aperture collimation.

References