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A YAP camera for the biodistribution of ^{188}Re conjugated with Hyaluronic-Acid in "in vivo" systems

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Abstract

The aim of the SCINTIRAD experiment is to determine the radio-response of ^{188}Rhenium (Re) in in vitro cells and the biodistribution in different organs of in vivo mice, and subsequently to assess the therapeutic effect on liver tumours induced in mice. Both the γ- and β- emissions of ^{188}Re have been exploited in the experiment. The in vivo biodistribution in mice was studied also with a γ-camera using different parallel hole collimators. In the ^{188}Re spectrum, while the 155 keV γ-peak is useful for imaging, the photons emitted at larger energies and the β-particles act as noise in the image reconstruction. The γ-cameras previously used to image biodistributions obtained with ^{99}Tc are, therefore, not optimized for use with ^{188}Re. A new setup of the γ-camera has been studied for ^{188}Re: 66 × 66 YAP:Ce crystals ($0.6 \times 0.6 \times 10\,mm^3$, 5 μm optical insulation) guarantee a FOV of $40 \times 40\,mm^2$, a Hamamatsu R2486 PSPMT, 3 in. diameter, converts their light into an electrical signal and allows reconstructing the spatial coordinates of the light spot; incoming photon directions are selected through a lead collimator with 1.5 mm diameter hexagonal holes, 0.18 mm septa, 40 mm thickness. Using this setup, results have been obtained both with ^{99}Tc filled and ^{188}Re filled capillaries and wells. The energy spectrum of the collected photons and the spatial resolutions obtainable with the ^{188}Re source will be presented.

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Keywords: Nuclear medicine; γ-ray imagers; YAP camera; Rhenium-188; Small animals imaging

1. Introduction

Rhenium (Re)-188, a β- and γ-emitter, is a promising candidate for the application in nuclear medicine. While the β-emission ($E_{max} = 2.12$ MeV) is fundamental for therapeutic purposes, the γ-rays (with a 15% branching ratio in the interesting 155 keV line) can be detected to evaluate the biodistribution of the radionuclide and for a real-time SPECT monitoring of regional drug concentration during radiation therapy. Furthermore, its chemical properties, similar to the widely used congener Technetium

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(Tc)-99 m, allow to use all the information in the biodistribution of ^{99m}Tc-radiopharmaceuticals for the research of useful ^{188}Re-radiotherapeuticals.

Hyaluronic Acid (HA) is a molecule already adopted as suitable vector of chemotherapeutic drugs. ^{99m}Tc–HA labeling procedure and biodistribution studies have been previously reported in literature. HA has also been adopted as vector for ^{188}Re. Preliminary results on the effect of ^{188}Re–HA on a series of tumor cell lines obtained "in vitro" are also available in these proceedings [1].

^{188}Re decays to ^{188}Os (70%) or ^{188}Os* (30%) in about 17 h, via the emission of a β-ray with a maximum energy of 2.12 MeV (0.78 MeV average energy). In addition, ^{188}Os* emits promptly (0.69 ns) a γ-ray, mainly in the line at 155 keV (about 15% of the original ^{188}Re decays end up with the emission of a 155 keV photon) but with the photon spectrum extending up to ~2 MeV.

The different emission properties of ^{188}Re, compared to ^{99m}Tc, which emits just one single γ-ray at the fixed energy of 140 keV, imply a different design of the imaging camera, to cope with the higher image background due to both β-rays interference, given the secondary interactions those electrons can generate everywhere in the field of view (FOV), and higher energies γ-rays, given their larger penetration compared to those from the main line.

Preliminary results were presented in a previous publication [2], where a different mechanical setup and collimator was used, however. Here, results are presented on the setup of the camera optimized for ^{188}Re and its measured energy and spatial resolutions for the 155 KeV photons. Ongoing developments and a proposed new setup will also be briefly reported.

2. The experimental setup

To study the effect of metabolic radiotherapy in small animals (mice), a small high-sensitivity γ-camera has been built, following the experience of the YAP camera [3–5] which is routinely used to image mice with ^{99m}Tc–HA at the Laboratori Nazionali di Legnaro, Italy (e.g. Ref.[6]).

The γ-camera is based on a matrix of 66×66 yttrium aluminum perovskite doped with cerium (YAP:Ce or $YAlO_3$:Ce) crystals [7], each measuring $0.6 \times 0.6 \times 10\,mm^3$, with 5 μm thick optical insulation between them. A FOV of $40 \times 40\,mm^2$ is thus achievable. The scintillator is read out by a R2486 Hamamatsu position sensitive photomultiplier (PSPMT) [8], with a 3 in. diameter photocathode. The anode consists of 16 plus 16 wires crossing at 90° and connected by two resistive chains, defining the x and y directions. A 40 mm thick lead parallel hexagonal holes collimator [9], with hole diameter 1.5 and 0.18 mm septa, is placed in front of the YAP matrix. The detector is triggered using the last dynode and the ends of the x and y resistive chains. Its signals are amplified, stretched and read out by a NI 6023E card [10] connected to a PC.

Fig. 1 shows the experimental apparatus and its readout boards, as it is used in the laboratory.

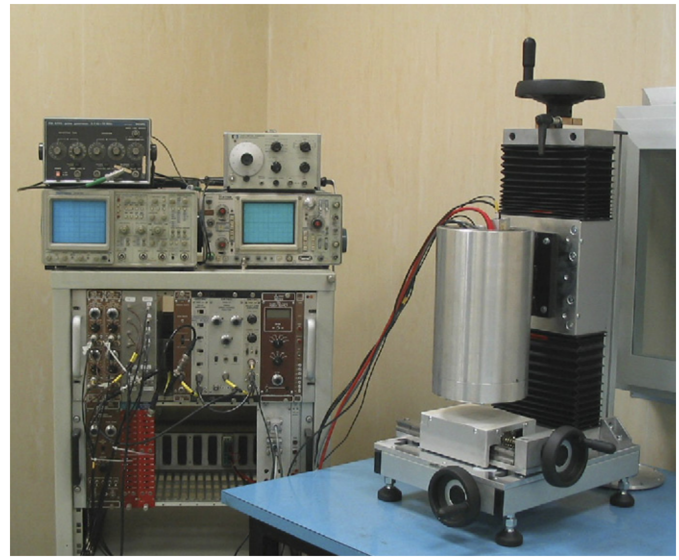

Fig. 1. The experimental apparatus which is taking data at the National Laboratories of INFN in Legnaro. On the right one can see the mechanical structure and source positioning system, which contains the scintillator, the PMT and the collimator inside the cylinder. On the left is the rack containing the readout electronics.

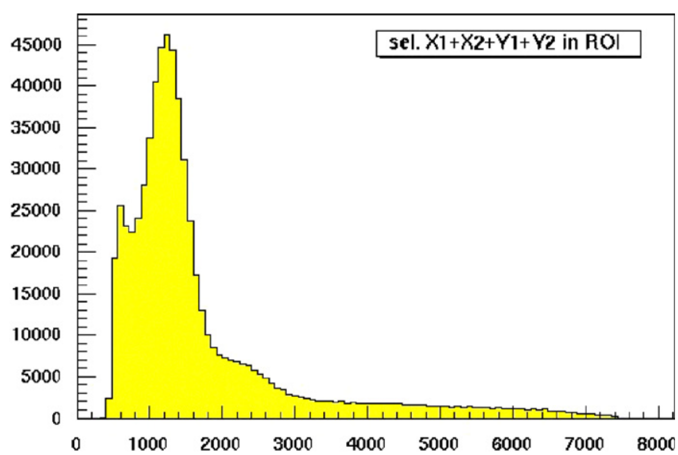

Fig. 2. The total energy of a cylindrical ^{188}Re source measured in the YAP-camera. In the horizontal axis, the photon energy is expressed in arbitrary units, while in the vertical axis the corresponding counts are listed.

All collected data are saved event by event on file for the offline analysis.

3. Energy resolution of the YAP camera

A 6.8 mm diameter and 10 mm height plastic well filled with a solution with ~0.3 GBq of ^{188}Re activity was put under the YAP-camera setup and data were acquired during 3 h. The total energy spectrum obtained from all the points originating from within the position of the well (region of interest (ROI) is shown in Fig. 2. To obtain such a spectrum, the energy response of the camera was calibrated as a function of the source position. For the calibration, a flat field of a solution containing ^{99m}Tc was taken, and the measured energies of the 140 keV photon were all equalized to the same value, everywhere in the FOV of the camera.

The energy resolution of the setup was thus determined as the width of the fitted Gaussian of the photon-energy peak (while a binomial shape was considered for the background). For the 155 keV ^{188}Re line, the energy resolution obtained in that way is 40% FWHM.

4. Position resolution of the YAP camera

The digital resolution (i.e., 1 mm in the FOV expressed in image pixels) was determined using a set of three parallel capillaries, 0.7 mm wide and spaced 1.0 and 1.5 cm apart, filled with a solution of ^{99m}Tc. The image obtained from them is visible in Fig. 3.

The spatial resolution obtainable in the present YAP-camera setup with ^{188}Re, at 10 mm distance from the collimator was then determined by acquiring an image (as in Fig. 4) from the same 6.8 mm diameter and 10 mm height plastic well filled with a solution with ~0.3 GBq of ^{188}Re activity during 3 h. The spatial resolution was measured separately in the horizontal and in the vertical directions by deconvoluting a Gaussian shape from the known geometrical shape of the well in thin horizontal and vertical slices [11]. The results give a FWHM of (2.76 ± 0.10) mm in x and (2.72 ± 0.10) mm in y. These numbers are comparable to the ones of the YAP camera for ^{99m}Tc at similar object to camera distance [12], the slightly larger FWHM values being due to the larger holes of the collimator employed for ^{188}Re.

5. Perspectives

To increase the space resolution without losing sensitivity, and to obtain different projections simultaneously, we

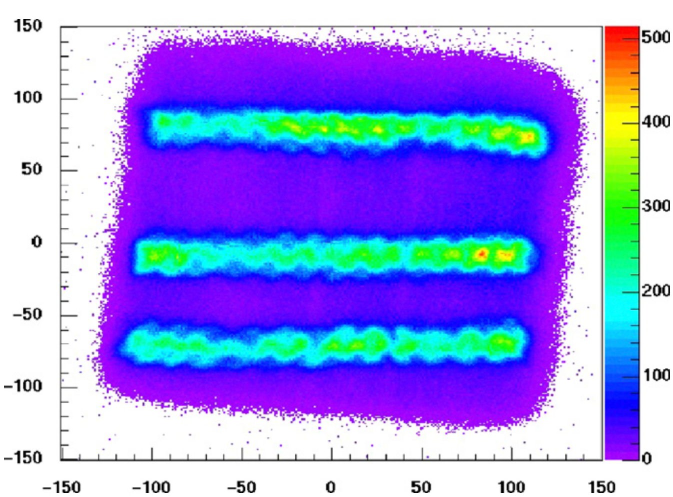

Fig. 3. Image obtained with three capillaries (0.7 mm inner diameter, at a distance of 10 and 15 mm each other) filled with a solution containing ^{99m}Tc.

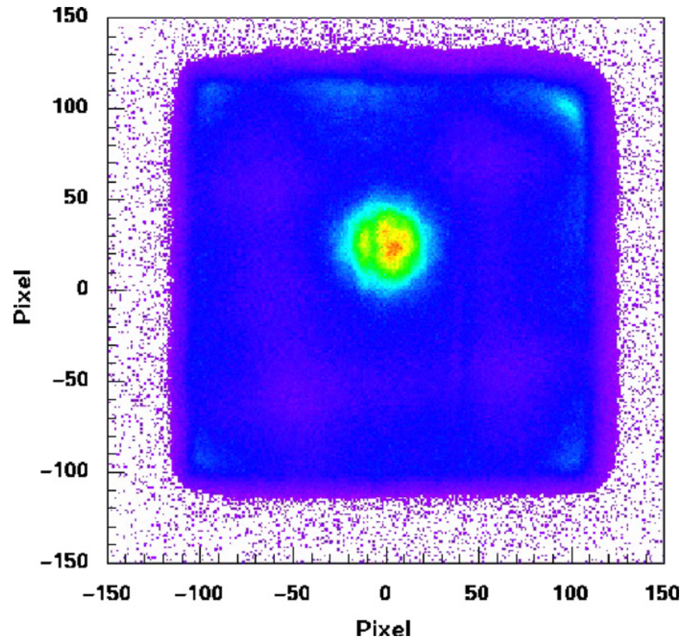

Fig. 4. Image obtained with a plastic well of cylindrical shape, with a base diameter of 6.8 mm and a height of 10 mm, filled with a solution of ^{188}Re. The activity of the liquid was about 0.3 GBq.

are building two new cameras to be positioned at 90° around the animal. They use as scintillators where two planar crystals of lanthanium bromide doped with cerium ($LaBr_3$:Ce), 50×50 mm wide and 4 mm thick, read out by one H8500 Hamamatsu Flat panel PMT [8] each, with a glass window 1.8 mm thick protecting the crystal. The front-end electronics for the 64 channels of the H8500 has been designed using MPX-08 chips. The system will be mounted on a rotating support, in order to produce tomographic images.

$LaBr_3$:Ce γ-cameras show superior spatial and energy resolution than the previous generation detectors based on scintillation arrays of pixellated crystals [13]. The better energy resolution is expected to ease the separation of the 155 keV line of ^{188}Re with respect to the background photons produced in a large fraction of that isotope decay.

Acknowledgments

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