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# Projections for dual radioisotope applications in PET imaging

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## Abstract

Positron emission tomography (PET) are widely accepted and used as an effective medical imaging method. We have studied on the dual radioisotopes C11 and Cu60 together by modifying the isotopes used in Standard cyclindirial PET through GATE imaging simulation. We scan the proper resolution intervals and the distances between the sources and present the differences in parameters such as full width at half maximum (FWHM), intensity and contrast. Applying statistical $\chi$^2 method, we aim to show the significance limits of above parameteric differences in PET simulations. These results may help determine in which conditions the imaging devices can be used with dual isotope method in clinical applications.

## Article info

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## 1. Introduction

Molecular imaging technology used in nuclear medicine includes specific imaging methods such as optical imaging and scintigraphy. The main devices of scintigraphy are positron emission tomography (PET) and single photon emission computed tomography (SPECT). These imaging methods use images generated by radiation emitted in the body as a result of the application of radiopharmaceuticals to patients. This image provides useful information not only for diagnostic purposes such as detection of functional abnormalities or early imaging of tumors, but also for treatment planning and follow-up. Nuclear imaging is a diagnostic medical imaging method that uses radionuclides to study the physiology and metabolism of the body [1].

In parallel with the developing new techniques, the number of publications in the literature has been increasing recently in the field of medical imaging. The use of dual radioisotope, that is one of these techniques, is considered to be effective in imaging of complicated tumor structures and nested tissues in the field of SPECT as well as in PET imaging [2]. Myocardial perfusion and brain imaging have been reported to be highly conclusive if this technique is succesfully implemented [3].

The dual isotope (DI) technique is based on the detection and visualization of two different gamma-emitting radionuclides at one time, which are injected into the patient, via the different energy decay windows. Especially for the PET device, the fact that positron-electron annihilations occur at 511 KeV energy for each time does not create an energy difference and requires extra gamma radiation to be used by the radioisotope. Thus, the selection of dual radioisotopes and measuring triple coincedence of gammas in PET imaging becomes utmost important. Not that, dual and multi tracer techniques mostly offer similar solutions but different timings and algorithms. [4,5,6]

The outline of the paper as following: we explain the simulation setup and GATE software in the next section, the statistical methods and calculations of parameters that will shed on light of a feasible DI technique will be mentioned in section III, we give analysis results and additional comments in section IV and conclude our study in the section V.

## 2. PET Simulation Setup With GATEv.8

GATEv.8 is an advanced opensource software developed by the international OpenGATE collaboration and dedicated to numerical simulations in medical imaging and radiotherapy. Using an easy-to-learn macro mechanism to configurate simple or highly sophisticated experimental settings, GATE v.8 now plays a key role in the design of new medical imaging devices, in the optimization of acquisition

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protocols and in the development and assessment of image reconstruction algorithms and correction techniques. It can also be used for dose calculation in radiotherapy experiments [7].

A cylindrical PET system that is a benchmark in GATEv.8 and composed of 4 rsectors (head), 64 cubic crystals (8 x 8) and 2 scintillation layers of BSO for inner and LSO for outer is implemented. Boxed world geometry with 0.4x0.4x0.4 m and water phantom with 20x20x20 cm is created. No CT system is added but the coincediences from standart read-outs are collected with rotating heads 30 deg/s for every 4 seconds (Total: 16 seconds). Most importantly two sources (C11 and Cu60) are implemented with their ion structures, half-lifes, activities and decay energies at different placements. We have chosen those sources since they are commonly used radioisotopes in PET imaging and known as gamma emitters in addition to positron emissions. Figure 1 shows the visualization of the system before the irradiation step. For digitization of the data, with 10 ns. Coincedence window, 350 – 650 KeV thresholder and upholder are used respectively. Not any of the PET systems has been referenced throughout the study. It is aimed to present the detectability parameters of the different radioisotopes. Standart physical interactions are implemented as Photoelectric, Compton, Rayleigh, Bremstrahlung scatterings and radioactive decays and positron annihilations are enabled.

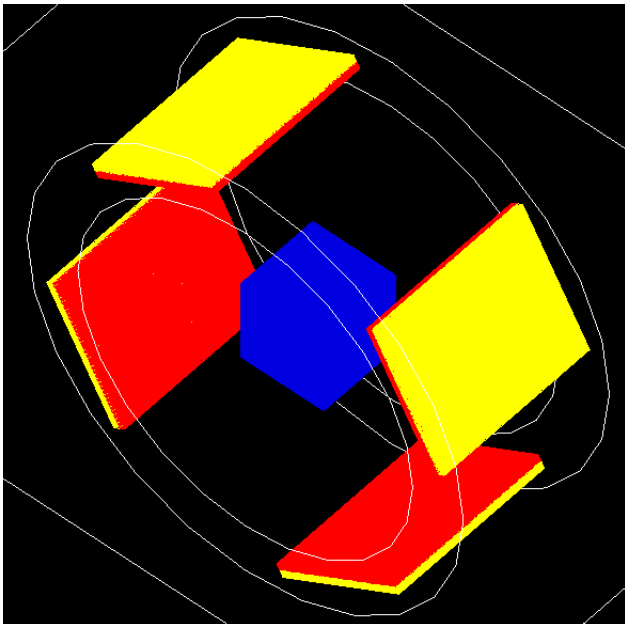

**Figure 1.** PET system design consisting of rotating BSO and LSO layers (red and yellow) and cubic water phantom (blue).

## 3. Material and Methods

In simulation, we scanned over different placements taking an interval between two sources starting from 0.4 cm to 4 cm. For each placements, we obtained two kind of outputs: Detector hits and coincedences (after digitization) with the histograms containing time lapse, energy, spatial distributions of gammas...etc. We also acquired data for blurred image resolutions 0.1, 0.26, 0.75 and 1 in digitization process respectively. All datas are analysed with a simple macro using ROOT [8].

In analysis step, we assume that the spatial distributions of sources are gauss curves with mean, standard deviations (σ) and total entries (hits). Thus, one can calculate that FWHM = (2.35 × σ) and take into account the Rayleigh criterion that says two point-like objects can be distinguished if the FWHM resolution of the optics is 0.82 times the distance of their images. As an example, two sources with 1 cm distance can be distinguished if the signal FWHM is no more than 0.82 cm. One can take this ratio for calculation optimal spatial resolution. Moreover an intensive analysis over σ distributions, as we present in this work, can give opportunity calculate optimal spatial resolutions with above mentioned blurring resolution set of PET device.

We also present contrast rates as a difference between two intensities as the following:

$$C = \frac{I_1 - I_2}{I_1 + I_2} \tag{1}$$

where the intensities I1 for first source C11 and I2 for the second source Cu60 can be calculated as follows;

$$I(r) = I_0\, exp\left(\frac{-2r^2}{w^2}\right) = \frac{2P}{\pi w^2}\, exp\left(\frac{-2r^2}{w^2}\right) \tag{2}$$

where $r$ is the spatial resolution, and w is the width taken as (0.849 × FWHM) in accordance with Rayleigh criterion. Moreover, as another feature of a PET device, we calculated digitization rate of the signal as digitizated signal entries over detector entries. Lastly, we applied chi-square method to determine if FWHM differences in PET data is significant.

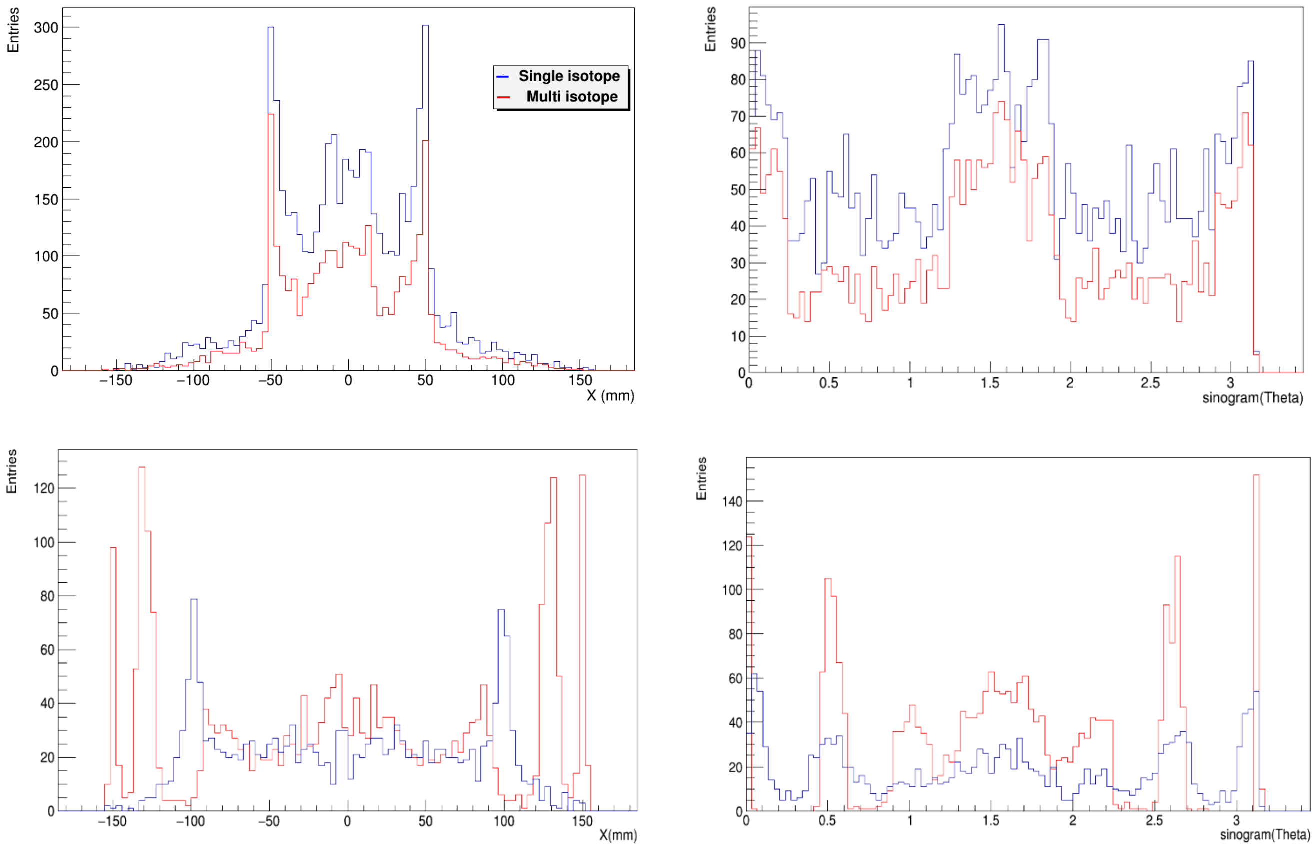


**Figure 2**. Sinograms for X axis (left) and scattering angle θ (right) in radians. Point-like $C^{11}$ is implemented for single isotope (blue) at +50 and -50 mm distances (top row) and +100 and -100 mm distance (below row). Dual isotope histograms (red) for $C^{11}$ and $Cu^{60}$ are plotted in stacks with same distances.

## 4. Comparison and Analysis

A first observation from the comparison of sinograms that at small distances between dual sources (e.g.: 2 mm), anhilation of electron-positron pairs are dominant but at longer distances than 50 mm (in our setup) one can expect more entries indiviually from dual-pairs as seen in Fig. 2. The same situation is good for energy plots as seen in Fig. 3. This also indicates that one can get a stronger overall signal using of dual isotopes regardless of the distances. However, one can realise the huge data acquisition differences between detector hits and coincedences in Fig 4. Roughly, 1.5% of total data has been labelling as coincedence while the remaining data has not been processing at all.

An observation from the energy perspective shows that while two resources emits energies at 511 KeV and 1330 KeV, annihilation processes occurs with only energetic electrons at proper range. We have chosen semi free energy window between 510 – 1400 KeV to work on near signal strenghts. One can get higher amount of data by setting another energy references for additional isotopes. Surely, that corresponds to a modification on the detectors of PET device.

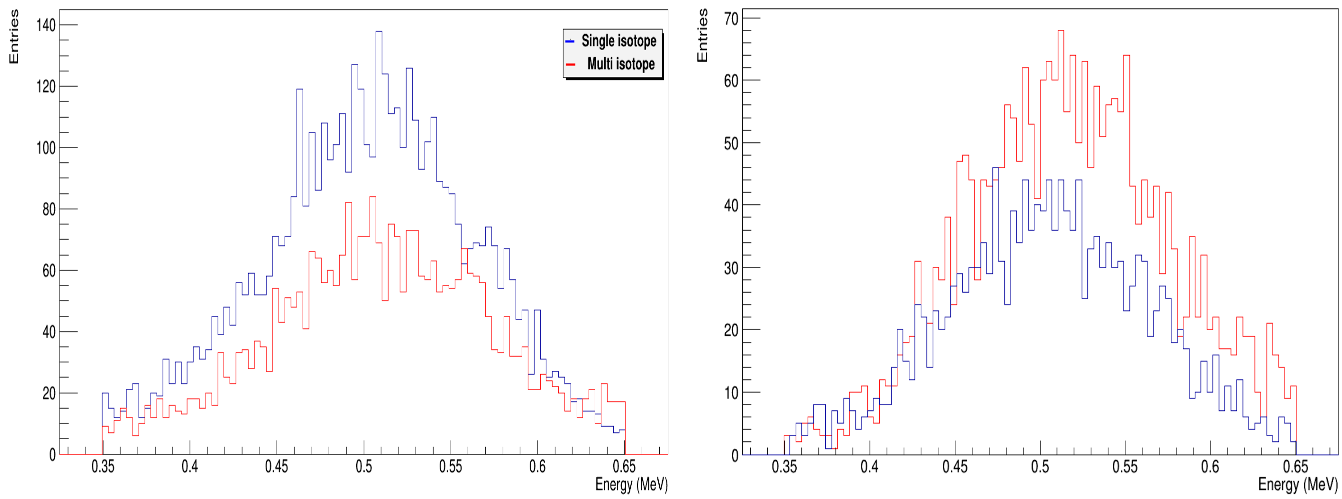


**Figure 3.** Total detected energy distributions in coincedences for +50 and -50 mm distances (left) and +100 and -100 mm distance (right). $C^{11}$ has been placed for single isotope (blue), $C^{11}$ and $Cu^{60}$ together placed for dual isotope (red) measures.

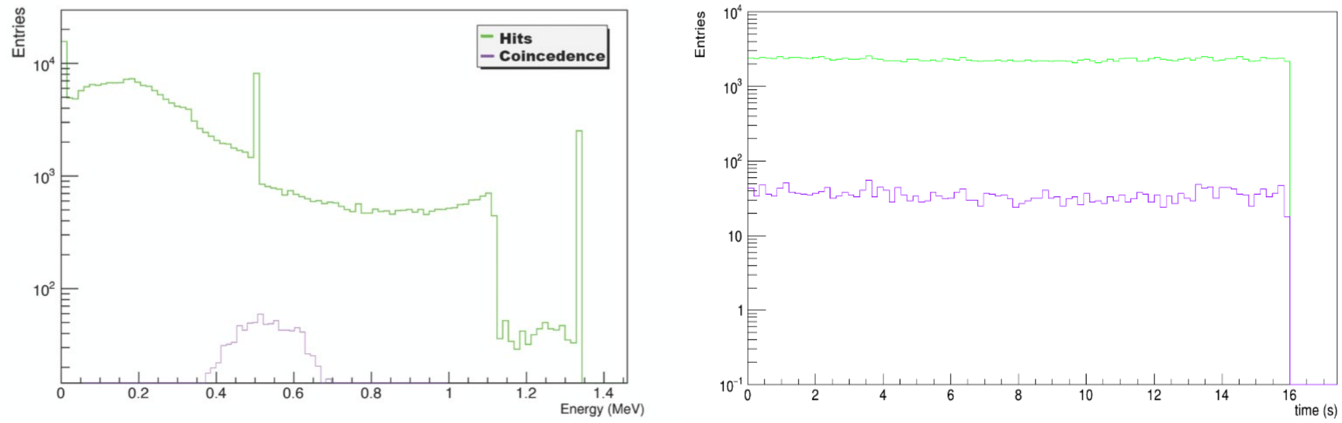


**Figure 4 -** For dual isotope resources of $C^{11}$ and $Cu^{60}$ energies that are considered at 511 KeV and 1330 KeV respectively, PET energy (left) and time (right) distributions in stacks with detected hits (green) and coincedences (purple).

It is analyzed the effects of dual isotope usage on PET device resolution as follows: We have placed $C^{11}$ and $Cu^{60}$ sources opposite to each other at several distances starting from (-2,+2) mm to (-20,+20) mm respectively as in Fig. 5 (left). Note that sources placed at (-2,+2) mm corresponds to 4 mm distance that is good for Rayleigh criterion since our smallest standart deviations is about 0.9. We mean that all distances are chosen in accordance with this criterion. We have repeated those similar runs changing the image resolutions of PET device as 0.1, 0.26, 0.75 and 1 mm. In profile histograms along (x,y,z), we have observed that the total entries are decreasing with the higher resolution for both single hits and coincedences. The same degredation is obtained also for enegy histograms as Fig. 5 (right). We have also observed that for the coincedences that total entries are higher if the distance is small. However, we searched that if the resolution cut for entries are significant between dual isotope and single isotope usage. One can construct a null-hypothesis as “there is no difference from dual isotope and single isotope usage in any image resolutions” as well as “there is no difference bewtween $C^{11}$ and $Cu^{60}$ usage in any resolutions”. Chi-square analysis is selected to apply on standard deviations (σ) as they are related with Rayleigh criterion as mentioned above. In analysis, we have compared σ values of signals from all resolutions with the smallest possible resolution (0.1 mm). After collecting σ values, we have calculated the chi-square values as follows:

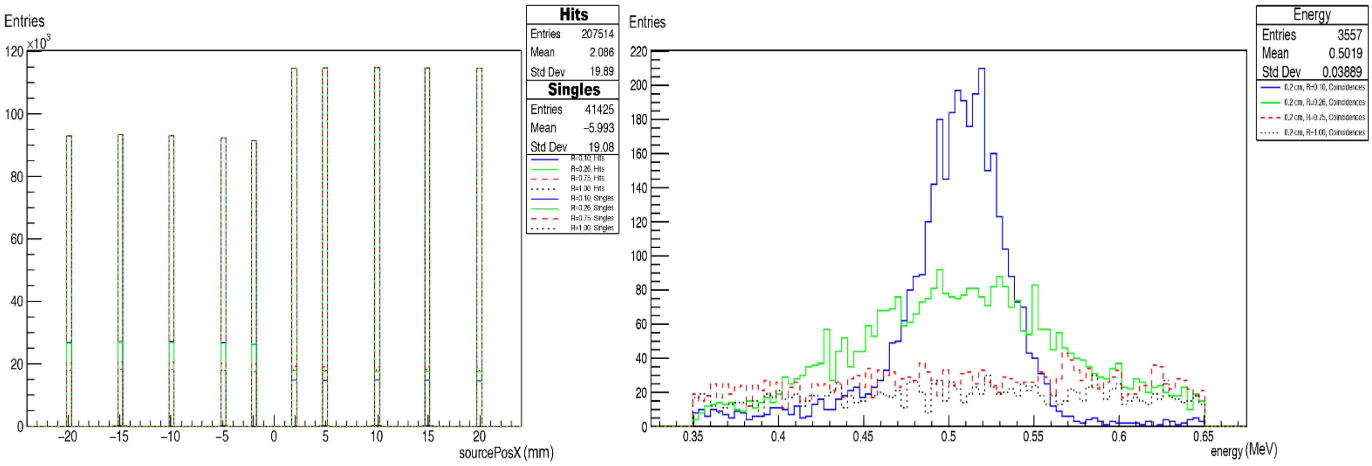


**Figure 5 –** (Left) Comparison of entries for dual isotopes placed at (-2,+2), (-5,+5), (-10,+10), (-15,+15), (-20,20) mm distances for hits and singles. (Right) Comparison of energy levels of entries from coincedences in different resolution as above. No major difference observed for singles and hits. Colors indicate different resolutions for both plots as 0.1 (blue), 0.2 (green), 0.5 (red dotted) and 1 (dashed) mm.

$$\chi^2 = \sum_{Distances} \frac{(\sigma_{0.1} - \sigma_{resolution})^2}{\sigma_{0.1}} \quad (3)$$

where $\sigma_{resolution}$ are collected values in 0.26, 0.75 and 1 mm image resolutions. We have summarized the results as in Table 1. According to chi-square values of single isotope simulations, one can see that resolution between 0.1 – 0.26 are low chi-square values indicate that the PET machine can distinguish two sources easily. It is also acceptable if the resolution is higher as 0.75 and 1 mm but significance level (α) drops about 0.975. For dual isotope simulations, low chi-square values show that the resolution is enough to distinguish two sources easily. For a comparison between dual isotope and single isotope simulations, PET device seems to be approx. 10 times (6 times) more precise at dual isotope usage for the worst case (best case).

We also calculated dual isotope image contrast values as in Table 2. Intensities are calculated normalising to highest intensity 1 and contrasts are obtained in percent in accordance with the equation (2). It can be seen directly that higher contrasts are obtained in small resolutions. Although all contrast values are good, 0.1 – 0.26 mm resolutions are give the best possible result. Note that the distances of sources are has no effect on contrast or intensities.

**Table 1 –** Chi-Square values over two different PET simulations: Single isotope and Dual isotope.

| | PET Energy Single İsotopes | | PET Energy Dual Isotopes |
|---|---|---|---|
| | $C^{11}$ | $Cu^{60}$ | $C^{11} + Cu^{60}$ |
| R=0.10-0.26 | 0.0808 | 0.0630 | 0.0116 |
| R=0.10-0.75 | 0.2476 | 0.2114 | 0.0253 |
| R=0.10-1.00 | 0.2554 | 0.3580 | 0.0262 |

**Table 2 –** Calculated contrast and intensity values over $C^{11}$ and $Cu^{60}$ source distances and resolutions.

| PET SOURCE POSX2 COINCIDENCES | | | | |
|---|---|---|---|---|
| Resolution (mm) | Distance (cm) | Intensity $C^{11}$ | Intensity $CU^{60}$ | Contrast (%) |
| R=0,10 | 0,2 | 0,018639911 | 0,000834623 | 0,914 |
| R=0,26 | | 0,010386333 | 0,001278318 | 0,781 |
| R=0,75 | | 0,002229608 | 0,000891843 | 0,431 |
| R=1,00 | | 0,001375709 | 0,000687855 | 0,330 |
| R=0,10 | 0,5 | 0,003064223 | 0,000094284 | 0,940 |
| R=0,26 | | 0,001596620 | 0,000149683 | 0,830 |
| R=0,75 | | 0,000332145 | 0,000142348 | 0,400 |
| R=1,00 | | 0,000195623 | 0,000108679 | 0,286 |
| R=0,10 | 1,0 | 0,000650233 | 0,000039408 | 0,886 |
| R=0,26 | | 0,000391067 | 0,000048131 | 0,781 |
| R=0,75 | | 0,000088933 | 0,000041502 | 0,364 |
| R=1,00 | | 0,000051728 | 0,000032671 | 0,226 |
| R=0,10 | 1,5 | 0,000291441 | 0,000018215 | 0,882 |
| R=0,26 | | 0,000176340 | 0,000022392 | 0,775 |
| R=0,75 | | 0,000036463 | 0,000018231 | 0,333 |
| R=1,00 | | 0,000021637 | 0,000014425 | 0,200 |
| R=0,10 | 2,0 | 0,000187356 | 0,000008922 | 0,910 |
| R=0,26 | | 0,000094633 | 0,000012411 | 0,769 |
| R=0,75 | | 0,000020771 | 0,000009644 | 0,367 |
| R=1,00 | | 0,000013141 | 0,000007608 | 0,267 |

## 5. Conclusion

As in this work, one can conclude that PET devices in GATE simulations can gain ability to distinguish dual isotope sources without extra modifications to virtual device. Although this kind of modifications are beyond the scope of this work, we have showed that there are quite amount of data that is excluded and expected to be processed simultenously with the process of capturing annihilated particles and coincedences. Note that we have carried on an analysis upon two distinct sources and observed quite low total entries after processing. Therefore, a complex analysis over tissues and real PET images can be a future work.

## Conflict of interest

The authors state that did not have conflict of interests.

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