Monte Carlo Simulations of a Non-Invasive Positron Detector to Measure the Arterial Input Function for Dynamic PET

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Abstract. This work presents Monte Carlo (MC) study of a novel non-invasive positron detector, hereinafter called NID, designed to measure the arterial input function (AIF) through the wrist of a patient for use with dynamic positron emission tomography (PET). The goal of the study was to optimize a previously developed NID prototype, to determine its efficiency and ability to distinguish between the arterial and venous portions of the signal escaping a wrist phantom. A user code based on the Geant4 MC toolkit was developed to model the NID and a wrist phantom. The scintillator based detectors were modelled as 64 polystyrene cylinders, 0.97 mm in diameter, 10 cm long and capped with cylindrical photomultiplier tubes. The scintillator fibers were arranged in a single band around a 64.13 mm polyethylene cylinder representing a model of the wrist. Two cylinders, 2.30 mm in diameter were placed 6 mm apart, 2 mm below the surface of the wrist phantom representing the radial artery and vein. Two simulations were performed by placing 100 million decay events of oxygen-15 (15O) or fluorine-18 (18F), randomly distributed between the artery and vein. Visible wavelength photon tracking was enabled, and Photomultiplier tubes were simulated to collect the visible photons. Deposited energy per event and location of energy deposition were calculated. A python algorithm was used to analyse the results. The arterial signal produced a 5.28 mm and 10.32 mm FWHM for 15O and 18F respectively. The algorithm could determine the correct location of interaction 98% of the time. The NID can resolve the arterial and venous signal and is thus suitable for determining the AIF for dynamic PET.

1. Introduction
Clinical interest in dynamic positron emission tomography (PET) has increased in recent years[1-4]. One example of this is detection of recurrence in prostate cancer (PS). The current standard for this is to perform a gadolinium-68 (68GD) labelled prostate specific membrane antigen (PSMA) PET scan. A static acquisition is performed 60 minutes post injection [5]. This protocol detects recurring lesions post treatment but is limited by the hyper-intense bladder which can mask lesions near the bladder. It has been demonstrated that dynamic PET performed up to 11 minutes post-injection, can in addition to all lesions detected with static PET also detect lesions near the bladder [6-7]. Dynamic PET has many other applications such as monitoring heart disease[8] and planning cancer treatments [3].

Unfortunately, this nuclear medicine technique is rarely used in a clinical setting due to three main disadvantages. Traditionally, dynamic PET scans are much longer than static scans, they can only
acquire a small field of view and they require knowledge of the radiation concentration in the patient’s arteries as a function of time, called the arterial input function (AIF). While the first two concerns are being worked on [1, 9], the acquisition of the AIF remains an unsolved problem.

The gold standard for AIF measurement is through arterial blood sampling. This is a costly and time-consuming technique that most nuclear medicine centers wish to avoid [10]. There also exists population averaging techniques [11] and image-derived input functions [12] but none have seen widespread clinical use. We are developing a non-invasive positron detector, hereinafter called non-invasive detector (NID), that can measure the AIF through the patient’s wrist. This is possible due to the relatively shallow placement of the radial artery, 2 mm +/- 0.99 mm [13], compared to the maximum travel distance of common PET radioisotopes in tissue [14]. In an earlier study, a prototype of this detector was built and benchmarked against an invasive microfluidic type detector [15]. It was found that the detector was capable of measuring clinically relevant activity concentrations of $^{18}$F, $^{11}$C and $^{68}$Ga through a wrist phantom. Figure 1 shows a regression analysis comparing the results of the two detectors. The present work presents Monte Carlo simulations to evaluate a new design for the detector to optimize its setup.

2. Methods

A user code based on the Geant4 MC toolkit was developed to model the NID and a wrist phantom. The NID geometry was composed of 64 plastic scintillating fibers, 0.97 mm in diameter and 10 cm long. These fibers had a 0.03 mm cladding layer and a 0.0250 mm plastic protective layer. Each fiber end was coupled to a photomultiplier tube (PMT) to collect photons in the visible range. These fibers were arranged in a single band wrapped around a 64.13 mm in diameter polyethylene cylinder that represents a wrist phantom. Two 2.30 mm diameter cylinders were placed inside the wrist to simulate the radial artery and vein of a patient. These cylinders were 6 mm apart and 2 mm below the surface of the wrist. Simulations were performed by simulating 100 million decay events of either oxygen-15 ($^{15}$O) or fluorine-18 ($^{18}$F), randomly distributed between the artery and vein. Particle transport was performed by using the Penelope low-energy electromagnetic physics and optical photon processes. Interactions were recorded when energy was deposited in the scintillator core. Total deposited energy in the scintillator was calculated and the location of interaction for each event was scored. The number of optical photons that accumulated in each PMT were also calculated. Figure 2 shows the geometry of the simulation.
The data was analyzed using a python algorithm to separate the arterial signal from the venous signal. For each event, the PMT with the highest photon count is considered as true location of interaction on the y-axis. The data points from positrons originating from the artery are considered and a histogram is built. A mask of this histogram is created using kernel density estimate. This mask can then be overlaid on a y-axis position histogram of a mixed arterial/venous signal which yields the arterial component of the signal. Figure 3 shows a graphical flowchart of this script.

Figure 3. Flowchart of data analysis script

3. Results/Discussion
The arterial signal produced a 5.28 mm and 10.32 mm full width half max (FWHM) for $^{15}$O and $^{18}$F respectively. Since these two signals are 6 mm apart, for $^{15}$O, this results in two distributions that are readily resolvable. For $^{18}$F, the FWHM of both components of the signal are larger than their spatial separation which makes them difficult to resolve. The data analysis script takes advantage of the fact that on the first pass through the detector, the bolus will be exclusively in the patient’s artery. This allows us to train the detector and use the mask at later timepoints when there will be a mixed signal. Using the script, we could calculate 104 % and 110 % of the true signal as calculated by the Monte Carlo simulation for $^{15}$O and $^{18}$F respectively. The number of detected positrons was overestimated by the script because the tail of the vein distribution overlaps with the arterial distribution. Currently, the script scales the mask to fit the given distribution. To improve this matching, we propose that an ultrasound of the wrist be taken before the dynamic PET scan which would allow us to measure the depth and size of the radial artery and vein. This would allow for Monte Carlo simulations to be performed on a patient-to-patient basis to match their specific biology.

4. Conclusion
We have simulated the sensitive volume of a novel non-invasive positron detector designed to detect positrons through a wrist phantom. The simulated detector can resolve the venous and arterial components of the signal and represents a promising method to non-invasively measure the arterial input function for dynamic PET.

5. References
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