Positronium Imaging

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***Abstract*–During the positron emission tomography about 40% of positrons annihilations occur through the creation of positronium which may be trapped within and between molecules. Positronium decays in the patient body are sensitive to the nanostructure and metabolism of the tissues. This phenomenon is not used in the present PET diagnostics, yet it is in principle possible to use environment modified properties of positronium as diagnostic biomarkers for cancer therapy. First in-vitro studies show differences of positronium mean lifetime and production probability in the healthy and cancerous tissues, indicating that they may be used as indicators for in-vivo cancer classification. Here we present a method of positronium lifetime imaging in which the lifetime and position of positronium atoms is determined on an event-by-event basis. The method requires application of β+ decaying isotope emitting prompt gamma (e.g. ^{44}Sc). We discuss the possibility of determining the time and position of positronium annihilation from the back-to-back photons originating from the interaction of positronium with the surrounding atoms and bio-active molecules. The prompt gamma is used for the determination of the time of the formation of positronium. We estimate that with the total-body PET scanners the sensitivity of the positronium lifetime imaging, which requires coincident registration of the back-to-back annihilation photons and the prompt gamma is comparable to the sensitivities for the metabolic imaging with standard PET scanners.**

I. Introduction

Positron emission tomography (PET) is well-established diagnostic technique enabling metabolic imaging of the living organisms. In PET, the radiopharmaceuticals administered to the patient are labeled with isotopes emitting positrons. Positron annihilates with the electron in the body. The annihilation may lead to the emission of two or more photons and it may proceed directly or via intermediate formation of the metastable positronium atom. Positronium atoms are produced in the patient's body in up to about 40% of cases of positron-electron annihilation [1]. One quarter of these cases constitute short lived spin-zero para-positronium (with mean lifetime in vacuum of 125 ps), and in three-quarters of cases a long-lived spin-one ortho-positronium is created (with mean lifetime in vaccum of 142 ns). Ortho-positronium mean lifetime depends strongly on the size of free volumes between atoms while its formation probability depends on their concentration. In addition, both these characteristics depend on the availability of bio-fluids and bio-active molecules such as e.g. oxygen which can interact with the emitted positrons as well as with positronium. The lifetime of ortho-positronium trapped within molecules in the body decreases to a few ns due to the additional possibilities of the annihilation via interaction of positronium with electrons from the surrounding molecules and via interactions with bio-active molecules. In Fig. 1, on example of hemoglobin, main channels of positronium annihilation in tissue are illustrated.

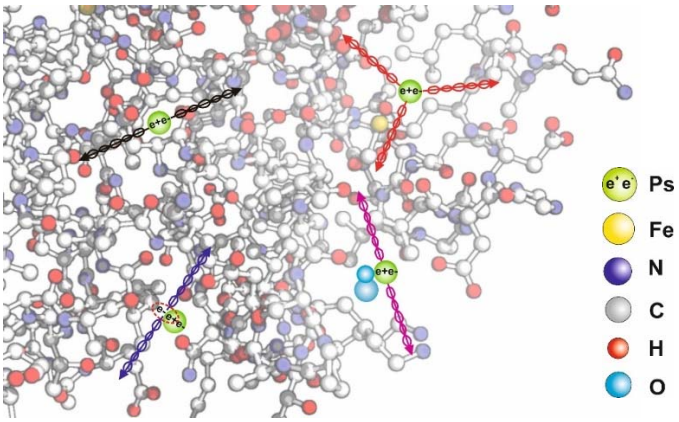

Fig. 1. Fragment of the hemoglobin molecule with pictorial representation of the possible ways of decays of positronium atoms trapped in the intermolecular voids. Black and red arrows depict photons from the decay of para- and ortho-positronium inside free space between atoms, respectively. Violet and magenta arrows indicate annihilation of positronium through the interaction with the electron from the surrounding molecule (violet) and conversion of ortho- into para-positronium via interaction with the oxygen molecule and subsequent decay of para-positronium to 2γ (magenta) [2].

In references [1,2,3] it was suggested that positronium properties may serve as indicators which in addition to the currently used standardized uptake value, would deliver complementary diagnostic information telling about the nano-structure of tissues and concentrations of bio-active molecules. At present the J-PET collaboration is carried out in-vitro measurements of properties of positronium in healthy and cancerous tissues operated from patients [4,5]. The first results obtained for uterine-, cardiac myxoma and colon cancers indicate that there are measurable differences between the life-time of positronium in healthy and cancerous tissues and that it is possible to measure positronium lifetime with the J-PET tomograph. In order to test the correlation of the mean ortho-positronium lifetime with the grade of development of metabolic disorders in cancer cells the investigations are ongoing with cancer and healthy tissues. At present about one sample from patients are examined per week. One of the working hypotheses connecting the lifetime of positronium with the grade of the cancer is the concentration of oxygen which differs for most cancers (hypoxia) from its

Manuscript received December 19, 2019. This work was supported in part by the Foundation for Polish Science through the TEAM POIR.04.04.00-00-4204/17 program, the National Science Centre of Poland through grant no. 2016/21/B/ST2/01222, and the Polish Ministry for Science and Higher Education through grant no. 7150/E-338/SPUB/2017/1.

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978-1-7281-4164-0/19/$31.00 ©2019 IEEE

concentration in normal tissues. However, for the clinically useful conclusions, due to the dependence of ortho-positronium lifetime on the bio-active molecules the decisive studies will need to be conducted in vivo. In this presentation it is argued that presently such investigations become possible with the advent of the total-body PET scanners [6,7,8,9] characterized by the high imaging sensitivity.

II. POSITRONIUM IMAGING

In general positronium imaging may be defined as a method for the position-sensitive reconstruction of positronium properties within the imaged object. The following properties can be considered as candidates for new diagnostic indicators [1,3,10] correlated with the nanostructure and concentration of bio-active molecules: (i) the mean lifetime of ortho-positronium, (ii) positronium production probability, and (iii) the ratio of annihilation rates into two and three photons. The $3\gamma/2\gamma$ rate ratio is accessible with all kinds of $\beta+$ emitting isotopes, while determination of lifetime and its formation probability requires applications of isotopes emitting prompt gamma. An example of an isotope appropriate for positronium lifetime imaging is ^{44}Sc, which emits positron via following process: $^{44}\mathrm{Sc} \rightarrow {}^{44}\mathrm{Ca}^{*}\, e^{+}\, \nu \rightarrow {}^{44}\mathrm{Ca}\, \gamma\, e^{+}\, \nu$, where excited ^{44}Ca* nucleus emits 1.16 MeV prompt gamma on the average after about four femtoseconds [11,12]. The measured time of the prompt gamma emission is used to determine the moment of the positronium formation since nuclear deexcitation and positronium thermalization in tissue is much faster (tens of picoseconds) than ortho-positronium lifetime. The time of the emission of annihilation photons is used to determine the moment of the positronium decay. In order to reconstruct the image of mean positronium lifetime, for each registered event the positronium lifetime and annihilation point need to be determined. Here there are two possibilities: one can either use the decay of positronium into three photons or into two photons. The registration of three photons decay allow for reconstruction of the annihilation point on an event-by-event base (e.g. using a trilateration-based method [13]) with the spacial resolution higher than the one achievable for the two-photon decay. The feasibility study of the 3γ decay positronium lifetime imaging is described extensively in ref. [1]. On the other hand, in the tissue the fraction of three-photon annihilation is less than 0.5% and this limits significantly the statistics of events to about 700 per cubic centimeter [1]. Here we estimate the sensitivity of the positronium lifetime image reconstruction based on the registration of annihilations of ortho-positronium into two photons which in the tissue occurs about 70 times more frequent than annihilation into three photons [1], and which can be registered with the higher detection sensitivity (2γ vs 3γ measurement) [14]. With the continuous improvement of the time resolution [15] (current TOF-PET achieve 250 ps [16] and the single detectors reach even 30 ps equivalent to position resolution of 4.5 mm along the line of response [17]) it may become feasible in the near future to reconstruct an image directly as a density distribution of annihilation points. Therefore, the main objective of this article is the estimation of the sensitivity for the positronium life-time imaging using ^{44}Sc isotope and 2γ annihilations of ortho-positronium atoms.

III. SENSITIVITY OF POSITRONIUM IMAGING WITH TOTAL-BODY PET SCANNERS

In this section the sensitivity gain of the standard PET 2γ imaging and of the $2\gamma + \gamma_{prompt}$ registration is estimated as a function of the length of the axial field of view (AFOV) of the scanner. The calculations are performed for the two types of scintillator material: LYSO crystal and plastic scintillators. Estimations were performed assuming that the scanners are in the form of cylinder with the diameter of 40 cm and the thickness of 2 cm (LYSO) and 6 cm (plastic scintillator; optimum solution for the double layer J-PET scanner). $2\gamma + \gamma_{prompt}$ photons were emitted from the 2 m long line source positioned along the main tomograph axis. In the calculations the interaction probability as a function of the angle under which the photon is entering the detector, as well as the attenuation of photons were taken into account. The attenuation was estimated assuming that the source is inserted in the center of the 2 m long and 20 cm diameter water phantom. All needed attenuation coefficients for Compton and photoelectric effects were taken from nuclear data base [11]. Results are shown in Fig. 2. They indicate that for the total-body PET the sensitivity for the discussed positronium imaging would be comparable to the sensitivity for 2γ imaging with PET systems of AFOV = 20 cm. Dashed line indicates as expected that for the regular 2γ PET imaging the total-body PET sensitivity increases by more than a factor of 40 with respect to AFOV=20 cm and for plastic PET design (dotted line) it would increase more than 20 times.

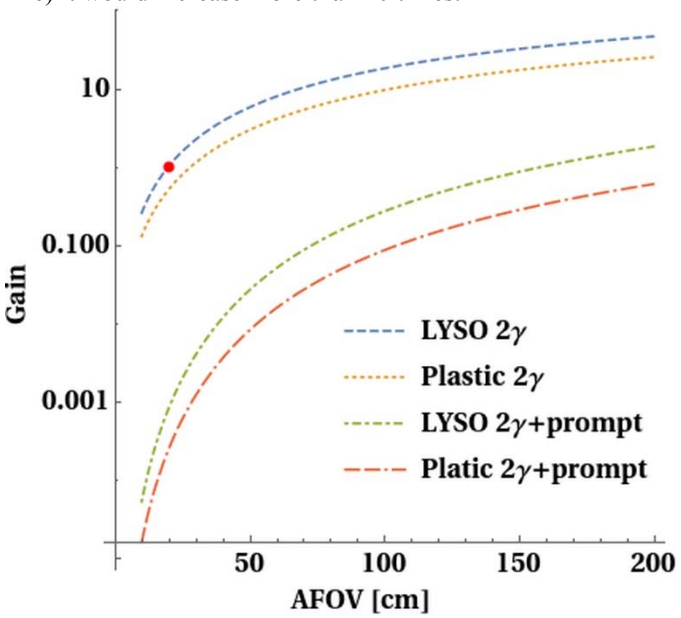

Fig. 2. Sensitivity gain for the 2γ and positronium imaging with respect to the LYSO based PET with AFOV =20 cm (red point). For details see text.

IV. CONCLUSIONS

Positronium imaging may bring a new in-vivo diagnostic indicator available during the PET scan. Sensitivity of the positronium lifetime imaging with a total-body PET scanner is

comparable to the sensitivities of the standard 2γ metabolic imaging with the PET scanners with AFOV = 20 cm.

ACKNOWLEDGEMENTS

Author is grateful to A. Kamińska and D. Kisielewska for help with figures and A. Gajos for correcting the manuscript.

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