RPE | Radiation Physics & Engineering
An International Peer-Reviewed Journal
Published by K.N. Toosi University of Technology
http://rpe.kntu.ac.ir
Research Article

Radiation Physics and Engineering 2022; 3(3):1–5
https://doi.org/10.22034/RPE.2022.336848.1072

Experimental investigation of the oxygen sensing ability of positron annihilation spectroscopy for tumor imaging

Mahshid Zare[a], Behjat Ghasemi[a], Omidreza Kakuee[b], Ali Biganeh[*,b]

[a] *Nuclear Engineering School, Shahid Beheshti University, Tehran, Iran*
[b] *Physics & Accelerators Research School, Nuclear Science & Technology Research Institute, P.O. Box 14395-836, Tehran, Iran*

HIGHLIGHTS

- Possible biomedical application of PAS is discussed.
- Oxygen sensing ability of the PALS technique is investigated.
- The capability of Positronium for identification of polar bond groups of polymers is confirmed.
- OEMS of the Doppler broadening spectroscopy is sensitive to the presence of oxygen.
- The presented approach provides a tool for measurement of oxygen in Carcinogenic tissues.

ABSTRACT

The potential biomedical application of Positron Annihilation Spectroscopy (PAS) for nonstructural characterization of normal and cancer cells was not thoroughly employed and researched. In this paper, the experimental investigation of the oxygen sensing ability of the PAS technique for tumor imaging is presented and discussed. This research is based on the validated hypothesis that tumor cells differ from the normal tissues in their value of oxygen concentrations. The components of Doppler Broadening and positron annihilation lifetime spectra are measured with our homemade spectrometer to determine the mechanism behind the positron annihilation in oxygen content tissue-equivalent samples. The analysis of PAS data shows that the Orbital Momentum Spectrum (OEMS) of the Coincidence Doppler Broadening Spectroscopy (CDBS) and the positronium lifetime components of Positron Annihilation Lifetime Spectroscopy (PALS) are sensitive to the presence of oxygen. The results are applicable in the development of a tumor imaging system based on the PAS technique.

KEYWORDS

Positron annihilation spectroscopy
Tumor imaging
PET
Oxygen

HISTORY

Received: 9 April 2022
Revised: 7 May 2022
Accepted: 9 May 2022
Published: Summer 2022

1 Introduction

Positron Emission Tomography (PET) has already gained general acceptance for the detection of tumor cells and their response to therapy plans. Many efforts have been devoted to improving the accuracy of the PET results. The development of instrumentation for clinical PET is reviewed by Muehllehner and Karp (Muehllehner and Karp, 2006). PAS is also a well-established technique for defect assay and their chemical environments in solids and liquids (Jean, 1990). PAS includes the PALS technique to obtain the size and concentration of defects and CDBS analysis to explore the chemical environment of positron annihilation sites. Although the PAS analysis has been extensively used for defect characterization in metals and semiconductors, the possible biomedical application of PAS to support PET has not been thoroughly researched (Moskal et al., 2019). In low-electron density materials such as tissues and polymers, Positronium atom (Ps) significantly forms during the PAS analysis. Due to its charge neutrality, Ps is a suitable probe for the characterization of annihilation sites. Since the carcinogenic and healthy tissues differ significantly (Vaupel et al., 2004) by the concentration of oxygen in their contents, the development of a tumor imaging system based on the PAS technique is the subject of study.

A combined PALS-PET system is a conventional PET spectrometer that should be set-up such to record the data of annihilation radiation and gives information about the positron lifetime on the density distribution of the radiopharmaceutical in the body. The proposed PALS-PET imaging is based on the record of the times and hit positions of the photons in the list of data. The event-by-event

*Corresponding author: abiganeh@aeoi.org.ir

registration enables the reconstruction of the annihilation sites (for PET) as well as the O-Ps lifetime in each position (for PALS) using the list of data. This is a quite new concept and few studies and experimental data exist to support the idea. Moskal et al. presented the feasibility study of positronium imaging with the Jagiellonian PET scanner (Moskal et al., 2019). This scanner consists of lots of strip plastic scintillator detector equipped with a waveform digitizer that can record the annihilation events in a matrix contains $(X_i, Y_i, Z_i, T_i, E_i)$, where the first three components represent the position, T_i and E_i are the time stamp and energy of the recorded photon. Since the reconstruction of the positron lifetime needs two signals for the birth and death of the positron, a new positron emitter should be introduced for the PALS-PET scanner. This can be achieved using radiopharmaceutical labeled with Sc-44 that decays via the emission of both the positron and gamma through the following process (Walczak et al., 2015):

$$^{44}Sc \longrightarrow ^{44} Ca^* + e^- + \nu_e \qquad (1)$$

where ν_e is the produced neutrino and has negligible probability for interaction with detector and patient. However, very little systematic research has been done to describe the hypothesis of the concept. The basic questions that should be answered to establish the concept of the combined PALS-PET technique are fourfolds:

- Is the PALS technique sensitive to the oxygen concentration in tissues?
- Which parameters of the PALS can reveal the changes in oxygen concentration?
- What is the detection limit of oxygen sensing in the PALS technique?
- Which contribution of positron annihilation can be attributed to the cancer tissues?

Stepanov et al. have investigated the sensitivity of PALS to dissolved oxygen in tissue equivalent liquids (Stepanov et al., 2020). They have developed a special software (RooPositron) for PALS analysis with initial parameters including clear physical meaning for the description of positron annihilation via oxygen sites (Stepanov et al., 2020). The characterization of normal and cancer tissues by PALS has been done by Kubicz (Kubicz, 2020). The results confirm that the changes in cancer cells are significant enough to affect the positron annihilation parameter to a degree observable with PALS.

However, before working on biological samples, we have initiated a systematic investigation to answer the above-mentioned questions. In this paper, the sensitivity of the CDBS and PALS technique for the identification of different annihilation sites and the parameters of the PAS connected to annihilations related to oxygen sites are explored and discussed for some tissue-equivalent polymers.

2 Theoretical background

To understand the mechanism that correlates the existence of oxygen and annihilation properties, we focus on the main reaction channel of positron annihilation. Due to the opposite charges of electrons and positrons, they can bound to a system and form a stable semi-atomic state called Positronium (Ps) atom. The charge neutrality of the Ps atom allows it to penetrate the electronic structure of an atom and annihilate with core electrons. The annihilation of the Ps atom with the core electrons reveals the chemical environment of positron annihilation sites. Ps atom exists in two different states: The O-Ps where the spins of electrons and positrons are parallel ($S = 0$) and the Para positronium (P-Ps) with anti-parallel spins ($S = 0$). The fate of both states is annihilation with an electron and the emission of two gammas with the energy of about 511 keV. P-Ps atom self annihilates with the mean lifetime of about 125 ps. The value of P-Ps lifetime is within the limit of timing resolution of the PALS system and does not make sense in PAS analysis. On the contrary, the O-Ps lifetime (in the order of several nanoseconds) is easily measurable using conventional PALS systems and makes it possible to investigate how the changes in the oxygen concentration affect the yield of O-Ps formation and its mean lifetime.

However, the interaction of positronium in the oxygen-containing polymers can be affected by two mechanisms:

First, the inhibition of positronium formation (Lazzarini, 1986) in which the dipole distribution of electric charge for oxygen atoms in double bonds with carbons plays the role of a strong quencher and leads to a locally high-density electron regions. In consequence, before Ps formation, positrons simply annihilate with the free electrons. This mechanism is responsible for a significant decrease in the intensity of O-Ps annihilation without any changes in O-Ps lifetime.

Second, the O-ps conversion which the unpaired electrons of $2p^4$ orbitals initiate the conversion of O-Ps to P-Ps via Eq. (2) (Ferrell, 1956):

$$\mathrm{O-Ps} + O_2 \rightleftarrows [\mathrm{Ps-O_2}]^* \rightleftarrows \mathrm{P-Ps} + O_2 \qquad (2)$$

From the PALS point of view, the conversion mechanism leads to a slight decrease in the longest-lived component (τ_3) of the positron lifetime spectrum.

3 Sample preparation

The granule of four polymers including Polypropylene (PP), Low-Density Polyethylene (LDPE), Polytetrafluoroethylene (PTFE), and Polymethylmethacrylate (PMMA) are selected for PAS analysis. All the samples are purely melted into the hot liquid and then poured into a mold for the required shape. The samples are made thick enough (2 mm^2) to stop all the positrons inside them. The Differential Scanning Calorimetry (DSC) analysis up to 400 °C is carried out to obtain the degree of crystallinity for each sample because this parameter affects the results of the PAS technique. In DSC analysis the heat flow (mW) of the sample is measured versus temperature. Figure 1 shows the result of the DSC analysis for the LDPE sample. The exothermic reaction for the LDPE sample at 102.39 °C is shown with a negative peak in the DSC curve. By

Table 1: The results of DSC analysis.

Sample	Density ($g.cm^{-3}$)	Enthalpy of perfect crystal ($J.g^{-1}$) (Brandrup et al., 1999)	Measured fusion Enthalpy ($J.g^{-1}$)	Degree of crystalinity (%)
PP	0.0861	207.1	74.4	35.92
LDPE	0.930	193.6	59.81	20.4
PMMA	1.159	-	-	Amorphous
PTFE	2.2	82	13.03	15.9

integrating the peak, the fusion enthalpy can be calculated using Eq. (3):

$$\Delta H = K\,A \tag{3}$$

where is the fusion enthalpy ($J.g^{-1}$), K is the calorimetric constant, and A is the area under the peak. The percentage of the polymer crystallinity (C) is estimated from the fusion enthalpy of a perfect reference polymer (ΔH_{ref}) and the measured fusion enthalpy (ΔH_{exp}) (using Eq. (4)):

$$C(\%) = \frac{\Delta H_{exp}}{\Delta H_{ref}} \times 100 \tag{4}$$

The final results of the DSC analysis and the calculated degree of crystallinity for all the investigated samples are listed in Table 1. The DSC curve of the PMMA sample did not exhibit any phase transition and was considered as an amorphous polymer.

4 Experimental details

PALS and CDBS techniques are executed for prepared samples to explore the sensitivity of the PAS parameters to positron annihilation sites. All the experiments are carried out at the PAS laboratory of Nuclear Science and Technology Research Institute (NSTRI). The details of set-up, calibration, long-term stability, resolution, and positron source characterization of our 2d-CDBS and PALS spectrometer are presented in our previous works (Biganeh et al., 2019, 2020). Each experiment lasts 4 days to obtain the required statistics.

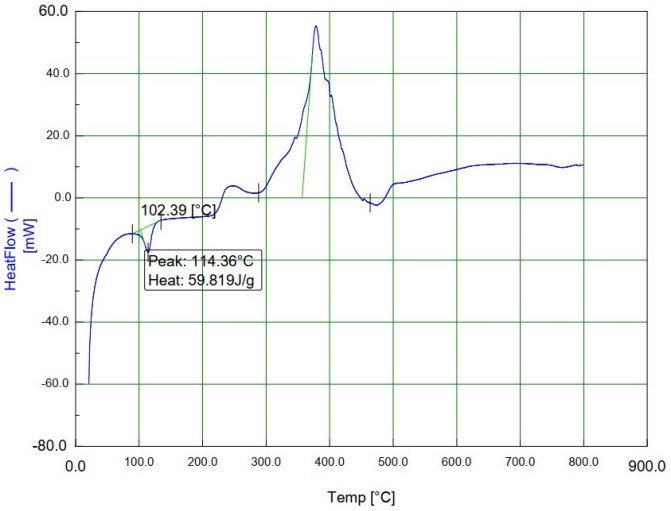

Figure 1: The measured DSC curve for the LDPE sample.

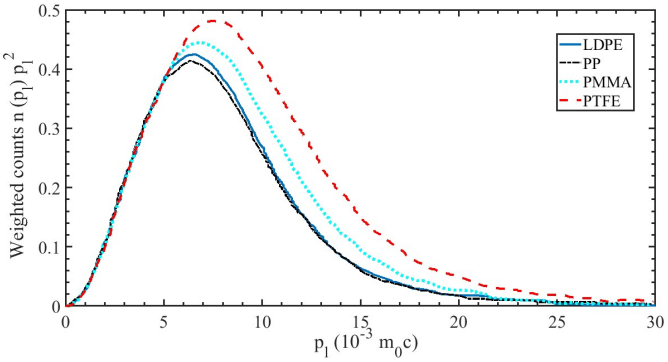

Figure 2: The OEMS of the investigated samples (Biganeh et al., 2020).

5 Results and Discussion

Figure 2 shows the Orbital Electron Momentum Spectrum (OEMS) of the samples. The OEMS is the weighted counts $n(p_1)p_1^2$ versus the longitudinal momentum of annihilated electrons (p_1) and describes the competition between valence and core electrons for annihilation with positrons. As shown in OEMS, the contribution of positron annihilation for low-momentum electrons is despised and this contribution for core electrons is magnified. So the OEMS peak is a signature of positron annihilation sites (Flores et al., 2002). For the PP and LDPE samples, the OEMS peaks show the positron annihilation with carbon atoms because the hydrogen atom has no core electrons. The position of OEMS peaks for PMMA and PTFE are mainly attributed to the positron annihilation with core electrons at polar groups (see the chemical bonds in Table 2). Compared to LDPE and PP samples the peak intensity for PMMA and PTFE is much higher because the polar groups (with higher positron affinity) trap positrons and force them to annihilate near the polar bonds. The OEMS peak position is a characteristic of each group of polymers and its intensity is attributed to the probability of positronium annihilation with core electrons. So it is expected that the intensity of the OEMS peak increases by an increase in the concentration of oxygen in the content because this peak is a characteristic of positron annihilation near oxygen and fluorine sites. This provides a systematic approach for relative measurement of oxygen concentration in carcinogenic tissues by CDBS technique. The other approach can be explored by the PALS technique. Figure 3 shows the positron lifetime spectrum for the PMMA sample. The positron lifetime spectrum of each sample is decomposed to the positron annihilation

Table 2: The results of the PALS technique for the investigated samples.

Sample	Characteristic bond	τ_1 (ns)	I_1(%)	τ_2 (ns)	I_2(%)	τ_3 (ns)	I_3(%)
PMMA	C=O	0.208 ±0.014	49.81 ±0.01	0.431 ±0.016	33.24 ±1.07	3.22 ±0.029	16.95 ±1.08
PTFE	C-F	0.231 ±0.05	59.43 ±1.01	0.521 ±0.047	28.41 ±1.28	3.85 ±0.018	12.16 ±1.17
PP	C-H	0.241 ±0.005	50.98 ±1.09	0.475 ±0.011	27.41 ±1.03	2.40 ±0.031	21.61 ±1.13
LDPE	C-H	0.217 ±0.003	46.07 ±1.05	0.496 ±0.019	24.51 ±1.24	2.61 ±0.015	29.42 ±1.11

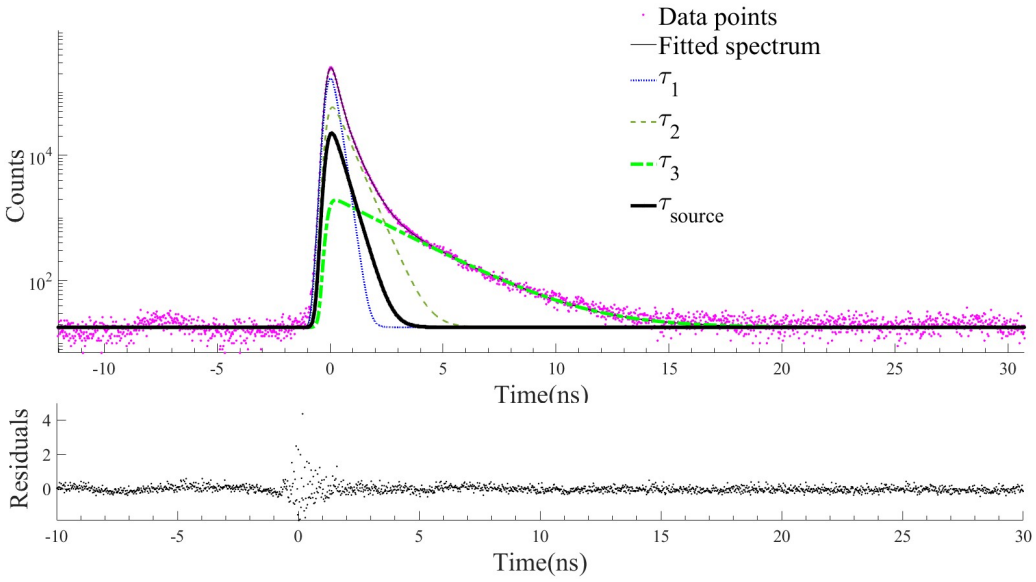

Figure 3: Positron lifetime spectrum of the PMMA sample fitted by LT-10 code.

lifetime τ_i (ns) and its related intensity I_1(%) using LT-10 software (Giebel and Kansy, 2012).

The results of the data analysis are listed in Table 2. The τ_1 component is related to P-Ps self-annihilation and does not make sense in our study. The intermediate component (τ_2) causes by the positron annihilation at the sites of lattice flow. The τ_3 parameter and its relative intensity with a lifetime greater than 2 ns are directly related to the O-Ps annihilation. As listed in Table 2, the I_3 parameter for PTFE and PMMA samples is much lower than PP and LDPE because the high electron density at polar groups sites reduces the probability of positronium formation. In brief, for samples with different concentrations of oxygen, we expect that I_3 decreases as the oxygen concentration increases in the content. So, with the hypothesis that PAS is sensitive to oxygen annihilation sites, we can examine the possibility to use positronium as a novel biomarker in cancer diagnosis systems.

6 Conclusions

In this paper, the capability of Positronium atoms for the identification of polar-bond positron annihilation sites is studied. The results of PAS analysis confirm that OEMS and the probability of positronium formation are sensitive to the presence of oxygen in the samples. Further to this work, we are going to initiate a systematic investigation of the tissue-equivalent samples with different concentrations of oxygen by the PALS technique. The potential application of such an investigation is to identify the carcinogenic tissues that suffer from the lack of oxygen by the PALS technique. If the PALS analysis shows the required sensitivity to distinguish between healthy and tumor tissues, PALS and PET techniques can combine in one clinical tomography system to provide data with a higher degree of precision to support the cancer diagnostic tests.

References

Biganeh, A., Kakuee, O., Rafi-Kheiri, H., et al. (2019). Development of a 2d digital coincidence Doppler broadening spectrometer. *Journal of Instrumentation*, 14(02):P02017.

Biganeh, A., Kakuee, O., Rafi-Kheiri, H., et al. (2020). Positron annihilation lifetime and Doppler broadening spectroscopy of polymers. *Radiation Physics and Chemistry*, 166:108461.

Brandrup, J., Immergut, E. H., Grulke, E. A., et al. (1999). *Polymer handbook*, volume 89. Wiley New York.

Ferrell, R. A. (1956). Theory of positron annihilation in solids. *Reviews of Modern Physics*, 28(3):308.

Flores, K., Suh, D., Dauskardt, R., et al. (2002). Characterization of free volume in a bulk metallic glass using positron annihilation spectroscopy. *Journal of Materials Research*, 17(5):1153–1161.

Giebel, D. and Kansy, J. (2012). LT10 program for solving basic problems connected with defect detection. *Physics Procedia*, 35:122–127.

Jean, a. C. (1990). Positron annihilation spectroscopy for chemical analysis: a novel probe for microstructural analysis of polymers. *Microchemical Journal*, 42(1):72–102.

Kubicz, E. (2020). *Biomedical applications of Positron Annihilation Lifetime Spectroscopy: nanostructural characterization of normal and cancer cells and tissues*. PhD thesis, Jagiellonian University.

Lazzarini, E. (1986). A comprehensive model for positronium formation and related phenomena of its inhibition and enhancement. *International Journal of Radiation Applications and Instrumentation. Part C. Radiation Physics and Chemistry*, 28(1):49–54.

Moskal, P., Kisielewska, D., Curceanu, C., et al. (2019). Feasibility study of the positronium imaging with the J-PET tomograph. *Physics in Medicine & Biology*, 64(5):055017.

Muehllehner, G. and Karp, J. S. (2006). Positron emission tomography. *Physics in Medicine & Biology*, 51(13):R117.

Stepanov, P., Selim, F., Stepanov, S., et al. (2020). Interaction of positronium with dissolved oxygen in liquids. *Physical Chemistry Chemical Physics*, 22(9):5123–5131.

Vaupel, P., Mayer, A., and Höckel, M. (2004). Tumor hypoxia and malignant progression. In *Methods in Enzymology*, volume 381, pages 335–354. Elsevier.

Walczak, R., Krajewski, S., Szkliniarz, K., et al. (2015). Cyclotron production of Sc-43 for PET imaging. *EJNMMI physics*, 2(1):1–10.