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Experimental investigation of the effect of oxygen on the positron annihilation mechanisms in liquids

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HIGHLIGHTS

- Systematic experiments by PALS and DBS was performed to assess the effect of Oxygen on PAS parameters.
- Cu-64 was produced for DBS experiment.
- Three mechanisms of positron annihilation in oxygen content liquids was described.
- The main reason for the O-Ps quenching in the presence of oxygen was discussed.

ABSTRACT

Treatment of cancer patients requires high-sensitivity diagnostic techniques. Recently, the Society of Positron Annihilation Spectroscopy (PAS) has been working on hypoxia detection using positron lifetime and hopes to diagnose cancer at its initial phases. The accepted hypothesis for the use of positron as a biomarker of tumor hypoxia is that due to the distance between the blood vessels and the cancerous tissues, the oxygen concentration strongly decreases in cancerous tissues. The point that can put the PAS technique in the category of cancer diagnosis tools is its potential capability for oxygen-sensing in tissues. So, the partial pressure of oxygen in the patients tissues can be measured from the Positron Annihilation Lifetime Spectroscopy (PALS). However, before the positron lifetime imaging technique can be established, it is essential to verify the oxygen-sensing capability of the PALS in various chemical environments. In this paper, the mechanisms of positron annihilation in the deionized water and air-bubbled water samples were investigated via systematic experiments by our homemade Doppler Broadening Spectroscopy (DBS) and PALS spectrometer. Three mechanisms for positron annihilation in the investigated liquid samples including oxidation, Positronium conversion, and Positronium inhibition were described. The outcome of this investigation could advance the development of the PALS method for detecting tumors before metastasis, using the J-PET machine, which is still under development at Jagiellonian University.

KEYWORDS

Positronium
Lifetime
PAS
Tumor
Hypoxia

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1 Introduction

Positron Annihilation Spectroscopy (PAS) is a well-established technique for assessing the sub-nanometer size of free volume and its concentration in polymers, metals, semiconductors, and liquids (Biganeh et al., 2020b). Currently, using the PAS technique for analyzing biological samples is gaining international recognition (Bass et al., 2023; Moskal et al., 2023). The Society of PAS aims to develop a new concept for detecting cancer sites and pinpointing the exact location of altered tissues at the earliest stages of molecular abnormalities. Histopathology is considered the definitive method for diagnosing oncological conditions. Histopathological studies confirm that cancerous tissues exhibit lower oxygen levels compared to normal tissues, as a result of their abnormal blood vessels and heightened metabolic activity (Moskal and Stepień, 2022). Hypoxia refers to a condition where the oxygen is deficient in the tissues due to the reduced oxygen supply, impaired oxygen utilization, and structural abnormalities. In the case of cancerous tissues, abnormal blood vessels and increased metabolism may decrease the oxygen concentration in tissues, resulting in a specific type of hypoxia known as tumor hypoxia. A hypoxic environment in the body can significantly reduce the effectiveness of radiotherapy in treating cancer due to reduced

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oxygen enhancement, increased radioresistance, tumor aggressiveness, and altered cellular response (Chaudary and Hill, 2007). Hypoxic conditions also can contribute to the spread of cancer cells from the primary tumor to the other part of the body mainly due to metabolic reprogramming (Pavlides et al., 2009), altered immune response (Noman et al., 2014), and increased survival signaling (Courtney et al., 2010). Although measuring hypoxic regions is vital for understanding cell biology and designing effective radiotherapies, addressing hypoxia in tumors is a significant challenge in radiation oncology. The application of PAS in the context of tumor hypoxia is an area of emerging interest with potential implications for cancer diagnosis. The key aspect that makes the PAS technique relevant for hypoxia detection is its potential ability to sense the oxygen concentration in the material. The sensitivity of the PAS to the microenvironments makes it a promising tool for identifying and studying hypoxic regions within tumors or other pathological conditions. Oxygen molecules interact with positrons via electron transfer, direct positron annihilation, and positronium formation. Describing these mechanisms in the presence of oxygen molecules is crucial for understanding how positrons can be used to probe the microenvironment of biological tissues or materials, especially in medical imaging. These interactions impact both the positron's lifetime and the properties of the gamma rays emitted during annihilation. By gaining insight into how interactions with oxygen influence these factors, we can better utilize positron-based methods to conduct in-depth analyses of biological tissues, materials, and their surrounding environments.

Moskal et al. at the Jagiellonian University of Krakow introduced an innovative imaging device known as the J-PET scanner, specifically designed for positronium (Ps) imaging of biological tissues. This advanced scanner represents a significant advancement in medical imaging technology by enabling detailed visualization of positronium interactions within tissues (Bass et al., 2023). J-PET scanner is made of a large number of plastic scintillators which are capable of imaging the whole body with the Ortho-positronium (O-Ps) lifetime by reconstruction method. The feasibility study of the Ps imaging using positron annihilation lifetime spectroscopy has been investigated in (Moskal et al., 2019). The first positronium imaging of a cardiac myxoma phantom using the developed J-PET scanner was demonstrated by the J-PET group (Moskal et al., 2021). A simulation study of a novel preclinical total body imaging with the J-PET technology was investigated by Dadgar et al. (Dadgar et al., 2022).

Before the technique can be implemented in the clinical stage, it is essential to first evaluate its capability to sense oxygen. This involves thoroughly investigating how effectively the PAS method can detect and respond to variations in oxygen concentration. In our previous work, we measured the parameters of the (PALS) and Coincidence Doppler Broadening Spectroscopy (CDBS) for four tissue-equivalent polymers (Zare et al., 2022). The results of the PALS experiment confirmed that the positronium formation decreases with an increase in the oxygen concentration in the polymer content. The results obtained from the CDBS technique further validated that the Orbital Electron Momentum Spectrum (OEMS) serves as a distinctive signature for identifying characteristic elements. Additionally, it provides insight into the chemical environment surrounding hydrocarbon sites. However, for samples with similar oxygen concentrations, factors such as the chemical environment, degree of crystallinity, and presence of elementary free volumes can significantly impact the positron annihilation processes. Consequently, there is a limited amount of experimental data available to support the effectiveness of the technique in such scenarios (Stepanov et al., 2020). In this work, the positron annihilation parameters were investigated via systematic experiments using PALS and DBS for water samples.

2 Theoretical details

Standard PAS performs using Na-22 as a positron emitter source. Simultaneously by the emission of the positron from the source, a 1274 keV gamma also emits which is a signal for the birth of the electron (start signal). The positron with the endpoint energy of 540 keV penetrates inside the material and after thermalization, annihilates by the free electrons, valance, or core electrons of the material and provides the death signal (stop signal). The time differences between the start and stop signals (annihilation radiation) are precisely measured by the two similar fast plastic scintillators and provide the positron lifetime spectrum of the investigated material. This technique is called PALS and reflects the size and concentration of the positron annihilation site. The other technique called DBS concentrates on the measurement of the longitudinal momentum (P_l) of the annihilated electrons and reveals valuable information about the chemical environments of positron annihilation sites.

In materials with low electron densities, such as liquids and polymers, positrons can form an unstable hydrogen-like atom known as Positronium (Ps). Positronium exists in two states based on the relative spin orientations of the electron and positron:

1. **Ortho-Positronium (O-Ps)**: This is the triplet state with parallel spins ($S = 1, M_S = 1, 0, 1$). In a vacuum, O-Ps has a lifetime of approximately 142 nanoseconds (ns), while in materials, its lifetime ranges from 1 to 5 ns. Ortho-Positronium primarily decays into three gamma rays. Due to its relatively long lifetime and neutral charge, O-Ps can interact with core electrons, providing valuable information about the chemical environment before annihilation.

2. **Para-Positronium (P-Ps):** This is the singlet state with anti-parallel spins ($S = 0, M_S = 0$). P-Ps has a much shorter self-annihilation lifetime (about 125 ps). For the PAS data analysis, the self-annihilation of P-Ps provides no information for material characterization, as its short lifetime limits its interaction with the material's environment.

Regardless of their lifetimes, both positrons and positronium ultimately annihilate with free, valence, or

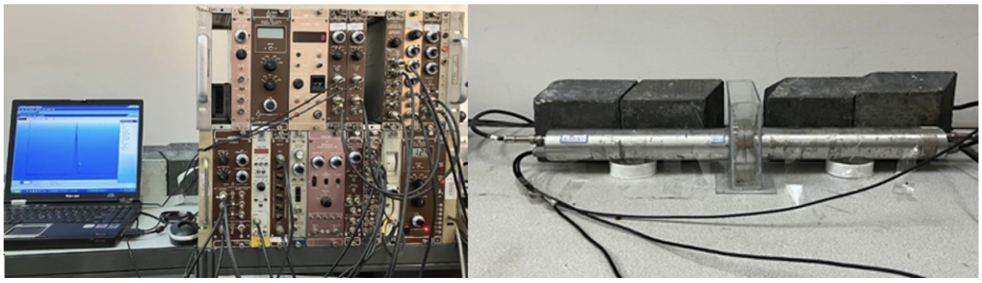

Figure 1: The setup of the PALS experiment.

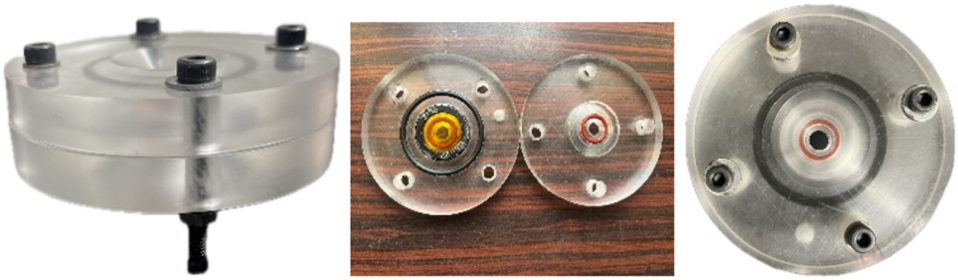

Figure 2: The support is made to place the source inside the water.

core electrons, resulting in the emission of either two or three gamma rays. The energy shift ($\Delta E = \frac{P_l\, c}{2}$) from the 511 keV gamma line is caused by the initial momentum of the annihilating electrons, where P_l is the longitudinal momentum of the electrons and c is the light velocity. DBS measures this energy shift using a high-resolution High-Purity Germanium (HPGe) detector.

3 Experimental details

In this section, the PALS and DBS techniques are presented for water and air-bubbled samples.

3.1 PALS experiment

Figure 1 shows the setup of the PALS experiment. The PALS technique was performed using two face-to-face plastic scintillators (NE-102) at the Nuclear Science and Technology Research Institute (NSTRI) in Iran. The positron lifetime was measured using a fast-slow spectrometer. The timing resolution of the spectrometer was measured at 320 ps using the coincidence gamma line of Co-60 (1173 and 1332 keV). The time calibration was determined at 24 ps using a pulse precision-time calibration module. The positron source is a 1 MBq Na-22 sandwiched between two 4 μm thick kapton foils. Kapton foils prevent the formation of Positronium (Ps) within the source, thereby minimizing errors in determining the lifetime of the longest-lived component of the investigated sample. This helps to enhance the accuracy of the measurements by ensuring that Ps formation does not interfere with the analysis. To avoid the penetration of water into the source, a sealed circular shape plexiglass with a hole in the center was made. Figure 2 shows how the source was sealed using plexiglass and O-rings. A $4 \times 20 \times 20$ cm^3 container was filled with deionized water and the source was placed at the common axis of the detectors. The positron lifetime was measured for the deionized water and ai-bubbled water for 21 days and 10^6 events were recorded on the spectrum. Figure 3 shows the positron lifetime spectrum for the deionized water.

Using the LT-10 software, the positron lifetime spectrum of each sample was analyzed by decomposing it into a sum of multi-exponential decays, expressed as $\sum_i \frac{I_i}{\tau_i}\, \mathrm{e}^{-t/\tau_i}$ convolved with the Full Width at Half Maximum (FWHM) of the PALS spectrometer (Giebel and Kansy, 2012), where τ_i (in ns) represents the lifetime and I_i (%) denotes the intensity of the i^{th} annihilation mechanism. For the analysis of PALS data, seven free parameters were taken into account: three lifetimes τ_i, three intensities I_i, and the lifetime of the positron in the source support (τ_{source}). The zero channel, channel width, and the spectrometer timing resolution were fixed during data analysis. The lifetime of the positron in the source (τ_{source}) was accurately determined through an experimental process involving a well-annealed nickel (Ni) sample. This particular nickel sample is known to have a precise positron lifetime of 110 picoseconds, which serves as a reference standard. By measuring the positron lifetime in this sample, the (τ_{source}) could be calibrated and validated, ensuring that the lifetime measurements for other samples are reliable and consistent. The (τ_1) component and its corresponding intensity (I_1) arise from the self-annihilation of para-positronium (P-Ps). However, this component is not relevant to our investigation and does not contribute to discussion on results. The medium-lived component (τ_2) and its associated intensity (I_2) are attributed to the annihilation of positrons

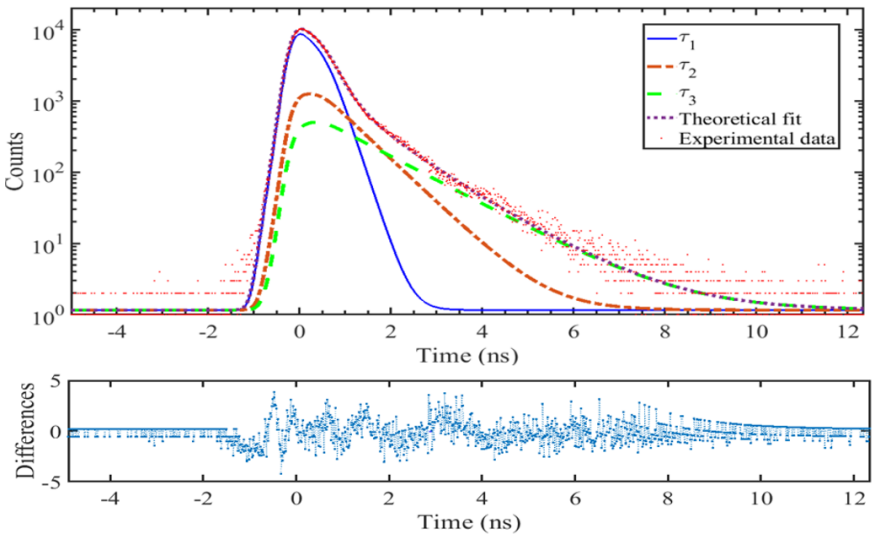

Figure 3: Positron lifetime spectrum of the deionized water (top) and the differences between the theoretical and experimental data (bottom).

Table 1: The results of PALS and DBS. The χ^2 parameter describes the quality of the multi-exponential fitting.

Sample	τ_1 (ns)	I_1 (%)	τ_2 (ns)	I_2 (%)	τ_3 (ns)	I_3 (%)	χ^2	S-parameter
Water	0.22	71.72	0.71	17.85	1.28	10.41	0.94	0.54473
Air-bubbled water	0.26	75.28	0.86	16.85	1.3	7.53	1.47	0.53922

with free electrons and electrons in the valence band. The component with the longest lifetime (τ_3) and its associated intensity (I_3) are primarily due to the annihilation of ortho-positronium (O-Ps) via the pick-off mechanism. This process involves the interaction of ortho-positronium, a bound state of a positron and an electron with parallel spins, with a nearby electron in its surrounding environment. The pick-off mechanism results in the annihilation of ortho-positronium with a longer lifetime compared to other annihilation processes, and this extended lifetime is reflected in the observed data as the longest-lived component. The results of the PALS data analysis are listed in Table 1.

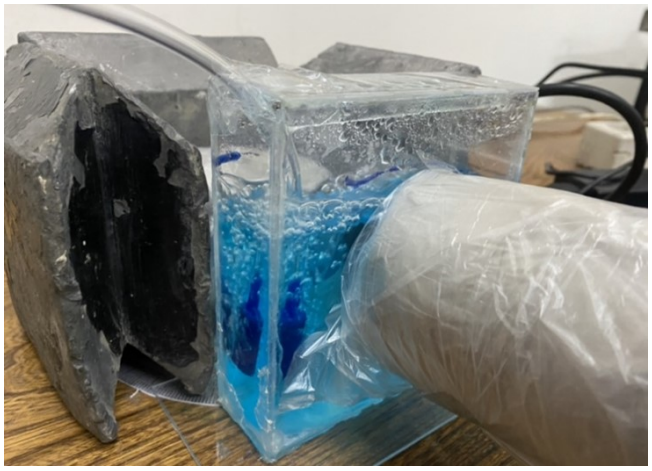

Figure 4: The activated Copper nitrate solution in the water in front of the HPGe detector. Bubbling in the sample has been done using an air pump.

3.2 DBS experiment

The DBS setup was configured using an HPGe detector (Canberra 20200) in conjunction with a waveform digitizer (CAEN DT5724). The digitizer samples directly at the preamplifier output of the detector and the analysis of the digitized signal performs by MC2 software. The digitizer is equipped with a Digital Pulse Height (PHA) algorithm that transforms the sampled data to pulse height. To achieve optimal energy resolution, the PHA control software is used to configure and manage the energy filter settings. The specifics of the optimal parameters for pulse shape analysis are detailed in our previous publication (Biganeh et al., 2019). The FWHM of the HPGe detector was measured at 2.1 keV for the 662 keV gamma line of Cs-137. For the DBS experiment, we used Cu-64 radioisotope ($T_{1/2}$ = 12.7 h) as the positron source with the positron endpoint energy of 653 keV. The 64Cu was produced using $^{nat}\mathrm{Cu}(n,\gamma)^{64}\mathrm{Cu}$ nuclear reaction at the Neutron Physics Laboratory (NPL) of the NSTRI. The Cu-64 was produced with 10 g of Copper (II) Nitrate ($Cu(NO_3)_2$ (H_3O)) powder. The powder was poured into a plastic container and placed in front of the 5 Ci Am-Be neutron source. To increase the reaction yield, the fast neutrons were thermalized using a 5 cm thick polyethylene rod in front of the Am-Be window. The flux of the thermal neutrons was measured at 3×10^3 n.cm^{-2}.s^{-1} at the target position using the foil activation technique. The irradiation time for the target was 63.5 hours and after 20 min cooling time for decay of short-lived radionuclide, the target was dissolved in 100 cc deionized water and placed in front of the HPGe detector for gamma spectroscopy. Figure 4 shows the activated copper nitrate

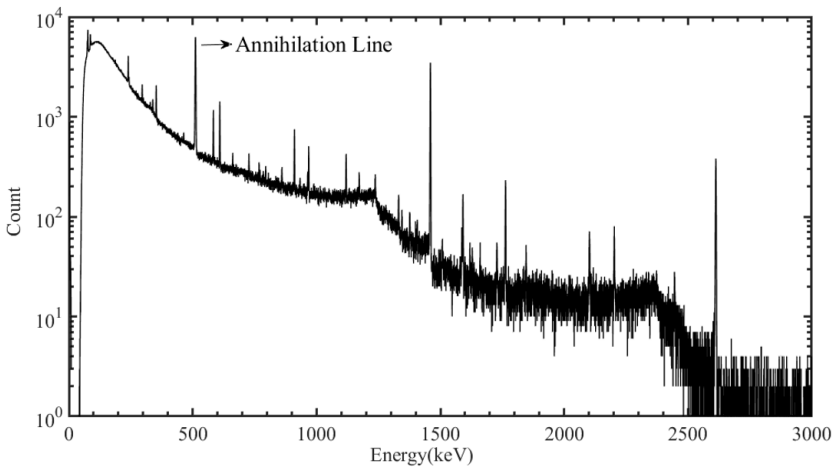

Figure 5: Gamma-ray spectrum of the activated copper nitrate solution used as the positron source for the DBS experiment. The positron annihilation line is shown in the spectrum.

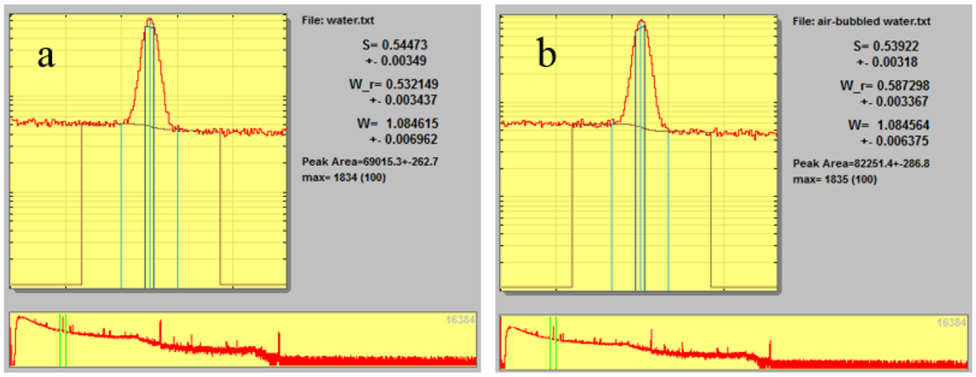

Figure 6: The result of DBS analysis by SP-1 code: a) water, b) air-bubbled water.

solution made for DBS. The gamma-ray spectroscopy of the solution is shown in Fig. 5. The DBS was performed for the deionized and air-bubbled water for 6 hours. The gamma-ray spectrum was analyzed using SP-1code (https://www.positronannihilation.net/). Figure 6 shows the results of the DBS analysis by SP-1 code. The Doppler broadened spectrum of the positron annihilation radiation is often described by S and W-parameters (Biganeh et al., 2020a). The S-parameter indicates the contribution of positron annihilation with free and valence band electrons, where the energy shift (ΔE) ranges from 0 to 0.8 keV. Where ΔE is the energy shift from the 511 keV gamma line caused by the initial momentum of the annihilated electrons. The W-parameter characterizes positron annihilation with core electrons, where the energy shift (ΔE) falls between 1.5 and 3.8 keV. Given that the probability of positron annihilation by core electrons is less than 10^4, accurately measuring the W-parameter requires a peak-to-Compton ratio exceeding 10^5. This level of precision is attainable through the use of two-dimensional Coincidence Doppler Broadening Spectroscopy (2D-CDBS) combined with long time data acquisition. So, the W-parameter can not be reported in our work. The results of the DBS for the investigated samples are listed in Table 1.

4 Discussion on results

The results of the PALS and DBS for the investigated samples are listed in Table 1. According to the results of the PALS experiment, the intensity of the longest-lived component (I_3) is significantly (37%) reduced for the air-bubbled sample. Consequently, the intensity of the P-Ps self-annihilation is increased significantly. The S-parameter of the DBS experiment also is decreased for the air-bubbled sample. An important question that should be addressed is the reason for the O-Ps quenching for the air-bubbled sample.

The reduction in ortho-positronium (O-Ps) formation can primarily be attributed to two key phenomena:

1. **Electron Sharing with Oxygen Molecules:** In this process, a positron interacts with an oxygen molecule, leading to a reaction where the positron shares an electron with the oxygen molecule. This interaction results in the conversion of positronium into a positron and an oxygen anion with a lower lifetime. The reaction is described by the Eq. (1):

$$\mathrm{Ps} + \mathrm{O_2} \longrightarrow \mathrm{e^+} + \mathrm{O_2^-} \tag{1}$$

2. **Conversion of O-Ps to P-Ps:** An unpaired electron in the 2p orbital of the oxygen atom can in-

teract with the electron of ortho-positronium (O-Ps), causing the transformation of O-Ps into para-positronium (P-Ps), which has a shorter lifetime. This process, known as O-Ps to P-Ps conversion, was first described by Ferrel et al. in 1956 (Ferrell, 1956). The reaction can be expressed as Eq. (2):

$$\text{O-Ps} + \text{O}_2 \longrightarrow \text{P-Ps} + \text{O}_2 \tag{2}$$

These mechanisms contribute to the observed reduction in the formation of ortho-positronium in the presence of oxygen, affecting the overall positron annihilation lifetime spectra and providing insights into the interactions between positrons and the oxygen content environment.

5 Conclusions

In this paper, the changes in the PAS parameters in the oxygen-content water samples were measured and described. The results show that the increase in the oxygen concentration leads to the quenching in the Positronium formation. The observed decrease in O-Ps intensity for the air-bubbled sample was mainly attributed to the underlying oxidation and conversion mechanisms, which were identified as the primary contributing factors. The results clearly demonstrated that Positronium intensity is not only sensitive but highly responsive to changes in oxygen concentration within liquid samples.

The measurement of oxygen concentration using the PALS method with the J-PET scanner, which is currently under development, offers several significant advantages over traditional techniques:

- **Enhanced Detection of Hypoxic Regions:** The PALS technique allows for the identification of hypoxic regions within tumors that may not be detectable using other PET imaging methods. This enhanced detection capability can lead to a more accurate assessment of tumor hypoxia.
- **Non-Invasive and Quantitative Hypoxia Measurement:** This method enables the precise, non-invasive measurement of hypoxia levels within tumor cells, providing valuable insights into the oxygenation status of the tissue without the need for invasive procedures.
- **Monitoring Hypoxia During Treatment:** The method can also be used to monitor changes in hypoxia levels throughout the course of treatment. This real-time monitoring can help evaluate the effectiveness of therapies and guide adjustments in radiotherapy, ultimately improving treatment outcomes.

The results of this research are expected to play a crucial role in advancing data analysis techniques for the J-PET scanner under construction at the Jagiellonian University in Krakow, Poland. Moving forward, the study will focus on measuring PAS parameters for samples with reduced oxygen concentration through argon-bubbling and for samples with elevated oxygen concentrations using hydrogen peroxide solutions. These measurements will further enhance the understanding of oxygen concentration effects and contribute to the optimization of the J-PET scanners capabilities.

Conflict of Interest

The authors declare no potential conflict of interest regarding the publication of this work.

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