J-PET scanner combined with Positron Annihilation Lifetime Spectroscopy as a tool for morphometric imaging

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Abstract

Jagiellonian Positron Emission Tomograph (J-PET) [1] is a multi-purpose detector which is used for investigations with positronium atoms in life-sciences as well as for development of medical diagnostics [2]. A prototype of the J-PET based on plastic scintillators was developed at the Jagiellonian University in Krakow, Poland [3,4].

Positron Annihilation Lifetime Spectroscopy (PALS) allows examining structure of materials at nano and sub-nanometer level. This technique is based on the lifetime and production intensity of ortho-positronium atoms in free volumes of given structures. It is mostly used for studies of organic materials. J-PET tomograph is capable of imaging of properties of positronium produced inside the human body [2]. Thus far, there exist few results, e.g. by group of Y. C. Jean [5-6] and J-PET [7-8], showing that morphology of cells is correlated with the PALS parameters.

Results of the first experiments with the cardiac myxoma tumor conducted by the J-PET collaboration will be presented. We performed PALS studies with J-PET first studies of human tissue (cardiac myxoma tumor and adipose mediastinal tissue). Results shown significance differences between tumor and normal tissue. As a result, we proved that PALS can be successfully used for studies of living organisms their dynamics and its relation to the cells morphology. This result opens perspective for simultaneous determination of early and advanced stages of carcinogenesis by observing changes in biomechanical parameters between normal and tumour cells and standard PET examination.

Positron Annihilation Lifetime Spectroscopy

Positronium is an atom consisting of an electron e^- and its anti–particle positron e^+, its diameter is about 0.2 nm. Therefore it is possible for positronium to be trapped in free spaces between molecules any kind of not conducting matter like cells and tissues (Fig. 1), which are investigated in this study. Since positron can annihilate with an electron not only from Ps, but also with electrons in surrounding matter, mean lifetime value of ortho-positronium trapped in these free volumes can be used to estimate their sizes. This together with intensity of o-Ps production gives us an information about porosity of given material.

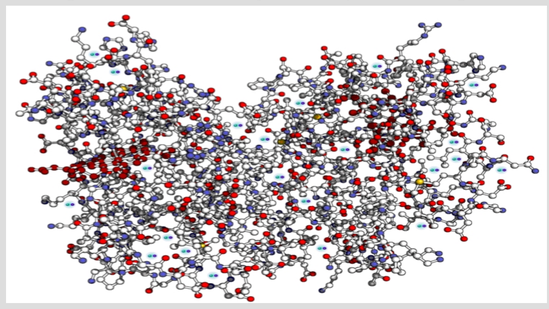


Fig. 1. Exemplary scheme presenting positronium trapping in molecule (hemoglobin).

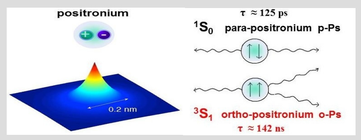


Fig. 2. (left) Positronium atom and the probability of spatial distribution of e^- and e^+ [9]. (right) Decays mode of the two ground states of positronium. (up) Singlet state of anti – parallel spins orientation, p-Ps. (bottom) Triplet state of parallel spin orientation, o-Ps.

Biomedical application of PALS technique

Until recently PALS was not used in biological or medical science. Some newly studies showed it can successfully be applied as a diagnostic technique, enabling to differentiate between cells, tissues and even molecules on accuracy level not achievable before. Due to positronium being trapped in free spaces between molecule and its time being shortened by presence of free radicals and Reactive Oxygen Species it is different for cancer cells or tissues, which produce more ROS than normal cells.

Jagiellonian-PET scanner

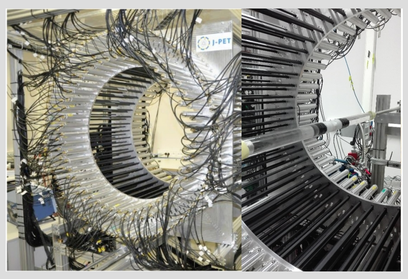
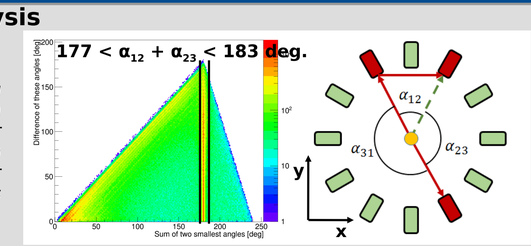


Fig. 3. Photo of J-PET scanner front view (right), sample with ^{22}Na source sealed in Kapton foil inside the scanner (left).

Data selection and analysis

Fig. 5. *To filter out events coming from annihilation of positronium into 2 gamma quanta, angular correlations are used. Graph shows angle dependence for events with 2 annihilation hits only.*



$$^{22}Na \rightarrow {}^{22}Ne^* + e^+ + \nu_e$$
$$^{22}Ne^* \rightarrow {}^{22}Ne + \gamma_{deexcitation}$$
$$e^+ + e^- \rightarrow n\,\gamma_{annihilation}$$

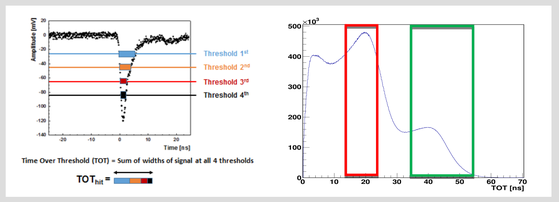


Fig. 4. (left) *The Time-Over-Threshold (TOT) values are calculated and used as a measure of Energy. (right) Applied cut on TOT: Annihilation 14-24 ns, deexcitation 35-55 ns.*

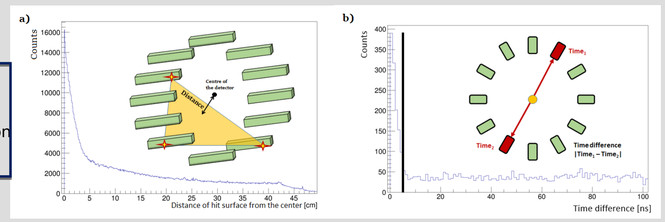


Fig. 6. (a) *Next criteria is checking coplanarity of annihilation hits. Because source with material was in the center of the detector the distance of decay plane from the center should be close to zero. (b) Next condition selecting true annihilations is checking the time difference between annihilation hits, knowing that the annihilation should take place in the center.*

Cardiac myxoma

Cardiac myxoma is very rare heart disease with an overall incidence of about 0.5 per million per year but accounts for approximately 50-75% of benign and about half of the all primary cardiac neoplasms. The tumor usually arises from the endocardium into the cardiac chamber. About 75% of cardiac myxomas are located in the left atrium, and 15-25% in the right atrium [10]. The only method of treatment of cardiac myxoma is radical surgical tumor excision using extracorporeal circulation.

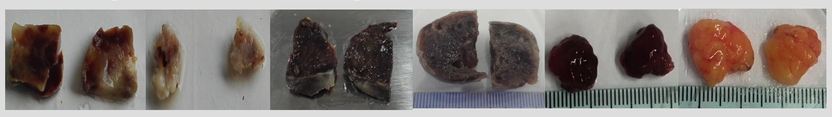


Fig. 7. Exemplary samples of measured cardiac myxoma from left: tumor I, tumor II, tumor III, tumor IV, tumor V (not fixed), adipose tissue (not fixed).

In case of this study four tumors of this kind fixed in aqueous solution of formaldehyde and one not fixed with mediastinal adipose tissue for comparison were measured.
First tumor (I) from 72 years old women was cut into 7 samples 2 mm thick each and second tumor (II) from 61 year old men was measured as one sample, third tumor (III) from 59 year old men was cut into 3 samples and fourth tumor (IV) from 54 year old women was cut into 3 samples. Fifth tumor (V) and adipose tissue from 77 year old men, were measured within 4 hours after surgery, not fixed in formaldehyde. (Fig. 5.)

PALS setup

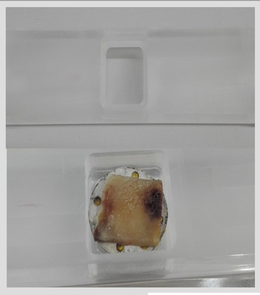


Fig. 8. Photo of measurement chamber without (up) and with the source and sample (bottom).

The gamma quanta corresponding to positron creation inside the source and positron annihilation inside the sample were collected using two detectors equipped with BaF_2 scintillators of sizes φ 1.5” x 1.5” each. Sodium – 22 isotope was used as positron source with activity of about 0.7 MBq. Signals were sampled with DRS4 evaluation board.

Coincidence criteria applied for measurement:
1) Signals for 511 keV with amplitudes > 14
2) Signals for 1274 keV with amplitudes > 7
3) Time window 120 ns

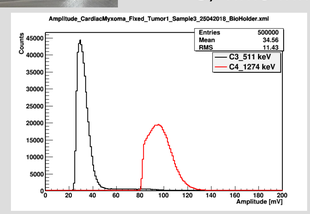


Fig. 9. Exemplary amplitude spectra.

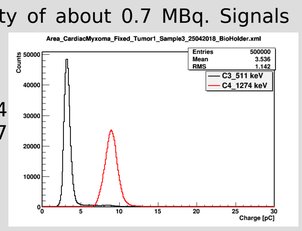


Fig. 10. Exemplary charge spectra

Time difference between two gamma quanta is calculated applying cut charge of the signal in analysis:
1) Signal for annihilation with charge 2-5 pC
2) Signal for deexcitation with charge 7-10 pC

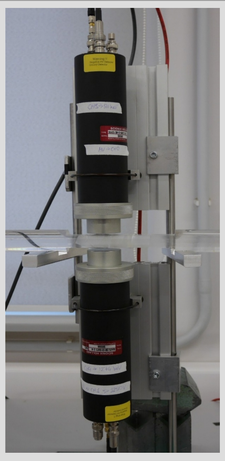


Fig. 11. Photo of PALS detectors.

Results

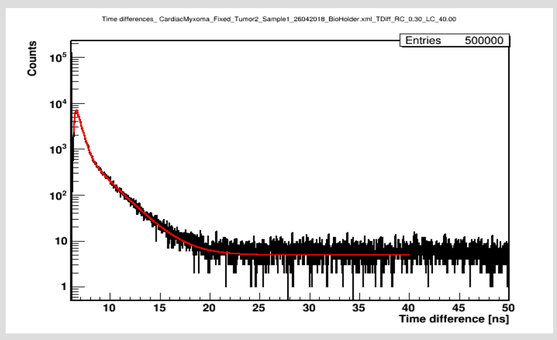


Fig. 12. Exemplary positronium lifetime spectra. Red line denotes fitted function.

In positronium lifetime spectra (Fig. 12) measured for all samples one component related to o-Ps annihilation in the free voids was found. Ortho-positronium lifetime are shown in Fig. 13-14 for fixed and not fixed samples respectively.

Obtained mean o-Ps lifetime value for fixed cardiac myxoma samples was of about **τ = 1.99(09) ns**, which corresponds to the free volumes radii estimated from the Tao-Eldrup model assuming spherical shape of void of about **r = 0.27 nm.**

Results for all samples from the same tumor are consistent with each other, which means that studied tumors had homogeneous structure on nanometer level. The determined ortho-positronium lifetime differs from the lifetime for water (1.8 ns), therefore it proves that this technique can be successfully applied in studies of hydrous biological samples. Different o-Ps lifetimes for tumors from different patients may be correlated to the tumor type, since cardiac myxoma can grow as a papillary type or calcified one. Separate microCT studies determined Tumors 1,2, 4 as papillary and tumor 3 as calcified one, and presents of this calcification may be the reason for lower lifetime values.
Additionally significant difference between cardiac myxoma and adipose tissue proves that this method can be applied with J-PET scanner as better and more effective diagnostic technique.

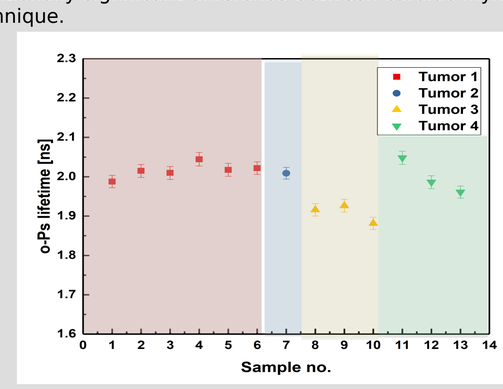


Fig. 13. o-Ps lifetime values as a function of sample number for Cardiac Myxoma fixed in formaldehyde.. Different colors denoted samples from given tumor

On Fig. 14 Results for not fixed cardias myxoma and healthy adipose tissue for comparison measured by PALS and J-PET are shown. Lifetime of o-Ps for cardiac myxoma was found to be **τ = 1.98(04) ns** - PALS and **τ = 1.85(06) ns** – J-PET, where for healthy mediastinal adipose tissue o-Ps lifetime was about **τ = 2.66(03) ns**, and **τ = 2.70(03) ns** respectively. Estimated free volumes radii of about **r = 0.35 nm.**

Significant difference between cardiac myxoma and adipose tissue with consistent results for both techniques proves that this method can be applied with J-PET scanner as better and more effective diagnostic technique.

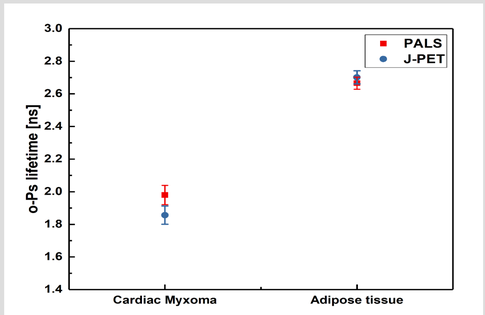


Fig. 14. o-Ps lifetime values for not fixed Cardiac Myxoma and adipose tissue, the same samples were measured by both standard PALS detectors and with J-PET scanner.

Conclusions

Presented results of the first experiments with the cardiac myxoma tumor conducted by the J-PET collaboration proved that PALS technique can be successfully applied for studies of biological samples. Results showed significant differences between tumor and normal tissue. Further studies of normal and cancerous cells, will enable determination of early and advanced stages of carcinogenesis by observing changes in biomechanical parameters employing PALS method combined with J-PET tomography system [2] which is currently being developed at Jagiellonian University [1-4]. These results opens perspective for simultaneous determination of early and advanced stages of carcinogenesis by observing changes in biomechanical parameters between normal and tumor cells and standard PET examination, therefore this techniques combined can be very effective diagnostic tool.

References

[1] Moskal P. et al. Time resolution of the plastic scintillator strips with matrix photomultiplier readout for J-PET tomograph. Phys. Med. Biol. 2016; 61:2025-2047.
[2] Moskal P. et al., Patent No: US 9851456; PL 227658; PCT/EP2014/068374.
[3] Moskal P. et al. A novel method for the line-of-response and time-of-flight reconstruction in TOF-PET detectors based on a library of synchronized model signals. Nucl. Instr. Meth. A. 2015; 775:54–62.
[4] Niedźwiecki S. et al. J-PET: A New Technology for the Whole-body PET Imaging. Acta Phys. Polon. B. 2017; 48(10):1567-1576
[5] Jean Y. C. et al. Applications of slow positrons to cancer research: Search for selectivity of positron annihilation to skin cancer. Applied Surface Science. 2006; 252:3166–3171.
[6] Liu G. et al. Applications of positron annihilation to dermatology and skin cancer. Phys. Stat. Sol. (c). 2007; 4(10):3912–3915.
[7] Jasińska B. et al. Human Tissues Investigation Using PALS Technique. Acta Phys. Polon. B. 2017; 48(10):1737-1747.
[8] Jasińska B. et al. Human Tissue Investigations Using PALS Technique - Free Radicals Influence. Acta Phys. Polon. A. 2017; 132:1556 – 1558.
[9]Y.H. Wang et al., Phys. Rev. A 89 (2014) 043624;
[10] L.E. Wold et al. Cardiac myxomas: a clinicopathologprofile. Am J Pathol. 1980 101(1):219-40.

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