NUKLEONIKA 2013;58(1):199–202

ORIGINAL PAPER

Influence of neoplastic therapy on the investigated blood using positron annihilation lifetime spectroscopy

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Abstract. The influence of neoplastic radiotherapy and chemotherapy was investigated using annihilation lifetime spectroscopy in blood types 0 Rh^+–AB Rh^+. Changes in the parameters of the longest lived component of the spectrum were analyzed depending on the time between the moment of taking the blood sample from a patient and that of taking measurements, and also the time passing from the cessation of radio- and chemotherapy.

Key words: blood • positron annihilation

Introduction

Achievements of contemporary physics find their extensive application in medical diagnosis and therapy, especially in cancer therapy, as well as in evaluation of its effects. As far as medicine is concerned, beginning with the 1970s, positrons have been used in the so-called positron emission tomography (PET) [1]. The first time, the phenomenon of positron annihilation was used in 1951 to locate brain tumor [8]. The majority of methods evaluating the effects of cancer therapy are based on the analyses of biological changes occurring in the patient's organism, following the applied therapy. It seems that the application of positron lifetimes spectroscopy can provide information about the changes induced by the therapy in the patient's organism. Information about the changes occurring at the atomic level can be useful in the future, to understand processes of destroying neoplastic cells and to create new drugs.

The aim of the present work was to check whether changes in the parameters of positron lifetimes spectra in patients' bloods after radio- and chemotherapy correlate with the biochemical changes observed by means of analyses applied in medicine [5]. Because these analyses are most frequently carried out on patients' blood tissues, the selection of such a tissue used in the examination is presented in this work.

Samples preparation

Spectra of positron lifetimes in blood plasma and hematocrit of blood types 0 Rh^+ and AB Rh^+ were investigated. The blood was obtained from 3 people

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Received: 14 June 2012
Accepted: 18 October 2012

who were diagnosed not having developed a neoplastic disease, therefore were not subject to cancer therapy, as well as from 3 women-patients who had been diagnosed with breast cancer, hence were undergoing neoplastic therapy through radiation with γ-rays (25×200 cGrey) and had undergone the first chemotherapy fraction. The results of the research presented in this work are the arithmetic means and the error marked in the graphs denotes the maximum error of the mean.

The blood samples were obtained from the Opole Oncological Centre. The women-patients subjected to cancer therapy had the blood taken after 1, 2, 3, 4 and 6 weeks, following the end of the therapy.

The examination of positrons annihilation in the women-patients' bloods 6 weeks after the end of the therapy resulted from the attempt to compare them with the results of biochemical examinations, considering which effects of the therapy were confirmed just after that time [5].

The separation of plasma from the hematocrit was executed by means of the standard method of centrifugation. The centrifugation and storing of the samples until the moment when they were placed in a positron lifetimes spectrometer were performed at a temperature of 4°C.

The examined samples were placed in two identical Plexiglas vessels with an inner diameter of 10 mm and a depth of 5 mm, which were covered with a Hostaphan foil, with the surface density of 0.9 mg/cm^2, between which there was a source of ^{22}Na positrons, also covered with a Hostaphan foil. The contribution of the source of positrons was determined experimentally through measuring lifetimes in foils of various thicknesses, which were put over the source of positrons. The contribution of the source amounted to 13.9%.

The positron lifetimes were measured with the use of a fast-fast spectrometer with the resolution of 226 ps, equipped with BaF_2 scintillators, with a diameter of 4 cm and a thickness of 15 mm.

The measured spectra of positron lifetimes always amounted to over 10^6 impulses, and in order to analyze them the computer program Lifetime 9 was used [3].

Results and their interpretation

The first aim of the conducted research was to examine whether the values of the determined lifetimes depended on blood types and on the time which elapsed from taking the blood for examination from persons who were diagnosed free from the disease, hence were not subjected to a cancer therapy. Since the blood is a substance composed mainly of erythrocytes, leukocytes, and thrombocytes dissolved in plasma, thus – for comparison of positron lifetimes spectra – the measurements were taken in both the plasma and the part separated from the plasma, known as hematocrit. Another goal of the research was also to check whether the spectra changed their parameters once the radiotherapy had been concluded. Spectra of positron lifetimes in the blood of patients, who underwent chemotherapy, were examined as well after 2 and 6 weeks following its finishing.

The experimentally obtained spectra were analyzed, accepting that they consisted of one, two, three and four free components. In order to analyze and interpret the results we chose the distributions into two components because the coefficient of fitting the experimental data to the selected annihilation model (χ^2) for these distributions was closest to unity (e.g., 1.002) and the scatter of points on the so-called error band did not display any systematic changes.

The so-called short-lived component of the spectrum (τ_1, I_1), both for the plasma and the hematocrit takes the values within the range from 0.192 to 0.252 ns, and its participation in the annihilation is within 53 to 77%.

The longest lived component of the spectrum with a greater value of positron lifetime took the values over 1.7 ns for the plasma and over 2.35 ns for the hematocrit. These values testify for the formation of *ortho*-positron (*o*-Ps) in the examined samples. The parameters of this component of the spectrum were denoted as $\tau_{o\text{-Ps}}$ and $I_{o\text{-Ps}}$. Positronium forms in determined geometric and energetic conditions. Generally speaking, it forms within areas of very low density of electrons (the so-called free volumes), such as porous polymers, molecular liquids. The appearance of the pick-off mechanism in annihilation of positronium causes very clear shortening of its lifetime to the value ranging from 1 to 2 ns. According to our knowledge, papers concerning the physical properties of blood, which suggest the way of creation of free volumes are not presented in the literature. However, the common appearance of the longest lived component of positron annihilation in the pick-off mechanism, suggest that such free volumes appear. At this stage of investigations, we are not interested in the mechanism of dynamic creation of free volumes with positronium. Therefore, additional studies are necessary. Also, a higher number of blood samples would be needed. Tao [6] and Eldrup [2] elaborated a simplified model of annihilation of positronium in materials containing free volumes. This model connects the mean lifetime of positronium that annihilates through the pick-off process with the sizes of the free volumes in which it is formed. For free volumes with spherical symmetry, this dependence is as follows:

$$\tau_{o\text{-Ps}} = \lambda_0 \left[1 - \frac{R}{R+\Delta R} + (2\pi)^{-1} \sin \frac{2\pi R}{R+\Delta R} \right]^{-1} \tag{1}$$

where $\lambda_0^{-1} = 0.5$ ns, ΔR – a certain constant depending on the shape of the free space, in which positron annihilates. For the spherical free volumes, its value amounts to 0.1656 nm.

The changes in the values of τ_1 and I_1 are hard to interpret, therefore – in the present work – we shall discuss only those connected to the longest-lived component of the spectrum.

Measurements of positrons lifetimes in the systems where positronium forms, allow assessing the so-called relative free volume *f*. This parameter is defined as follows:

$$f = \frac{(V - V)_0}{V} \tag{2}$$

where: V – total macroscopic volume of the system, V_0 – volume occupied by the molecules of the system.

Wang *et al*. as well as Kobayashi *et al*. [4, 7] proposed a semi-empirical equation which can be applied to assess

the values of this parameter on the basis of annihilation parameters of the positrons lifetimes spectrum.

$$f = A \times I_3 \times \tfrac{4}{3}\pi R^3 = A \times F \tag{3}$$

where $F = I_3 \times 4/3(\pi R^3)$, A – a normalizing constant.

According to Wang *et al*. [7], the value of this normalizing constant at room temperature is close to one.

Spectra of lifetimes of positrons in the blood of persons who were diagnosed with no neoplastic disease

Measurements were taken for blood samples of the types 0 Rh^+ and AB Rh^+ after 24 h and 6 weeks following the taking of the blood for examination. The values obtained from those measurements: lifetimes of the longest-lived component $\tau_{o\text{-Ps}}$, and its intensity $I_{o\text{-Ps}}$ and the fractional free volume f are presented in Figs. 1 and 2. It can be seen that these parameters for the plasma take values that are clearly different from those for the hematocrit. The obtained results testify for the fact that both in the plasma and in the hematocrit – after six weeks – the radii of the free volumes, in which positronium occurs and annihilates, increased by 11.1 ± 3.6% for the plasma, 16.5 ± 1.8% for the blood type AB Rh^+ and 13.2 ± 2.7% – for the blood type 0 Rh^+ (Fig. 3).

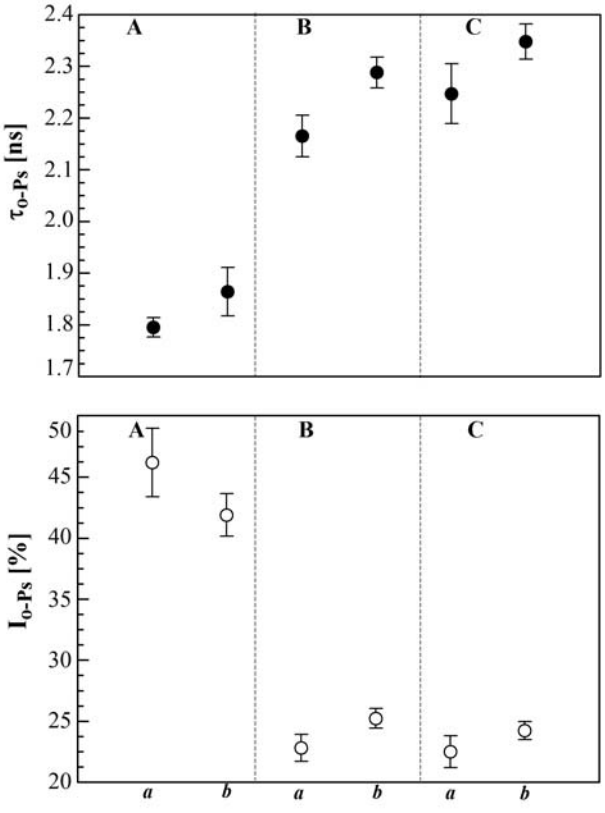

Fig. 1. Values of $\tau_{o\text{-Ps}}$ and $I_{o\text{-Ps}}$ of the *o*-Ps component of the spectrum for: plasma – (A), hematocrits of the blood types 0 Rh^+ – (B) and AB Rh^+ – (C) for subjects with no diagnosed neoplastic disease, after 24 h (a) and after 6 weeks (b) following the taking of the blood for examination.

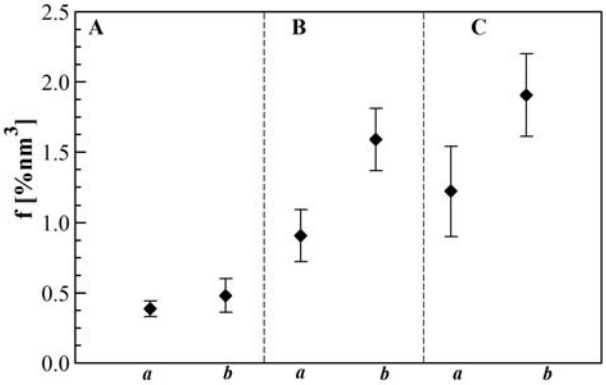

Fig. 2. Values of the fractional free volume f for: plasma – (A), hematocrits of the blood types 0 Rh^+ – (B) and AB Rh^+ – (C) for subjects with no diagnosed neoplastic disease, after 24 h (a) and after 6 weeks (b), following the taking of the blood for examination.

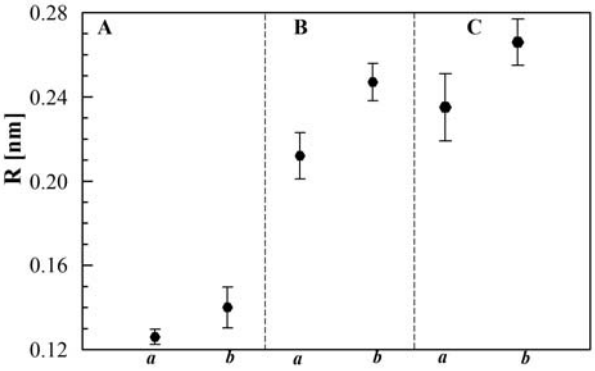

Fig. 3. Values of the radii R of voids, in which positronium forms for: plasma – (A), hematocrits of the blood types 0 Rh^+ – (B) and AB Rh^+ – (C) for subjects with no diagnosed neoplastic disease, after 24 h (a) and after 6 weeks (b), following the taking of the blood for examination.

Spectra of lifetimes of positrons in the blood of persons undergoing a cancer therapy

The influence was investigated of the time that elapsed from the completion of radiotherapy applied to a woman-patient with a beam of γ-rays and from the completion of chemotherapy to the moment of conducting annihilation measurements on spectra of lifetimes of positrons in blood hematocrits. Figures 4 and 5 present the values: $\tau_{o\text{-Ps}}$, as well as the intensity $I_{o\text{-Ps}}$, and f after 1, 2, 3, 4 and 6 weeks following the radiotherapy. The last two bars in the diagrams denote the value of the parameters 2 and 6 weeks after the completion of the chemotherapy-based treatment. The results relate to the investigation of blood type 0 Rh^+. The analysis of the results of the changes in the fractional free volumes f, points to the noticeable changes in these parameters which are visible already after 2 weeks, following the end of radiotherapy with the beams of γ-rays or following the end of chemotherapy. However, the changes in the value of the *o*-Ps component of spectrum $\tau_{o\text{-Ps}}$ cease to occur already after 2 weeks following the completion of this type of therapy. The intensity of this component of the spectrum is not clearly higher until after 6 weeks, following the completion of the radiotherapy (by 10.7%). Much greater values of $I_{o\text{-Ps}}$ can be noticed after 2 weeks, following the completion of chemotherapy (by 20.8%).

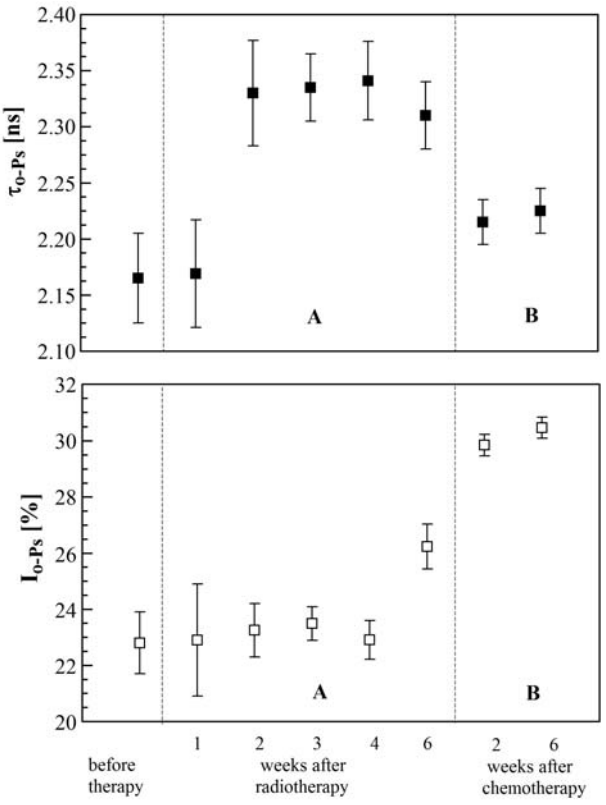

Fig. 4. Dependence of the $\tau_{o\text{-Ps}}$ and $I_{o\text{-Ps}}$ of the *o*-Ps component of the spectrum in hematocrits of the blood type 0 Rh^+ on the time which elapses from the completion of radiotherapy (A) and chemotherapy (B).

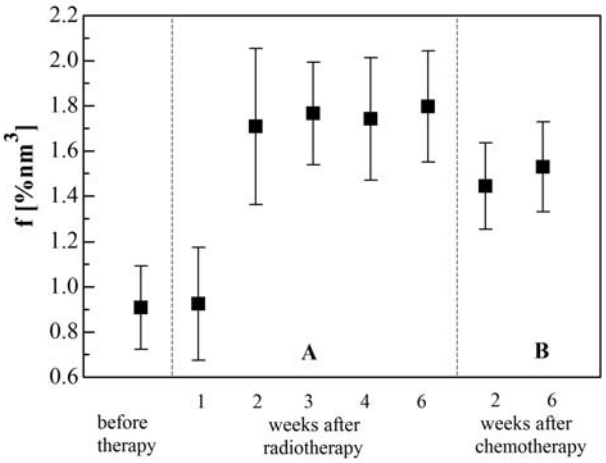

Fig. 5. Dependence of the fractional free volume *f* in hematocrits of the blood type 0 Rh^+ on the time which elapses from the completion of radiotherapy (A) and chemotherapy (B).

The obtained results point to different mechanisms of the changes occurring in the blood at the subatomic level for both types of treatment. From the atomic point of view, radiotherapy is connected with expanding of the radii of the free volumes, in which positronium forms, without changes in their concentration, whereas following the chemotherapy their concentration in the blood changes, although their radii remain practically unchanged.

Conclusions

The conclusions presented below follow from the conducted research:

1. The parameters of positron lifetimes spectra for the blood types 0^+ and AB^+ take the same values.
2. There are geometrical and energetic conditions for positronium to form in the blood and in the plasma.
3. The radii of the free volumes, in which positronium forms, are greater for hematocrits than those in the plasma.
4. The radii of the free volumes in blood hematocrits with a neoplastic disease (0.250 ± 0.006 nm) are greater six weeks after the completion of radiotherapy than those in the blood freshly taken for examination (0.219 ± 0.011 nm).
5. The radii of the free volumes, in which positronium forms, in the blood of patients subjected to radiotherapy and healthy persons, are just the same six weeks after the completion of the treatment in error limits: (0.254 ± 0.009) and (0.247 ± 0.009) nm.
6. In the blood of patients subjected to chemotherapy, the concentration of the free volumes, in which positronium forms, is greater than that in the blood of healthy patients six weeks following the completion of the treatment.

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