CALCULATION OF ABSORBED DOSE DUE TO THE ^{90}Y-DOTATOC PEPTIDE RECEPTOR RADIONUCLIDE THERAPY BY MCNP5/X

by

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Strong beta emitters, like ^{90}Y, ^{177}Lu labelled peptide, are used for treatment of neuroendocrine tumours where there is a good expression of somatostatin receptors. In this work, MCNP5/X computer software and ORNL human phantoms were used to calculate absorbed dose due to ^{90}Y labelled DOTATOC in the peptide receptor radionuclide therapy. Tumour was considered as a sources of beta radiation and represented as a sphere with diameter of 1-4 cm and 5 cm in liver, pancreas, and lungs. Results are expressed as absorbed dose per unit of cumulated activity, S – value in units mGy·(MBq·s)$^{-1}$. The far largest dose is in tumour itself, then in organ which contains the tumour. Doses in other organs, where the metastasis are the most frequent, due to the bremsstrahlung radiation, are much smaller and could be neglected. The largest dose, $8.66 \cdot 10^{-3}$ mGy·(MBq·s)$^{-1}$ was obtained for tumour with size of 3 cm.

Key words: Monte Carlo simulation, ^{90}Y-DOTATOC, radionuclide therapy, dosimetry

INTRODUCTION

Peptide receptor radionuclide therapy (PRRT) with radioactive somatostatin analogues was developed recently [1, 2]. It is a targeted molecular therapy based on somatostatin analogues which uses short-lived strong beta emitters like ^{90}Y, ^{177}Lu, or their combination labelled peptide molecules as DOTA-TOC, DOTA-TATE, DOTA-NOC, DOTABOC-ATE *etc*., [3-9]. It has been recommended to use ^{90}Y for tumours larger than 2 cm, and ^{177}Lu for the treatment of smaller ones, both labelled peptide [10]. This recommendation is based on physical characteristics of ^{90}Y, which emits beta particles with the maximal energy of 2.28 MeV, with the range of 11.3 mm in soft tissue. On the other side, ^{177}Lu emits gamma radiation and beta particles with maximal energy of 0.497 MeV, whose range is below 2 mm in tissue [11]. This kind of therapy is standard nowa days in nuclear medicine practice for curing of the neuroendocrine tumours (NET).

The NET do not have specific symptoms, and mainly are diagnosed by the case in later phases of the illness (median, 9.2 years) [12], when numerous metastasis were already spread out through the body. Usually NET appear in gastrointestinal tract, although they can be found at in other organs in human body [13].

The PRRT is applied intravenously and patients spend relatively short period in hospital, up to 3 days. Therapy is usually divided in several portions, where each one is with activity of about 5.5 GBq. Peptide molecules are nephrotoxic [14-16] and relatively large; they could be absorbed in proximal tubules, being retained for long time in renal interstitium [17, 18]. In order to prevent re-absorption of PRRT drugs, positively charged amino acids (like L-Lysine and L-Arginine), which compete for drug transporters, are administered simultaneously [19, 20]. As a consequence, dose delivered to kidney could be large and kidney functions could deteriorate seriously [21]. Some authors proposed to limit the dose in kidney down to 23 Gy [20]. Due to this, it is very important to optimize the dose in pre therapeutic dosimetric study [22-25].

The ^{90}Y is very convenient for this kind of therapy because it is a pure beta emitters with maximal energy of 2.28 MeV, the average energy of beta particles is 0.934 MeV and half-life is 64 h. Maximal range of these beta particles in tissue is 11.3 mm [11]. On the other side, it is difficult to detect and measure ^{90}Y distribution in human body. This can be done by measuring of bremsstrahlung radiation emitted by beta particles.

The objective of this work is to calculate absorbed dose per one emitted beta particle from ^{90}Y, in

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different organs of human body, for various locations and sizes of tumour.

MATERIAL AND METHODS

To perform dose calculation, well known computer software, MCNP5/X [26] was used. Human body is represented with ORNL phantom [27] where organs are given as geometrical bodies filled with various materials. Dose calculations was performed assuming that tumour is spherical in shape with diameter of 1-4 cm and 5 cm, localized in liver, pancreas and lungs, where NET tumours appear most frequently. Tumour was considered as a source of beta particles since up to 30 % of applied activity is deposited and retained in tumour tissue. Such choice of tumour locations was made after 10 years of experience in application of PRRT therapy in Department of Nuclear Medicine in Kragujevac Clinical Centre. The results obtained from MCNP are expressed in MeV g^{-1} per one emitted particle. Results are later recalculated in mGy/(MBqs).

Tumour locations in patients were determined based on diagnostic OCTREO scan, which was done using Dual Head gamma camera (SIEMENS, HOFFMAN ESTATES, ILLINOIS, USA), with low energy – high resolution collimators, in matrix 256 1024 pixels, with the table speed 5 cm/min. This is the standard procedure for patients with NET illness. Totally 740 MBq of ^{99m}Tc-Tectrodyd produced by POLATOM, Poland, was applied intravenously in a single dose.

Figure 1 shows images of human body obtained by gamma camera and longitudinal cross-section view of corresponding ORNL phantoms (on the left side of gamma camera images).

Monte Carlo simulations were carried out for the following organs: liver, pancreas and lungs, as well as the central area of the abdomen, where the tumour was assumed:

The liver (volume is 1830 cm^3) is given as an elliptical cylinder

$$\frac{x}{a}^2 \quad \frac{y}{b}^2 \quad 1 \qquad (1)$$

intersected with a plane

$$\frac{x}{x_m} \quad \frac{y}{y_m} \quad \frac{z}{z_m} \quad 1 \quad \text{and} \quad z_1 \quad z \quad z_m \qquad (2)$$

Parameters a and b are 16.50 and 8, respectively. Values for x_m, y_m, and z_m are: 35, 45, and 43, respectively (all in cm).

The pancreas is an ellipsoid with a section removed and defined by

$$\frac{x \quad x_0}{a}^2 \quad \frac{y}{b}^2 \quad \frac{z \quad z_0}{c}^2 \quad 1 \text{and} \; x \quad x_0 \qquad (3)$$

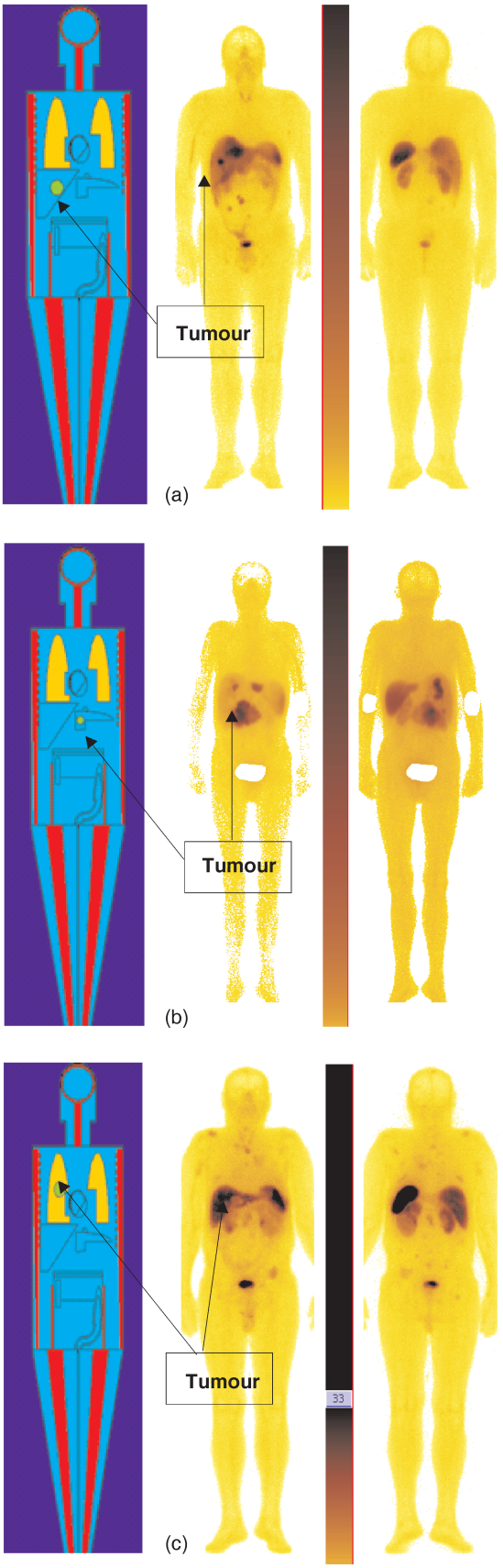

Figure 1. The images of whole body scintigraphy in AP, and PA projection, of three patients with NET tumours in (a) liver, (b) pancreas, and (c) right lung lobe. Left of scintillation images, the graphical output from MCNP code with ORNL phantom are shown, with the tumour locations used in calculations

where parameters x_0, z_0, x_1, a, b, and c are: –1, 37, 3, 16, 1.20, and 3.30 (in cm), respectively.

Each lungs lobe is represented as a half ellipsoid, where upper part is removed. The lungs (volume is 1810 cm^3 for right, and 1560 cm^3 for left lung) are defined as

$$\frac{x \quad x_0}{a}^2 \quad \frac{x}{y}^2 \quad \frac{z \quad z_0}{c}^2 \quad 1 \text{ and } z \quad z_0 \quad (4)$$

If $z_{1R,L} \quad z \quad z_{2R.L}$ and $y \quad y_{1R,L}$, $x \quad x_{1R,L}$. The letters R and L refer to the right and left lungs. The appropriate values (in cm) for x_0, z_0, x_{1R}, x_{1L}, y_{1R}, y_{1L}, z_{1R}, z_{2R}, z_{2L}, a, b, and c are: 8.50, 43.50, -5.40, 8, 1.50, 1, 46, 54, 55, 5, 7.50, and 24, respectively.

According to ORNL, human phantom consists of three types of tissues, skeletal, lung and soft, with different densities and elemental compositions. All equations for organs of ORNL phantom, with other relevant information (chemical compositions, volumes, masses *etc*.), were programmed in input files for MCNP code [28]. By combining surfaces through Bull algebra, MCNP forms cells, representing various organs.

To calculate the mean absorbed doses in other organs, when the source of radiation is located in the tumour, ORNL phantom of human body was also used. This model does not give details of human kidneys, liver and tumour. In addition, uniform distribution of activity in these organs is assumed. The dose in other organs originated from bremsstrahlung radiation, emitted by beta particles in tumour.

Since the kidneys appear in pair, they are presented in MCNP as the union of regions which contain left and right kidney. The number on histories must be increased to ensure low statistical error. As the calculation time in this case would be enormous, calculations were done separately.

For the calculations, a spectrum of electrons emitted by ^{90}Y is needed. Continuous spectrum of beta (β) radiation emitted by ^{90}Y was taken from reference [29]. Particle energy was sampled according to yields using random method incorporated in MCNP software. In order to simulate emission of whole spectrum of β^- radiation, large number of histories was created (10^8), to ensure uncertainty lower than few percent. As a result of computation, the F6 MCNP tally produces the output in MeVg^{-1} per particle, which was recalculated in the absorbed dose in Gy in targeted organs, per one emitted (β) particle of radiation from the source, *i*. *e*. from the tumour in this case.

Since the yields for beta emission of ^{90}Y is equal to 0.9982 ~ 1, results obtained by MCNP calculations can be expressed as absorbed dose per unit cumulated activity, S – value (mGy(MBqs)$^{-1}$) [30], which is the most often used units in literature in this field

$$S(k \quad h) \quad \sum_i \Delta_i \Phi(k \quad h) \quad (5)$$

where k is a target organ and h is a source organ, $\Delta_i = n_i E_i$ and E_i is the energy emitted for radiation type i with probability n_i, a $(k \quad h)$ is specific absorbed fraction (SAF) defined as the ratio of the absorbed fraction divided by the mass of target organ m_k

$$\Phi(k \quad h) \quad \frac{\phi(k \quad h)}{m_k} \quad (6)$$

$\phi(k \quad h)$ is the absorbed fraction (AF) given as

$$\phi(k \quad h) \quad \frac{E}{E_0} \quad (7)$$

the ratio of the energy, E, absorbed in target region k, to the energy E_0 emitted in source region h.

RESULTS AND DISCUSSION

Results are presented in tabs. 1-3. The S-values in organs of human body, assuming that source is in liver, pancreas and lung, respectively. As it was previously written, calculation was performed for the beta spectrum of ^{90}Y. Dependence of S-value on tumour size is also shown in fig. 2.

Location of the tumour/source was chosen to fit the images obtained from the real patients who were treated with this therapy (see fig. 1). Post therapeutic scintigraphy is not performed in practice because ^{90}Y is almost pure beta emitter. It is possible to obtain bremsstrahlung scintigraphy, but it does not satisfy criteria for quantitative estimation of distribution of ^{90}Y-DOTATOC [31]. Due to this reason, pre therapeutic prediction of ^{90}Y distribution in human body is often conducted with radiopharmaceutical with similar bio kinetic [32]. Nevertheless, in some publications bremsstrahlung scintigraphy was used to measure ^{90}Y distribution [33].

By inspection of tabs. 1-3 it is seen that doses are dependent on the tumour diameter. Doses in tumour decreases with its size. This is due to the increasing of tumour volume and mass with the r^3, while the tumour surface increases with r^2, where r is the tumour radius. In this way, fraction of beta particles which escape from the tumour decreases with the tumour size, but the mass of the tumour increases with r^3.

In tab. 1 doses are given when the tumour is in liver. The largest doses are in gall bladder and adrenals.

In tab. 2 doses are given for the tumour in pancreas. Again, doses are larger in pancreas and adrenals than in other organs.

In tab. 3 results are given for the tumour in lung. Here doses in adrenals are much smaller, while the thyroid and stomach are larger than in previous cases.

However, doses in tumour do not depend on distribution of ^{90}Y within the tumour. Similar finding was observed in ref. [34].

In organs where the tumour is located, dose is larger 4 to 5 order of magnitude than in other organs. As it was expected, doses are larger in organs closer to

Table 1. The S-values in mGy/(MBqs) to the target *k* per unit cumulated activity in the source region *h* for different tumour size when the tumour is in the liver. Comparison with Stabin *et al*. [35]

Organs	Diameter 1 cm	Stabin *et al*. [35] for point source	Diameter 2 cm	Diameter 3 cm	Diameter 4 cm	Diameter 5 cm
Adrenals	$0.20\cdot10^{-7}$	$0.28\cdot10^{-7}$	$0.20\cdot10^{-7}$	$0.20\cdot10^{-7}$	$0.21\cdot10^{-7}$	$0.21\cdot10^{-7}$
Bladder	$0.45\cdot10^{-9}$	$0.95\cdot10^{-9}$	$0.49\cdot10^{-9}$	$0.49\cdot10^{-9}$	$0.49\cdot10^{-9}$	$0.48\cdot10^{-9}$
Bone surface	$0.29\cdot10^{-8}$	$0.66\cdot10^{-8}$	$0.29\cdot10^{-8}$	$0.29\cdot10^{-8}$	$0.3\cdot10^{-8}$	$0.3\cdot10^{-8}$
Stomach	$0.42\cdot10^{-8}$	$0.91\cdot10^{-8}$	$0.42\cdot10^{-8}$	$0.42\cdot10^{-8}$	$0.43\cdot10^{-8}$	$0.42\cdot10^{-8}$
Small intestine	$0.39\cdot10^{-8}$	$0.71\cdot10^{-8}$	$0.38\cdot10^{-8}$	$0.38\cdot10^{-8}$	$0.39\cdot10^{-8}$	$0.39\cdot10^{-8}$
Colon	$0.36\cdot10^{-8}$	–	$0.36\cdot10^{-8}$	$0.36\cdot10^{-8}$	$0.36\cdot10^{-8}$	$0.37\cdot10^{-8}$
Gall bladder	$0.35\cdot10^{-7}$	$0.58\cdot10^{-7}$	$0.35\cdot10^{-7}$	$0.35\cdot10^{-7}$	$0.35\cdot10^{-7}$	$0.36\cdot10^{-7}$
Kidneys	$0.18\cdot10^{-7}$	$0.18\cdot10^{-7}$	$0.18\cdot10^{-7}$	$0.18\cdot10^{-7}$	$0.18\cdot10^{-7}$	$0.18\cdot10^{-7}$
Liver	$0.32\cdot10^{-4}$	$0.17\cdot10^{-6}$	$0.17\cdot10^{-4}$	$0.11\cdot10^{-4}$	$0.87\cdot10^{-5}$	$0.67\cdot10^{-5}$
Lungs	$0.64\cdot10^{-8}$	$0.13\cdot10^{-7}$	$0.64\cdot10^{-8}$	$0.64\cdot10^{-8}$	$0.65\cdot10^{-8}$	$0.65\cdot10^{-8}$
Pancreas	$0.14\cdot10^{-7}$	$0.23\cdot10^{-7}$	$0.14\cdot10^{-7}$	$0.14\cdot10^{-7}$	$0.14\cdot10^{-7}$	$0.14\cdot10^{-7}$
Spleen	$0.25\cdot10^{-8}$	$0.44\cdot10^{-8}$	$0.25\cdot10^{-8}$	$0.24\cdot10^{-8}$	$0.25\cdot10^{-8}$	$0.25\cdot10^{-8}$
Thyroid	$0.07\cdot10^{-9}$	$0.66\cdot10^{-9}$	$0.15\cdot10^{-9}$	$0.12\cdot10^{-9}$	$0.14\cdot10^{-9}$	$0.17\cdot10^{-9}$
Tumour	0.16	–	$2.68\cdot10^{-2}$	$8.66\cdot10^{-3}$	$3.81\cdot10^{-3}$	$2.0\cdot10^{-3}$

Table 2. The S – values in mGy/(MBqs) to the target *k* per unit cumulated activity in the source region *h* for different tumour size when the tumour is in the pancreas

Organs	Diameter 1 cm	Diameter 2 cm	Diameter 3 cm	Diameter 4 cm	Diameter 5 cm
Adrenals	$0.47\cdot10^{-7}$	$0.46\cdot10^{-7}$	$0.47\cdot10^{-7}$	$0.48\cdot10^{-7}$	$0.49\cdot10^{-7}$
Bladder	$0.58\cdot10^{-9}$	$0.56\cdot10^{-9}$	$0.55\cdot10^{-9}$	$0.61\cdot10^{-9}$	$0.60\cdot10^{-9}$
Bone surface	$0.44\cdot10^{-8}$	$0.45\cdot10^{-8}$	$0.45\cdot10^{-8}$	$0.45\cdot10^{-8}$	$0.47\cdot10^{-8}$
Stomach	$0.29\cdot10^{-7}$	$0.29\cdot10^{-7}$	$0.29\cdot10^{-7}$	$0.29\cdot10^{-7}$	$0.30\cdot10^{-7}$
Small intestine	$0.51\cdot10^{-8}$	$0.51\cdot10^{-8}$	$0.51\cdot10^{-8}$	$0.51\cdot10^{-8}$	$0.51\cdot10^{-8}$
Colon	$0.43\cdot10^{-8}$	$0.43\cdot10^{-8}$	$0.44\cdot10^{-8}$	$0.42\cdot10^{-8}$	$0.43\cdot10^{-8}$
Gall bladder	$0.36\cdot10^{-7}$	$0.34\cdot10^{-7}$	$0.37\cdot10^{-7}$	$0.36\cdot10^{-7}$	$0.38\cdot10^{-7}$
Kidneys	$0.19\cdot10^{-7}$	$0.18\cdot10^{-7}$	$0.19\cdot10^{-7}$	$0.19\cdot10^{-7}$	$0.19\cdot10^{-7}$
Liver	$0.18\cdot10^{-7}$	$0.18\cdot10^{-7}$	$0.19\cdot10^{-7}$	$0.19\cdot10^{-7}$	$0.19\cdot10^{-7}$
Lungs	$0.52\cdot10^{-8}$	$0.53\cdot10^{-8}$	$0.53\cdot10^{-8}$	$0.52\cdot10^{-8}$	$0.53\cdot10^{-8}$
Pancreas	$0.65\cdot10^{-3}$	$0.33\cdot10^{-3}$	$0.16\cdot10^{-3}$	$0.79\cdot10^{-4}$	$0.33\cdot10^{-4}$
Spleen	$0.16\cdot10^{-7}$	$0.16\cdot10^{-7}$	$0.16\cdot10^{-7}$	$0.16\cdot10^{-7}$	$0.16\cdot10^{-7}$
Thyroid	$0.12\cdot10^{-9}$	$0.14\cdot10^{-9}$	$0.12\cdot10^{-9}$	$0.02\cdot10^{-9}$	$0.08\cdot10^{-9}$
Tumour	0.16	$2.68\cdot10^{-2}$	$8.66\cdot10^{-3}$	$3.81\cdot10^{-3}$	$2.0\cdot10^{-3}$

Table 3. The S – values in mGy/(MBqs) to the target *k* per unit cumulated activity in the source region *h* for different tumour sizes when the tumour is at the lung

Organs	Diameter 1 cm	Diameter 2 cm	Diameter 3 cm	Diameter 4 cm	Diameter 5 cm
Adrenals	$0.47\cdot10^{-8}$	$0.45\cdot10^{-8}$	$0.47\cdot10^{-8}$	$0.45\cdot10^{-8}$	$0.43\cdot10^{-8}$
Bladder	$0.70\cdot10^{-10}$	$0.75\cdot10^{-10}$	$0.82\cdot10^{-10}$	$0.86\cdot10^{-10}$	$0.68\cdot10^{-10}$
Bone surface	$0.41\cdot10^{-8}$	$0.41\cdot10^{-8}$	$0.40\cdot10^{-8}$	$0.40\cdot10^{-8}$	$0.39\cdot10^{-8}$
Stomach	$0.12\cdot10^{-8}$	$0.12\cdot10^{-8}$	$0.12\cdot10^{-8}$	$0.12\cdot10^{-8}$	$0.12\cdot10^{-8}$
Small intestine	$0.41\cdot10^{-9}$	$0.40\cdot10^{-9}$	$0.41\cdot10^{-9}$	$0.39\cdot10^{-9}$	$0.39\cdot10^{-9}$
Colon	$0.36\cdot10^{-9}$	$0.35\cdot10^{-9}$	$0.35\cdot10^{-9}$	$0.34\cdot10^{-9}$	$0.35\cdot10^{-9}$
Gall bladder	$0.20\cdot10^{-8}$	$0.18\cdot10^{-8}$	$0.20\cdot10^{-8}$	$0.19\cdot10^{-8}$	$0.19\cdot10^{-8}$
Kidneys	$0.15\cdot10^{-8}$	$0.15\cdot10^{-8}$	$0.15\cdot10^{-8}$	$0.15\cdot10^{-8}$	$0.15\cdot10^{-8}$
Liver	$0.60\cdot10^{-8}$	$0.59\cdot10^{-8}$	$0.58\cdot10^{-8}$	$0.58\cdot10^{-8}$	$0.57\cdot10^{-8}$
Lungs	$0.63\cdot10^{-4}$	$0.33\cdot10^{-4}$	$0.22\cdot10^{-4}$	$0.17\cdot10^{-4}$	$0.13\cdot10^{-4}$
Pancreas	$0.25\cdot10^{-8}$	$0.27\cdot10^{-8}$	$0.25\cdot10^{-8}$	$0.25\cdot10^{-8}$	$0.26\cdot10^{-8}$
Spleen	$0.11\cdot10^{-8}$	$0.11\cdot10^{-8}$	$0.11\cdot10^{-8}$	$0.10\cdot10^{-8}$	$0.11\cdot10^{-8}$
Thyroid	$0.12\cdot10^{-8}$	$0.12\cdot10^{-8}$	$0.98\cdot10^{-9}$	$0.11\cdot10^{-8}$	$0.11\cdot10^{-8}$
Tumour	0.16	$2.66\cdot10^{-2}$	$8.62\cdot10^{-3}$	$3.80\cdot10^{-3}$	$1.99\cdot10^{-3}$

the tumour than in other distal organs. Similar values were published in [35]. Stabin *et al*. [35] calculated absorbed dose from point like ^{90}Y source at the distance of 3 cm as $1.61\cdot10^{-4}$ GyMBq^{-1}, while in this work value $8.66\cdot10^{-3}$ mGy(MBqs)$^{-1}$, was found. However, in this work calculation was performed for spherical source while Stabin *et al*. [35] used point source, so, the results are not directly comparable.

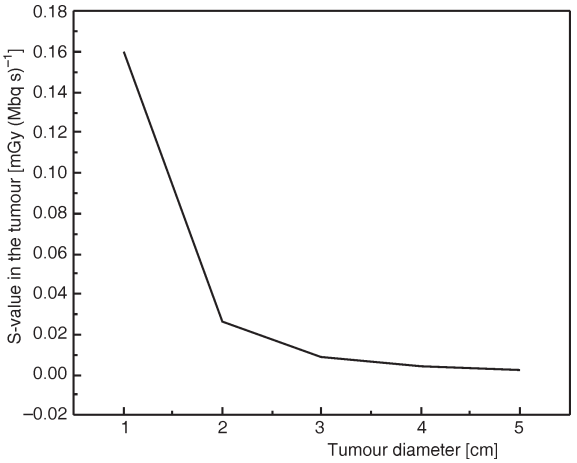

Figure 2. Dependence of absorbed dose per unit cumulated activity (S-value) on the tumour size

Nevertheless, comparison with Stabin *et al.* [35] is given in third column in tab. 1. Comparison shows that the same order of magnitude is in all organs, but the difference is smaller for distal organs, and larger for organs closer to the source. Ahangari *et al*. [36], also calculated dose from various sizes of spherical sources but, the results again are not directly comparable.

Calculations performed here – were done with 10^8 simulations in order to obtain results with statistical uncertainty smaller than 1 %. Other uncertainties are possible due to variability of size of human body, tissue density and its chemical composition, *etc*.

CONCLUSION

Absorbed dose per unit exposure, *i. e.*, S-value in mGy/(MBqs) from ^{90}Y, in different organs of human body, were calculated in this work. As expectable, doses are largest in tumour and in organ where the tumour is situated. In addition, doses are larger in organs near the tumour and much smaller in distant organs where they could be neglected. In addition, doses in organs out of tumour weakly depend on tumour size.

According to European directive 2013/59/, there is a need for estimation of absorbed doses in all medical exposure of ionizing radiation [37]. Since there is no bio kinetic model for ^{90}Y recommended by the ICRP, it is necessary to develop such model where the previously given results of S-values could be used for dose assessment.

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AUTHOR'S CONTRIBUTIONS

Conceived and designed the computations: M. Ž. Jeremić and D. Ž. Krstić. Performed the computations: D. Ž. Krstić. Analyzed the data: all authors. Wrote the paper: D. R. Nikezić, M. Ž. Jeremić, and D. Ž. Krstić. All the authors participated in the discussion of the results presented in the final version of the manuscript.

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РАЧУНАЊЕ АПСОРБОВАНЕ ДОЗЕ ПРИ ^{90}Y-DOTATOC ПЕПТИДНОЈ РАДИОНУКЛИДНОЈ ТЕРАПИЈИ, ПОМОЋУ MCNP5/X

Пептиди (DOTATOC, DOTATATE) обележени јаким бета емитерима, као што су ^{90}Y и ^{177}Lu, користе се у терапији неуроендокриних тумора који имају јак афинитет за соматостатинске рецепторе. У овом раду коришћени су MCNP5/X софтвер и ORNL фантоми људског тела, за рачунање апсорбованих доза услед примене ^{90}Y-DOTATOC. Тумори су разматрани као извор бета зрачења и представљени су у облику сфера дијаметара 1-4 cm и 5 cm у јетри, панкреасу и плућима. Резултати су изражени у облику апсорбоване дозе по јединици кумулативне активности, S- вредност у јединицама (mGy·(MBqs)$^{-1}$). Највећа доза је у самом тумору, мања је у органу у коме се тумор налази али није занемарљива. Дозе у осталим органима, које потичу од закочног зрачења су далеко мање и могу се занемарити. Максимална доза је добијена за пречник тумора од 3 cm, 8.66 10^{-3} mGy·(MBqs)$^{-1}$, док је за остале пречнике тумора добијена мања вредност.

Кључне речи: Монте Карло симулација, ^{90}Y-DOTATOC, терапија радионуклидима, дозиметрија