# Estimation of Photon Specific Absorbed Fractions in Digimouse Voxel Phantom using Monte Carlo Simulation Code FLUKA

Sinha A.[1]*, Patni H. K.[2], Dixit B. M.[1], Painuly N. K.[3], Singh N.[3]

[1]Faculty of Physical Sciences, Shri Ramswaroop Memorial University, Lucknow, India
[2]Bhabha Atomic Research Center, Mumbai, India
3Department of Radiotherapy, King George Medical University, Lucknow, India

## ABSTRACT

**Background:** Most preclinical studies are carried out on mice. For internal dose assessment of a mouse, specific absorbed fraction (SAF) values play an important role. In most studies, SAF values are estimated using older standard human organ compositions and values for limited source target pairs.

**Objective:** SAF values for monoenergetic photons of energies 15, 50, 100, 500, 1000 and 4000 keV were evaluated for the Digimouse voxel phantom incorporated in Monte Carlo code FLUKA. The organ sources considered in this study were lungs, skeleton, heart, bladder, testis, stomach, spleen, pancreas, liver, kidney, adrenal, eye and brain. The considered target organs were lungs, skeleton, heart, bladder, testis, stomach, spleen, pancreas, liver, kidney, adrenal and brain. Eye was considered as a target organ only for eye as a source organ. Organ compositions and densities were adopted from International Commission on Radiological Protection (ICRP) publication number 110.

**Results:** Evaluated organ masses and SAF values are presented in tabular form. It is observed that SAF values decrease with increasing the source-to-target distance. The SAF value for self-irradiation decreases with increasing photon energy. The SAF values are also found to be dependent on the mass of target in such a way that higher values are obtained for lower masses. The effect of composition is highest in case of target organ lungs where mass and estimated SAF values are found to have larger differences.

**Conclusion:** These SAF values are very important for absorbed dose calculation for various organs of a mouse.

## Keywords

Specific Absorbed Fraction, Digimouse Voxel Phantom, Monte Carlo Simulation, FLUKA

## Introduction

Most preclinical studies are carried out on mouse and based on the success of these studies; the human clinical trial will be carried out. Therefore, the correctness of mouse modelling has a large impact on success rate of the clinical trials as well as the development of new experimental drugs for treatment [1]. For applications related to radionuclides incorporated in body, preclinical studies require the estimation of internal organ doses delivered to mouse. The medical internal radiation dose (MIRD) methodology [2] for estimation of internal organ and whole body dose require the quantities known as

*Corresponding author:
A. Sinha
Faculty of Physical Sciences, Shri Ramswaroop Memorial University, Lucknow, India
E-mail: ashutosh22jan@gmail.com

Received: 18 June 2015
Accepted: 25 August 2015

specific absorbed fraction (SAF) values. SAF values are the absorbed fractions per mass unit of the target tissue. The absorbed fraction is the fractional energy deposited in target organ due to the emission from source organ [3]; therefore, the estimation of SAF values on mouse is an important step in preclinical trial studies. Earliest methods adopted for the estimation of mouse SAF values involved using point kernel method [4-5] in conjunction with stylized phantoms [4-6] with mouse organs represented by ellipsoids, spheroids and cylinders. With time, approximate point kernel methods were replaced by full Monte Carlo simulations [4-9] using the particle transports which are more accurate. Similarly, stylized phantoms have the issue of non-realistic representation of internal organs due to their simple mathematical form and non-overlapping organs. Mouse volume pixel (voxel) phantoms are modern computational phantoms based on medical imaging of mouse. Mouse voxelized phantoms are free from the above mentioned problems associated with stylized phantoms. There are several studies using mouse-based voxelized phantoms with Monte Carlo codes for the estimation of SAF values of photons [7-9]. For these simulations, organ compositions of human have been used. Most studies are used older organ composition based on International Commission on Radiological Protection (ICRP) publication number 23 [10] or International Commission on Radiation Units and Measurements (ICRU) report number 44 [11]. Human organ compositions in ICRP 23 are based on studies carried out before 1975 whereas ICRU 44 contains composition of tissue substitute only. Previous studies also lac the aspect that SAF values are not provided for all source target pairs, which will be useful for computing all organ doses. Based on these facts, this study was proposed for the estimation of mouse SAF values for photons using recent organ compositions.

In this study, Digimouse voxelized phantom [12] was incorporated into Monte Carlo particle transport code FLUKA [13-14]. FLUKA shows the results similar to those obtained by EGS and MCNP codes for 3D patient specific dosimetry [15]. FLUKA code also shows results similar to those obtained by EGS and MCNP codes for the estimation of external organ dose conversion coefficients [16] and evaluation of SAF values [17] in ICRP reference voxelized phantoms. Source sampling was carried out in the following organs: lungs, skeleton, heart, bladder, testis, stomach, spleen, pancreas, liver, kidney, adrenal, eye and brain. The considered target regions considered were lungs, skeleton, heart, bladder, testis, stomach, spleen, pancreas, liver, kidney, adrenal and brain. Eye was considered as the target only when it was the source organ. Six photon energies from 15keV to 4000 keV were considered for these simulations. Material composition and density of the simulated organs were based on the values presented in ICRP publication number 110 [18]. Mouse organ masses were estimated based on these new compositions and densities. SAF values were estimated for all monoenergetic photons, and all source target pairs were considered. The effects of various factors on SAF values were also analyzed. The comparison between present study and the studies which used voxelized phantoms was also performed

## Material And Methods

### Digimouse Voxel Phantom in FLUKA Code

The Digimouse voxel phantom used in this study is a three-dimensional representation of whole body of a mouse. This phantom was developed by biomedical imaging group of the University of South California using medical image data such as x-ray CT and color cryosection images of a normal nude male mouse. The phantom is a matrix of 380 columns, 992 rows and 208 slices or 78407680 voxels. Each voxel is a cube of dimensions 0.1 mm. The structures which are segmented and labeled

with distinct organ identification numbers in this phantom are: medulla, cerebellum, olfactory bulbs, external cerebrum, striatum, rest of the brain, massetter muscles, eyes, lachrymal glands, heart, lungs, liver, stomach, spleen, pancreas, adrenal glands, kidneys, testes, bladder, skeleton and skin. The whole brain in this phantom consists of medulla, cerebellum, olfactory bulbs, external cerebrum, striatum and the rest of the brain. Digimouse voxelized phantom data was downloaded from the link provided in the reference.

A FORTRAN program was used to convert Digimouse voxelized phantom data into a suitable format to use in FLUKA code. This program was used to read the provided phantom data and generate the ".vxl" file for FLUKA with details such as name of the phantom, number of columns, rows and slices, the maximum organ identification numbers, voxel dimensions, anatomical data etc. Flair [19], an advanced user interface for FLUKA, has been used for creating input file and visualizing this phantom in FLUKA. The figure of Digimouse phantom incorporated in FLUKA code in X-Y, Y-Z and X-Z planes is shown in Figure 1. The elemental compositions and densities used for Monte Carlo simulation of Digimouse phantom are based on the most recent human anatomical data provided in ICRP publication number 110. ICRP 110 contains fifty three different organ compositions where various soft tissue compositions are based on ICRU 46 [20] and various skeleton tissue compositions are based on ICRP 70 [21].

## Simulations and Estimation of SAFs

Another FORTRAN program was used for Monte Carlo simulation of the uniform activity distribution and isotropic photon emission from the source organ. Details of the source sampling method can be found in this reference [16]. Using the mentioned FORTRAN program, masses of simulated organs in phantom were calculated by multiplying the total volume of organs (product of number of voxels and volume of voxel and related density). The organ sources considered in the present study are: lungs, skeleton, heart, bladder, testis, stomach, spleen, pancreas, liver, kidney, adrenal, eye and brain. The target organs considered are: lungs, skeleton, heart, bladder, testis, stomach, spleen, pancreas, liver, kidney, adrenal and brain. As stated above, eye was considered as the target only when it was a source organ. Six photon energies (15, 50, 100, 500, 1000 and 4000 keV) were considered in these simulations. In FLUKA code, USERBIN card was used to evaluate the energy deposited in target organs due to the activity in the source organ. SAF value [17] used as a common parameter in our studv which can be calculated

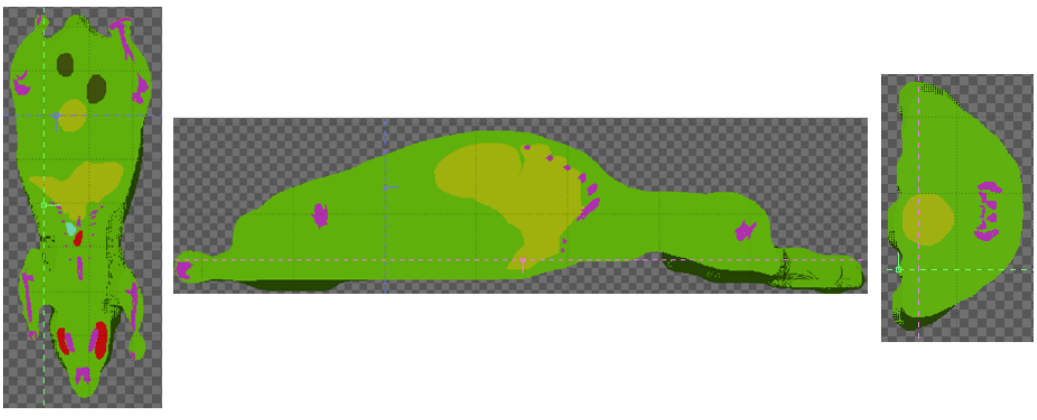


**Figure 1:** Digimouse Phantom Incorporated in FLUKA Code (different views)

by the following formula:

$$SAF = \frac{\text{Average energy deposited in target organ}}{\text{Primary energy emitted in source organ x mass of the target organ}} \quad (1)$$

For a particular energy and source-target combination, 2x108 histories were run to reduce the relative error (RE) in the estimated energy deposited in target organ due to the activity in source organ.

A separate FORTRAN program was used to compute SAF values and their REs for all source-target combinations and energies considered in this study.

## Results and Discussion

The estimated masses of various organs in Digimouse voxelized phantom are shown in supporting documents available on the website. A comparison of masses for various simulated organs in our study (organ composition based on ICRP 110) and in the paper of Mohammdi et al. [22] (organ composition based on ICRU 44) shows that masses are similar for most organs (difference <5%) except for skin, lungs and skeleton. The difference in mass is 7% for skin and 33% for lungs and skeleton.

The computed photon SAF values (from equation 1) for various source-target combinations and their REs at different energies are presented in supporting documents available on the website. The reported SAF values have REs less than 10%. The results of SAF values show that these values are dependent on the following factors: Source-to-target distance, primary photon energy, mass of target tissues and the effect of geometry in case of cross-irradiation.

### Source-to-target Distance

SAF values depend on source-to-target distance decreasing by increase in distance. If the source and target are the same (self-irradiation), SAF values are the highest, because the maximum energy absorption will occur. As the distance between sources-to-target increase, the influence decreases due to the increased attenuation in the intermediate organs or tissues.

When liver is the source organ, the highest SAF values are observed in liver in all energies. The SAF values for testis and brain are the smallest, because they are far from source organ liver. Similarly, in the case of brain being the source organ, the highest SAF values are observed in brain. It can be concluded that, bladder and testis also have the smallest SAF values because they are far from brain.

### Primary Photon Energy

As shown in Figure 2 (SAF values for self-irradiation in liver, stomach, heart, kidney and pancreas) and Figure 3 (SAF values for cross-irradiation in stomach, pancreas, spleen, heart and kidney with liver as source organ), photon SAF values for self-irradiation and cross-irradiation show a decreasing trend with increasing energy in the photon energy range of 15 keV to 100 keV and 500 keV to 4000 keV. There was a slight increase in SAF values when photon energies increased from 100 keV to 500 keV, which is due to multiple Compton scattering occurring in this energy region.

### Mass of Target Organs

Photon SAF values depend on the mass of target organs especially in case of self-irradiation. As shown in Figure 2, SAF values continuously increase with decreasing the target mass. The effect of the mass of target tissue on SAF values is due to energy deposition per mass unit less for larger size organs. The organ with similar masses (difference ~0.2%) such as stomach and heart have very small differences (<7%) in SAF values at all energies.

### Effect of Geometry in case of Cross-irradiation

Based on Figure 3, we can explain the independence of SAF values from mass of target

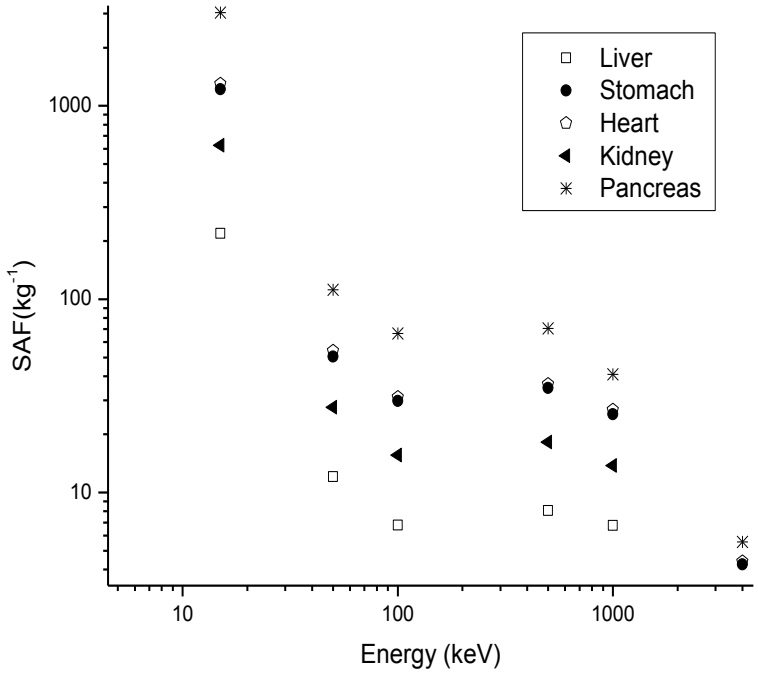


**Figure 2:** Self-irradiation in Organs such as Liver, Stomach, Heart, Kidney and Pancreas

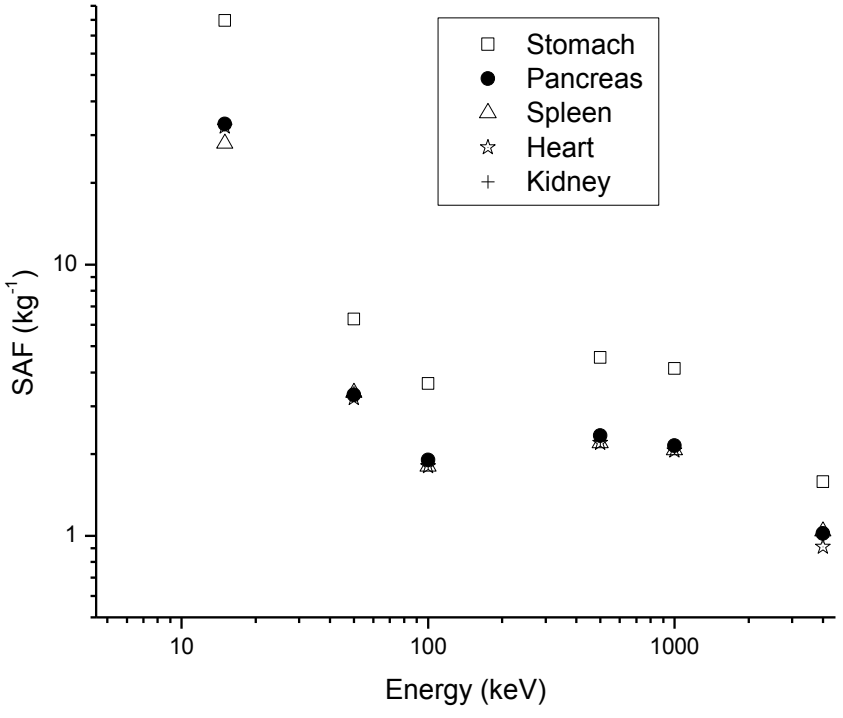


**Figure 3:** Cross-irradiation in Organs such as Stomach, Pancreas, Spleen, Heart and Kidney (Source: Liver)

organs in case of cross-irradiation while taking liver as a source organ. SAF values are different at all energies for stomach and heart (difference more than 73%) regardless of having the same mass. SAF values for heart and pancreas with large difference in mass (mass of heart > 4.9 times of mass of pancreas) have almost the same SAF values (difference less than 13%). We can conclude from these examples that SAF values for cross-irradiation is dependent on various geometrical factors such as source size, target size and their distance.

### Comparison with Contemporary Studies Using Digimouse Voxel Phantom

A comparison of SAF values for self-irradiation in lungs and spleen reported by Mohammadi et al. and with those observed in the present study are shown in Figure 4. The difference in SAF values of spleen between our study and the reference study is less than 11% at 15 keV as well as very smaller differences at higher energies (<2%). The difference in SAF values for lungs between our study and the reference study is up to 23%, which can be attributed to different compositions and masses for lung used in both studies.

SAF values for cross-irradiation in liver, while taking stomach as source organ between our study and the reference study, are shown in Figure 5 which has the maximum difference of 6%.

## Conclusion

In preclinical studies involving internal dose assessment of mouse, SAF values play an important role. Most studies on SAF values have used older standard human organ compositions and these values were for limited source target pairs. In this study, organ compositions and densities for photon SAF estimation in

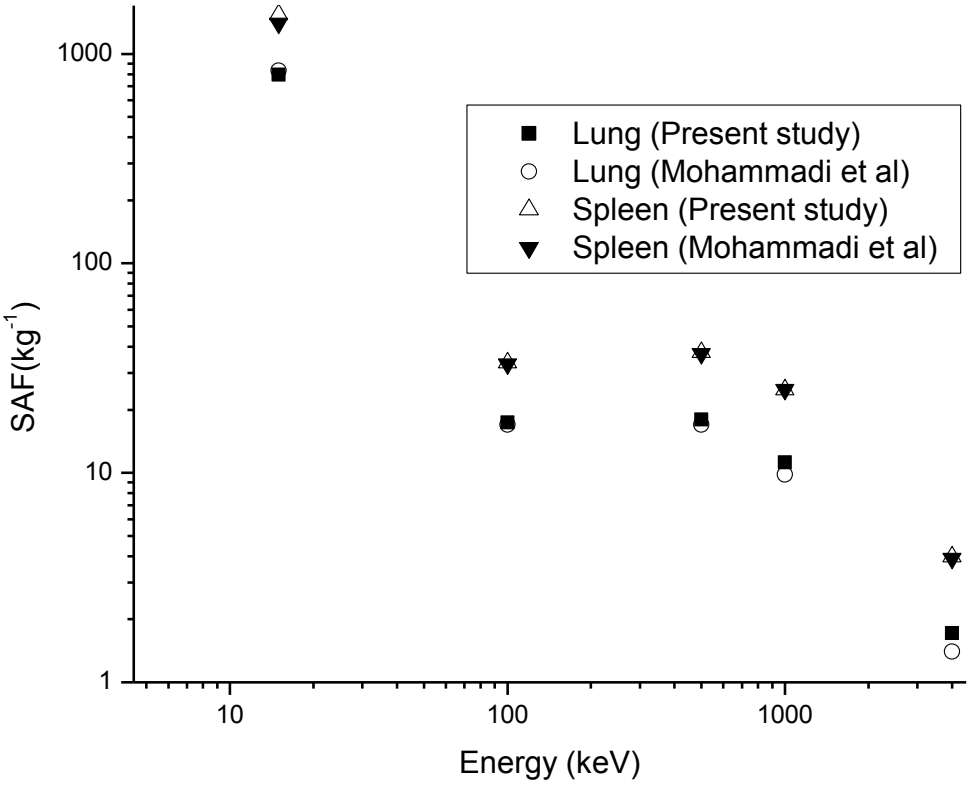


**Figure 4:** Comparison of Photon Specific Absorbed Fractions for Self-irradiation in Lung and Spleen between Present Study and Mohammadi et al. Study

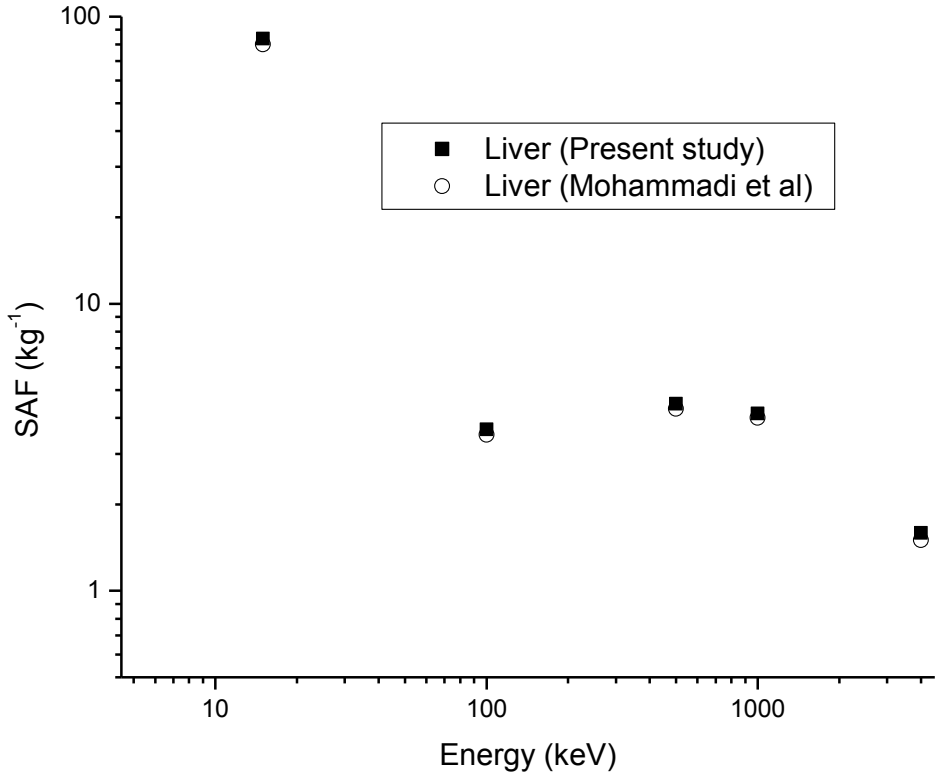


**Figure 5:** Comparison of Photon Specific Absorbed Fractions for Cross-irradiation in the Present Study and Mohammadi et al. Study (Source: Stomach)

Digimouse voxelized phantom are based on ICRP publication number 110. FLUKA code has been used as a Monte Carlo tool at 15, 50, 100, 500, 1000 and 4000 keV photon energies. Organ sources were lungs, skeleton, heart, bladder, testis, stomach, spleen, pancreas, liver, kidney, adrenal, eye and brain. Target organs were lungs, skeleton, heart, bladder, testis, stomach, spleen, pancreas, liver, kidney, adrenal, eye and brain. The SAF values obtained from this study are in agreement with other studies which used Digmouse voxelized phantom. It was observed that the SAF values are dependent on source-to-target distance decreasing with distance. For self-irradiation, SAF values decrease with increasing photon energy. SAF values for self-irradiation also depend on the mass of target, and higher values were obtained for lower masses.

## Acknowledgment

Authors would like to thank Dr. Akram Mohammadi, National Institute of Radiological Sciences, Chiba- Japan for her guidance in this work.

## Conflict of Interest

None

## References

1. Perrin S. Preclinical research: Make mouse studies work. *Nature*. 2014;**507**:423-5. doi. org/10.1038/507423a. PubMed PMID: 24678540.
2. Snyder WS, Fisher HL, Jr., Ford MR, Warner GG. Estimates of absorbed fractions for monoenergetic photon sources uniformly distributed in various organs of a heterogeneous phantom. *J Nucl Med*. 1969:Suppl 3:7-52. PubMed PMID: 5802194.
3. Eckerman KF. Dosimetric methodology of the ICRP. USA: Oak Ridge National Laboratory; 1994.
4. Hui TE, Fisher DR, Kuhn JA, Williams LE, Nourigat C, Badger CC, et al. A mouse model for calculating cross-organ beta doses from yttrium-90-labeled immunoconjugates. Cancer. 1994;73:951-7. PubMed PMID: 8306284.
5. Kolbert KS, Watson T, Matei C, Xu S, Koutcher

JA, Sgouros G. Murine S factors for liver, spleen, and kidney. *J Nucl Med*. 2003;**44**:784-91. PubMed PMID: 12732681.

6. Hindorf C, Ljungberg M, Strand SE. Evaluation of parameters influencing S values in mouse dosimetry. *J Nucl Med*. 2004;**45**:1960-5. PubMed PMID: 15534069.
7. Stabin MG, Peterson TE, Holburn GE, Emmons MA. Voxel-based mouse and rat models for internal dose calculations. *J Nucl Med*. 2006;**47**:655-9. PubMed PMID: 16595500.
8. Bitar A, Lisbona A, Thedrez P, Sai Maurel C, Le Forestier D, Barbet J, et al. A voxel-based mouse for internal dose calculations using Monte Carlo simulations (MCNP). *Phys Med Biol*. 2007;**52**:1013-25. doi.org/10.1088/0031-9155/52/4/010. PubMed PMID: 17264367.
9. Taschereau R, Chatziioannou AF. Monte Carlo simulations of absorbed dose in a mouse phantom from 18-fluorine compounds. *Med Phys*. 2007;**34**:1026-36. doi.org/10.1118/1.2558115. PubMed PMID: 17441249. PubMed PMCID: 3006169.
10. Snyder WS, Cook MJ, Nasset ES. Report of the task group on reference man : a report prepared by a task group of Committee 2 of the International Commission on Radiological Protection: adopted by the Commission in october, 1974. Oxford; New York; Tokyo: Elsevier Science; 1994.
11. International Commission on Radiation U, Measurements. Tissue substitutes in radiation dosimetry and measurement. Bethesda: International Commission on Radiation Units and Measurements; 1989.
12. Dogdas B, Stout D, Chatziioannou AF, Leahy RM. Digimouse: a 3D whole body mouse atlas from CT and cryosection data. *Phys Med Biol*. 2007;**52**:577-87. doi.org/10.1088/0031-9155/52/3/003. PubMed PMID: 17228106. PubMed PMCID: 3006167.
13. Ferrari A, Sala P, Fasso A, Ranft J. FLUKA: a multi-particle transport code, CERN 2005-10. *INFN/TC*. 2005;5:II.
14. Battistoni G, Cerutti F, Fasso A, Ferrari A, Muraro S, Ranft J, et al. The FLUKA code: description and benchmarking. *Hadronic Shower Simulation Workshop*. 2007;**896**;31-49.
15. Botta F, Mairani A, Hobbs RF, Vergara Gil A, Pacilio M, Parodi K, et al. Use of the FLUKA Monte Carlo code for 3D patient-specific dosimetry on PET-CT and SPECT-CT images. *Phys Med Biol*. 2013;**58**:8099-120. doi.org/10.1088/0031-9155/58/22/8099. PubMed PMID: 24200697. PubMed PMCID: 4037810.
16. Patni HK, Nadar MY, Akar DK, Bhati S, Sarkar PK. Selected organ dose conversion coefficients for external photons calculated using ICRP adult voxel phantoms and Monte Carlo code FLUKA. *Radiat Prot Dosimetry*. 2011;**147**:406-16. doi.org/10.1093/rpd/ncq462. PubMed PMID: 21147784.
17. Patni HK, Akar DK, Nadar MY, Ghare VP, Rao DD, Sarkar PK. Estimation of specific absorbed fractions for selected organs due to photons emitted by activity deposited in the human respiratory tract using ICRP/ICRU male voxel phantom in FLUKA. *Radiat Prot Dosimetry*. 2013;**153**:32-46. doi.org/10.1093/rpd/ncs087. PubMed PMID: 22645381.
18. Adult reference computational phantoms. International Commission on Radiological Protection. *ICRP*. 2009; Publication 110.
19. Vlachoudis V. FLAIR: a powerful but user friendly graphical interface for FLUKA. Proc. Int. Conf. on Mathematics, Computational Methods & Reactor Physics (M&C 2009), Saratoga Springs, New York; 2009.
20. Photon E. Proton and neutron interaction data for body tissues. International Commission on Radiation Units and Measurements. *ICRU report*. 1992;**46**:13
21. 2 ICorpC. Basic Anatomical and Physiological Data for Use in Radiological Protection: the Skeleton: A Report of a Task Group of Committee 2 of the International Commission on Radiological Protection Adopted by the Commission in July 1994: Pergamon Press; 1995.
22. Mohammadi A, Kinase S. Influence of voxel size on specific absorbed fractions and S-values in a mouse voxel phantom. *Radiat Prot Dosimetry*. 2011;**143**:258-63. doi.org/10.1093/rpd/ncq391. PubMed PMID: 21123241.