Overview and analysis of internal radiation dose estimates in experimental animals in a framework of international studies of the sprayed neutron-induced $^{56}$Mn radioactive microparticles effects

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ABSTRACT

The aim of overview is to present the pooled data of published internal dose estimates and the results of corresponding analysis of internal irradiation features of experimental mice and rats after exposure to sprayed neutron activated radioactive $^{56}$MnO$_2$. These dose estimates were conducted in a framework of multicenter international study to investigate biological effects as a result of exposure to sprayed radioactive $^{56}$MnO$_2$ microparticles. Radionuclide $^{56}$Mn ($T_{1/2} = 2.58$ h) is one of the main gamma-beta emitters during the first hours after neutron activation of soil following nuclear explosion. It was concluded that there are three groups of organs of mice and rats, the radiation doses of which differ by approximately an order of magnitude: the group with the highest radiation doses (large and small intestine, stomach, skin and lungs), the group with lowered radiation doses (eyes, esophagus, trachea), the group with the lowest radiation doses (liver, heart, kidneys). The radiation doses to organs are proportional to the activity of the sprayed radioactive powder. The distribution of internal radiation doses among organs of experimental mice of different strains but of the same age was practically the same in case of exposure to the same activity of sprayed $^{56}$MnO$_2$ powder. Doses of internal irradiation of experimental mice substantially exceed the doses of internal irradiation of experimental rats exposed to the same activities of the sprayed $^{56}$MnO$_2$ powder. The data presented in the overview can be helpful for further investigation and for interpretation of the biological effects of this type of irradiation.

Keywords: dosimetry of internal beta- and gamma-irradiation; neutron activation; $^{56}$Mn; spayed radioactive microparticles; laboratory animals

INTRODUCTION

Radiation effects from residual radioactivity resulting from nuclear explosions in Hiroshima and Nagasaki are the subject of discussions and research of the consequences of such kind of uncontrolled irradiation of population [1–4]. Radionuclide $^{56}$Mn ($T_{1/2} = 2.58$ h) is one of the main beta-gamma emitters during the first hours after neutron activation of soil at the time of a nuclear explosion [5–7]. The aim of this overview is to present the pooled data of published internal dose estimates [8–11] and the results of corresponding analysis of internal irradiation features of experimental animals after exposure to sprayed neutron activated radioactive $^{56}$MnO$_2$. Overview is based on the data obtained in a framework of international...
Internal radiation dose in mice and rats exposed to sprayed $^{56}$Mn microparticles

multicenter studies conducted at a nuclear reactor [8,12]. The data presented in overview can be helpful for further investigation and for interpretation of the biological effects of this type of irradiation.

GENERAL DESCRIPTION OF EXPERIMENTAL STUDIES

General description of the method for exposure of laboratory animals to sprayed neutron activated $^{56}$MnO$_2$ powder

Neutron activation of manganese dioxide powder was conducted at the IVG.1 M research reactor (Kazakhstan). The IVG.1 M reactor is a research water-moderated heterogeneous thermal neutron reactor [8–12] with a beryllium reflector designed for radiation studies of samples of various materials used in reactor construction, nuclear power engineering and for performing experiments with irradiation of biological objects.

Manganese dioxide is a finely dispersed powder weighing 100 mg with a particles size of about 3 microns [9–11,13]. A special construction for exposure of laboratory animals to sprayed powder $^{56}$MnO$_2$ has been developed.

The neutron activated manganese dioxide powder was sprayed into a cage with laboratory animals (mice and rats) [9–11]. Figure 1 shows a photo with laboratory rats placed in experimental cage [8].

Fig. 1. Cage with laboratory rats placed in it [8]. The pneumatic hose is connected to the cage with biological objects for supplying the radioactive powder from the shielded lead container with $^{56}$MnO$_2$ powder. The experimental cages with laboratory animals placed in it is equipped with forced ventilation system and air filters.

To exclude the possibility of $^{56}$MnO$_2$ powder particles to enter the working room, the cage with experimental animals (mice and rats) was placed in an external box [9]. Figure 2 shows a photo with general view of the external box and experimental cage for laboratory animals placed in it [8] at the moment of external dose rate measurements in order to control the safe level after exposure of animals to sprayed $^{56}$MnO$_2$ powder.

Fig. 2. General view of the external box and cage for experimental animals at the moment of external dose rate measurements in order to control the safe level after exposure of animals to sprayed $^{56}$MnO$_2$ powder [8].

Experimental animals and conditions of exposure

There were several experiments carried out. Experimental animals and conditions of exposure are described in detail in [9–11]. Briefly, experiments were performed with 11 week old male Wistar rats and with 10 week old CD-1, C57BL, BALB/C mice. The reason for usage of different strains and types of experimental animals was determined by the aims of corresponding biological investigations [13–21]. Experimental animals were exposed to 100 mg portion of sprayed radioactive manganese dioxide powder with various initial activities of $^{56}$Mn – in the range from $8.0 \times 10^7$ Bq to $8.0 \times 10^8$ Bq – as it was planned in biological experiments [13–21]. There were six to nine experimental animals placed in each cage in dependence on biological experiments' plans [13–21].

General description of methods used for internal dose estimation

Methods used for internal dose estimation are described in detail in publications [9–11]. In brief, after animal’s exposure, they were euthanized by injection of an excessive dose of pentobarbital according to Approval by the Ethical Committee of Semey State Medical University (Kazakhstan), and according to Directive 2010/63/EU of the European Parliament and the Council of the Office on the protection of animals used for scientific purposes [22]. The $^{56}$Mn activity in pieces of each extracted organ was measured by AMPTEC, Inc., Gamma-Rad5 spectrometer with the 76 mm $\times$ 76 mm NaI(Tl) scintillation detector. Volumes of extracted biological samples were small enough ($< 1$ ml) to consider these samples as point sources of irradiation (in comparison with the size of the detector and 50 mm distance from the sample to the detector).

Calibration of AMPTEC, Inc., Gamma-Rad5 spectrometer was performed by using a standard source with a neutron-activated $^{56}$Mn point source [10]. Shortly calibration procedure was as follows.

To produce this source, 0.1 mg MnO$_2$ powder was activated using thermal neutrons of the research reactor. The obtained initial activity of the $^{56}$Mn source was equal to $(0.36 \pm 0.021) \times 10^8$ Bq. The calibration procedure was performed two hours after end of activation using the
same geometry as the geometry used to measure the $^{56}$Mn activity in tissue and organ samples. At the moment of calibration the activity of the $^{56}$Mn source was equal to $(0.205 \pm 0.012) \times 10^7$ Bq. Results of the calibration procedure were as follows: $(2000 \pm 240)$ counts/min per kBq for the AMPTEK, Inc. Gamma-Rad5 spectrometer. All indicated numbers are related to the 846.8 keV gamma peak (98.9%) of $^{56}$Mn with a region of interest from 817 to 876 keV. The background spectrum was subtracted from the spectrum obtained with the $^{56}$Mn source.

The calculations of internal doses [9–11] were performed using MIRD methodology [23] and mathematical phantoms of rats and mice [25] with accounting for beta- and gamma- spectra irradiations of $^{56}$Mn [26,27]. In accordance with MIRD methodology, in order to assess internal radiation doses, in addition to the estimated accumulated activity of radionuclide in the organs and tissues of experimental animals, it is necessary to know the values of the absorbed energy in the ‘target’ organs expressed as ratio to the total energy irradiated by the ‘source’ organs – it is so called ‘absorbed fractions’ (AF). As a rule, the Monte-Carlo code and mathematical phantoms of experimental animals are used for calculation of the AFs or specific absorbed fractions (SAF). The term ‘specific absorbed fraction’ (SAF) means AF per ‘target’ organ’s mass. For calculations of SAF, it is also necessary to know the spectra of quantum and corpuscular ionizing radiations of the considered radionuclide [26,27]. Figures 3–6 show examples of calculated SAF values in various organs of experimental mice and rats when they are irradiated to gamma quanta and electrons of various energies [25]. These figures show examples with SAF values for cases where the source organ and the target organ are the same (‘specific self absorbed fraction’).

The calculations of SAFs were performed using the MCNP Monte-Carlo N–particle transport code (version C) [24] and mathematical phantoms of rats and mice [25]. In brief, the mathematical phantoms of experimental animals were constructed as follows [25]: the positions of organs of three-dimensional mathematical phantoms of laboratory mice and rats were considered relative to a rectangular coordinate system (with the center on the base of the body—point ’0’) and were set in the form of three-dimensional geometric figures; the vertical axis...
of the animals’ phantoms (axis Z) is directed towards the head of the animal; the X axis is directed from the center of coordinate system to the right, the Y axis is directed from the center of coordinate system to the back of the phantom. The shapes and sizes of animals’ organs were approximated by systems of mathematical equations in the rectangular coordinate system.

Comparison of the data presented in Figs 3–4 with the data presented in Figs 5–6 shows that the values of the SAFs for mice’ organs significantly exceed those for the organs of rats. This is explained by the fact that the masses of the organs of mice are much less than the masses of the organs of rats [28]. This leads to the fact that, for the same accumulated activities of radionuclides in the organs of mice and rats, the absorbed doses of internal irradiation in experimental mice will exceed those for rats.

ANALYSIS OF THE RESULTS OF INTERNAL DOSE ESTIMATES IN EXPERIMENTAL ANIMALS EXPOSED TO SPRAYED $^{56}$Mn RADIOACTIVE MICROPARTICLES

Internal radiation doses among organs of Wistar rats after exposure to different activities of sprayed neutron-activated $^{56}$Mn dioxide powder

Figures 7–9 show in graphical form the pooled values of internal radiation dose for various groups of organs versus sprayed neutron-activated $^{56}$Mn dioxide powder activity (based on the data published in [9–11]).

Figures 7–9 show that there are three groups of organs, the radiation dose of which differ by approximately an order of magnitude: the group with the highest radiation dose (large and small intestine, stomach, skin, lungs), the group with lowered radiation dose (eyes, esophagus, trachea), the group with the lowest radiation dose (heart, liver, kidneys).

The values of the radiation doses to organs are proportional to the activity of the dispersed radioactive powder.

Doses of internal irradiation among organs of mice from different strains after exposure to the sprayed neutron-activated $^{56}$Mn dioxide powder with various levels of activity

Tables 1 and 2 presents the pooled information regarding values of internal irradiation among organs of mice from different strains after exposure to the sprayed neutron-activated $^{56}$Mn dioxide powder with various levels of activity (based on the data published in [11]).

As it follows from the Table 1, the doses of internal irradiation in organs and tissues resulted from exposure to sprayed $2.74 \times 10^8$ Bq
Table 1. Doses of internal irradiation and corresponding standard deviations (D ± SD), Gy, in organs resulted from exposure to $2.74 \times 10^8$ Bq activity of sprayed neutron activated $^{56}$MnO$_2$ powder among different strains of 10 week old mice

| Activity of $^{56}$Mn, Bq, and strains | Dose (D ± SD), Gy, in investigated organs |
|---------------------------------------|------------------------------------------|
|                                       | Lungs                               | Small intestine          | Large intestine | Stomach | Whole body | Skin         | Esophagus   | Trachea | Eyes | Liver | Heart | Spleen | Kidney |
|                                       | D  SD          | D  SD          | D  SD          | D  SD          | D  SD          | D  SD          | D  SD          | D  SD          | D  SD          | D  SD          | D  SD          | D  SD          |
| $2.74 \times 10^8$ C57Bl               | 0.096 0.013    | 0.91 0.15      | 4.2 0.5        | 0.98 0.16      | 0.38 0.07      | 0.29 0.05      | 0.087 0.013    | 0.039 0.003   | 0.14 0.05      | 0.0066 0.0011  | 0.026 0.0025   | 0.0070 0.0005  |
| $2.74 \times 10^8$ C57Bl               | 0.14 0.02      | 1.1 0.2       | 4.5 0.5        | 1.2 0.2       | 0.33 0.07      | 0.34 0.06      | 0.079 0.013    | 0.047 0.008   | 0.13 0.02      | 0.0086 0.0014  | 0.07 0.01      | 0.0028 0.0006  | 0.0021 0.0006  |
| $2.74 \times 10^8$ BALB/C              | 0.11 0.03      | 0.86 0.21     | 3.8 0.6        | 0.91 0.22     | 0.41 0.09      | 0.31 0.07      | 0.093 0.016    | 0.05 0.1    | 0.01 0.16      | 0.0376 0.0012  | 0.061 0.014    | 0.0032 0.0008  | 0.0026 0.0004  |
| $2.74 \times 10^8$ CD-1                | 0.12 0.02      | 1.4 0.3       | 3.4 0.5        | 0.81 0.12     | 0.39 0.07      | 0.42 0.09      | 0.052 0.011    | 0.041 0.009   | 0.12 0.03      | 0.0081 0.0016  | 0.089 0.017    | 0.0036 0.0007  | 0.0023 0.0006  |

Table 2. Doses of internal irradiation and corresponding standard deviations (D ± SD), Gy, in organs resulted from exposure to $8 \times 10^8$ Bq activity of sprayed neutron activated $^{56}$MnO$_2$ powder among different strains of 10 week old mice

| Activity of $^{56}$Mn, Bq, and strains | Dose (D ± SD), Gy, in investigated organs |
|---------------------------------------|------------------------------------------|
|                                       | Lungs                               | Small intestine          | Large intestine | Stomach | Whole body | Skin         | Esophagus   | Trachea | Eyes | Liver | Heart | Spleen | Kidney |
|                                       | D  SD          | D  SD          | D  SD          | D  SD          | D  SD          | D  SD          | D  SD          | D  SD          | D  SD          | D  SD          | D  SD          | D  SD          |
| $8.0 \times 10^8$ C57Bl               | 0.25 0.05      | 2.3 0.2       | 10.1 1.4      | 2.4 0.5       | 0.97 0.22      | 0.96 0.21      | 0.29 0.05      | 0.14 0.06      | 0.39 0.08     | 0.023 0.002    | 0.12 0.02      | 0.006 0.001    | 0.007 0.002    |
| $8.0 \times 10^8$ C57Bl               | 0.34 0.07      | 2.8 0.4       | 11 2.1        | 2.2 0.3       | 1.01 0.21      | 0.16 0.17      | 0.24 0.04      | 0.16 0.04      | 0.32 0.07     | 0.022 0.004    | 0.18 0.04      | 0.008 0.002    | 0.006 0.002    |
| $8.0 \times 10^8$ BALB/C              | 0.38 0.07      | 2.4 0.4       | 9.5 2.1       | 3.2 0.5       | 1.02 0.3       | 0.23 0.04      | 0.13 0.03      | 0.34 0.07      | 0.024 0.005   | 0.15 0.04      | 0.007 0.002    | 0.007 0.002    |
activity of $^{56}$Mn dioxide powder are not statistically different in different strains of mice. A similar picture takes place under irradiation to $8 \times 10^8$ Bq activity (Table 2). This means that the distribution of the radioactive powder in the body of mice of different strains but of the same age was practically the same in case of exposure to the same activity of $^{56}$MnO$_2$ powder.

Figures 10–12 show the values of internal radiation dose in various groups of mice’s organs, versus the initial activity of sprayed neutron-activated $^{56}$Mn dioxide powder activity.

Figures 10–12 show, that similar to rats, there are three groups of organs of mice, the radiation dose of which differ by approximately an order of magnitude: the group with the highest radiation dose (large intestine, small intestine, stomach, skin, lungs), the group with lowered radiation dose (eyes, esophagus, trachea), group with the lowest radiation dose (heart, liver, kidneys). As in the case of rats, the values of the radiation dose to organs of mice are proportional to the activity of the dispersed radioactive powder.

**DISCUSSION**

Elevated doses of radiation to the lungs and trachea in both types of experimental animals (rats and mice) are fairly obvious. This can be explained by inhalation of a finely dispersed radioactive $^{56}$Mn dioxide powder. High levels of irradiation of the large and small intestines, stomach, and elevated irradiation of esophagus are associated with the characteristics of animal behavior: experimental animals (rats and mice) are swallowing radioactive powder in the process of their typical behavior, which consists in the cleaning of hair, which leads to increased irradiation of gastrointestinal tract. Elevated irradiation of skin is most likely due to the deposition of powder on animal’s hair.

Comparison of the data presented in Figs 7–9 and Figs 10–12 show that with the exposure to the same initial activity of sprayed $^{56}$MnO$_2$ powder, doses of internal irradiation of experimental mice substantially exceed the doses of internal irradiation of experimental rats. This is explained by the fact that for the beta-gamma radiation spectra of $^{56}$Mn, the values of the SAFs for the organs of mice (Figs 10–12) substantially exceed those for the organs of rats (Figs 7–9).

**CONCLUSION**

There are three groups of organs of mice and rats, the radiation doses of which differ by approximately an order of magnitude: the group with the highest radiation doses (large intestine, small intestine, stomach, skin, lungs), the group with lowered radiation doses (eyes, esophagus, trachea) and the group with the lowest radiation doses (heart, liver, kidneys). The radiation doses to organs are proportional to the activity
of the sprayed radioactive powder. The distribution of internal irradiation doses among organs of experimental animals of different strains but of the same age was practically the same in case of exposure to the same activity of 56MnO2 powder. Doses of internal irradiation of experimental mice substantially exceed the doses of internal irradiation of experimental rats exposed to the same activities of sprayed 56MnO2 powder.

Data related to the features of internal irradiation of organs and tissues of experimental animals after exposure to sprayed radioactive microparticles are useful for further studies and interpretation of the biological effects of this type of irradiation [13–16,18–21]. One of the important matters of further studies is investigation of the features of internal irradiation at the microstructures of organs and tissues of experimental animals exposed to radioactive microparticles. This is a separate matter, which is discussed in the publications [17,29].

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CONFLICT OF INTEREST
The authors declare that they have no conflicts of interest.

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