DEVELOPMENT OF A 3-D-PRINTED MOUSE PHANTOM TO REPLACE CURRENT MOUSE ANIMAL MODEL

by

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Evaluating the radiation dose of target organs of a laboratory mouse requires a glass dosimeter to be surgically inserted at the irradiated location. However, precisely inserting the glass dosimeter at the same location in different mice is rarely achieved, reducing the reliability of the measured radiation dose. To address this limitation, 3-D mouse phantom was developed using computed tomography scanning and 3-D printing technology. The radiation dose of target organs was assessed using four mouse models: laboratory mouse, 3-D mouse phantom, Monte Carlo N-Particle (MCNP) 3-D phantom, and MCNP simulation. In all the experiments, the brain, heart, lungs, and abdomen were irradiated with 100 mGy of measured air kerma at a 6 mGyh^{-1} air kerma rate. A small volume glass dosimeter was inserted into the mouse models to assess the radiation dose, and the reliability of the glass dosimeter reading system was evaluated using the dose-response curves. The dose values of the laboratory mouse and 3-D-printed mouse phantom were found to differ by up to 3.3 %. This study provides a method to accurately measure the radiation dose to target organs, enhancing the reliability of pre-experiments.

Key words: standard irradiation, glass dosimetry, 3-D mouse phantom, Monte Carlo simulation

INTRODUCTION

Owing to the recent increase in the utilization of 3-D printers, research on the use of output materials and products is being increasingly conducted in the medical field. Although many studies employ 3-D- printed mice, no research has been found on radiation dose evaluation of target organs in mice with a non-breakable traceability retrospective assessment chain. In this study, a realistic 3-D mouse phantom was created using computed tomography (CT) scanning and 3-D printing techniques [1-3]. The CT was used to capture the internal organs of the laboratory mouse to produce the 3-D phantom [4-7]. The 3-D mouse phantom was 3-D printed using acrylonitrile butadiene styrene (ABS), a material that is actively used as a tissue equivalent. The radiation dose of target organs was assessed using four mouse models: laboratory mouse, 3-D mouse phantom, Monte Carlo N-particle (MCNP) 3-D phantom, and MCNP simulation. Experiments were performed at the Dongnam Institute of Radiological and Medical Sciences (DIRAMS), an internationally accredited calibration and testing laboratory that belongs to the Korea Laboratory Accreditation Scheme (KOLAS). The absorbed radiation dose of the four mouse models was evaluated using the traceability of the calibrated ion chamber at the Korea Research Institute of Standards and Science (KRISS). A total of 100 mGy was irradiated using a ^{137}Cs gamma radiation field at a biologically low dose rate of 6 mGyh^{-1} to evaluate the dose irradiated inside the mouse models with a radio photo-luminescent (RPL) glass dosimeter and reading system [8-10]. The radiation dose in target organs was assessed and compared in the 3-D mouse phantom, MCNP 3-D phantom, MCNP simulation, and laboratory mouse.

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MATERIALS AND METHODS

This study conducted dose assessments of internal organs on four mouse models: laboratory mouse, 3-D mouse phantom, MCNP 3-D phantom, and MCNP simulation. The target organs for dose evaluation were the brain, heart, lungs (left and right), and abdomen, as well as organs that can confirm the effect of radiation attenuation in tissues. The laboratory mouse was dissected, and glass dosimeters were inserted into each target organ locations for irradiated dose assessments by gamma radiation which was emitted at 662 keV from ^{137}Cs source of each target organ.

To produce the 3-D mouse phantom, a 25.15 g laboratory mouse was CT scanned (Light SpeedTMRT16, GE Healthcare) in the T-B direction at 1.25 mm, P-A, and L-R direction at 2.5 mm intervals of a 512 matrix. Using the MIMICS software, a software used for 3-D printing, the captured DICOM images were bound by contour differences in the total body, brain, heart, lungs (left and right), and abdomen and were transformed into an STL output file statement [11]. A CT reader expert manually distinguished each mouse organ from the DICOM file. Each organ was made with a cylinder-shaped hole (0.3 mm in diameter and 9.7 mm long) to insert a glass dosimeter (GD-301, Asahi Techno Glass) for dose assessment in the STL file, as shown in fig. 1. For the lung, a 0.3 gcm^{-3} volume was applied by physically creating an internal space for density in the 3-D printing process. When a glass dosimeter was inserted, its volume occupied the entire internal lung space, therefore, the effect of lung density was negligible in assessing the radiation dose. The 3-D printed mouse phantom was assembled for glass dosimeter insertion, and a cross section was made at a perpendicular in the beam direction from the centre of glass dosimeter position.

The 3-D phantom was made using ABS material with a density of 1.05 gcm^{-3}, a tensile strength of 50 MPa, and a multi-body output via the poly-jet method [8]. For comparison, a linear algebra-based mouse was simulated using MCNP 6.2, and a MCNP 3-D phantom was produced using a 3-D printer as shown in fig. 2 [12]. The purpose of dose assessment by a linear algebra-based mouse

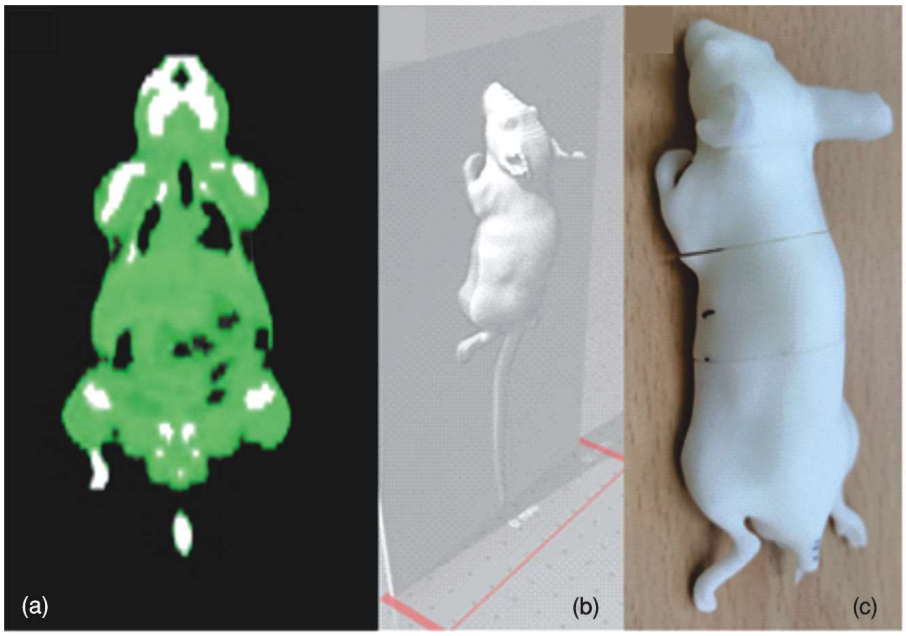

Figure 1. The CT scan of a laboratory mouse (a), STL file for 3-D printing (b), and 3-D mouse phantom (c)

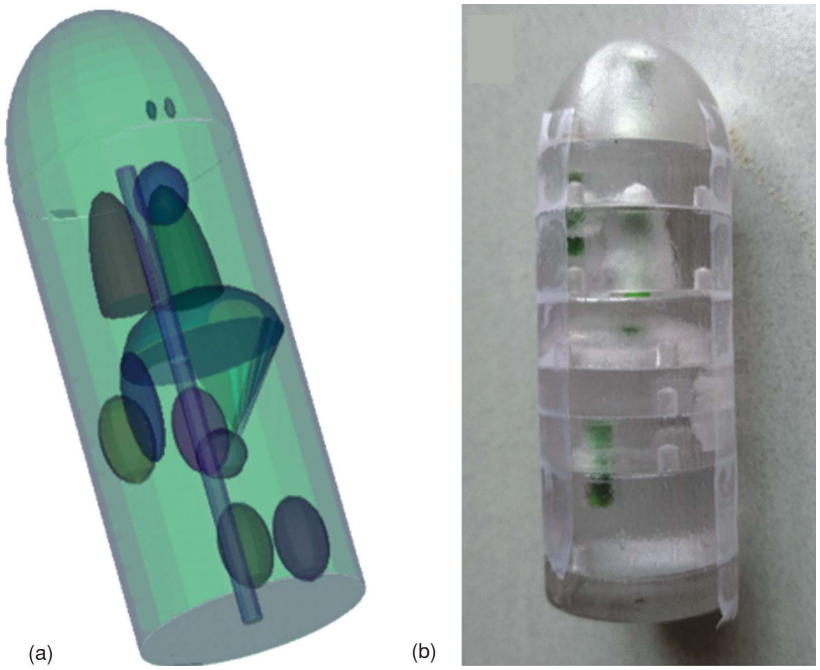

Figure 2. Geometric shape of linear algebra- based MCNP simulation (a) and MCNP 3-D phantom (b)

phantom is to secure the reliability of the computational simulation data by comparing the measurement results and simulation results. A MCNP 3-D phantom of linear algebra is a phantom that can represent mice of different size. The MCNP 3-D phantom was also prefabricated, likewise the 3-D mouse phantom.

A hole was built inside the 3-D mouse phantom to evaluate the radiation dose, such that two glass dosimeters on both sides of the spine could be mounted based on CT images. The small cylindrical glass dosimeter inserted into the phantom was a silvery active phosphate comprising P (31.55 %), O (51.16 %), Al (6.12 %), Na (11.0 %), and Ag (0.17 %). It was 1.5 mm wide and 8.5 mm long. Glass dosimeters with response stability, compact size, and readability are widely used in field of gamma dose assessment as passive detectors. The glass dosimeter, which was irradiated, underwent 30 minutes of pre-processing at 70 °C. The radiation dose was evaluated using a reader (FGD-1000SE, Asahi Techno Glass) with a holder size 2.8 mm wide and 9.5 mm long. The glass dosimetry system was calibrated by producing a dose-response curve using a glass dosimeter that maintains traceability that was standard gamma irradiation at 6 mGy and 2 Gy by ^{137}Cs source at KRISS.

It is important not only to accurately read the glass dosimetry system, but also to preserve the reliability of the measurement of the gamma dose rate to irradiate the phantom during the experiment. To retain the reliability of the irradiation dose rate, a radiation detection system that maintains traceability was used and compared with the results of MCNP simulation.

A standard calibrated EXRADIN ion chamber (A3, Standard Imaging) with traceability from the KRISS was used to evaluate the air kerma rate from the ^{137}Cs irradiator source (370 GBq, Chiyoda Technol. Corp.) to the detection positions at 1-5 m. Low-dose irradiation was performed with a total irradiation dose of 100 mGy at a rate of 6 mGyh^{-1} at 2 m from the ^{137}Cs source [8, 9]. Low-dose irradiation of the 3-D mouse

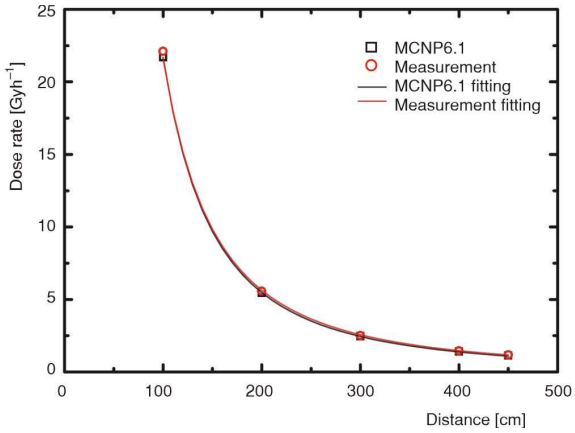

Figure 3. Irradiation dose assessment using an ion chamber with traceability and MCNP simulation

phantom was also conducted after dose evaluation of the photon irradiation devices using a standard calibrated A3 ion chamber [13-15]. The dose rate, according to the distance from the irradiator to the detection position, was evaluated by experimental results and MCNP simulation, as shown in fig. 3 [8, 9].

Figure 4 illustrates the experimental set-up for the irradiation experiments. The radiation direction of the laboratory mouse, 3-D mouse phantom, MCNP 3-D phantom, and MCNP simulation samples was P-A with positioning on a circular arc-shaped mouse-apartment system. The system built in the DIRAMS is designed to irradiate an uniform dose for each position. The distance from the source to the heart of the mouse models was 2 m. The MNCP simulation was set up for each irradiation experiment in ABS plastic cases that had a length, width, height, and thickness of 13, 12, 14, and 0.3 cm, respectively [16].

The laboratory mouse was dissected under the same conditions as the 3-D mouse phantom and MCNP 3-D phantom, and glass dosimeters were inserted into the target organs. After completion of gamma irradiation of a total of 100 mGy, the dose of the glass dosimeter was evaluated by own glass dosimetry system.

Figure 4. Experimental set-up for irradiation of laboratory mouse (a), MCNP 3-D phantom (b), and 3-D mouse phantom (c)

RESULTS AND DISCUSSION

In this study, a 3-D mouse phantom was created from a laboratory mouse using CT scanning and 3-D printing technology to evaluate radiation dose measurements of target organs. The radiation dose and uncertainty of the ^{137}Cs radiation units, measured at a distance of 2 m from the source and radiation point, were 6.49 mGyh^{-1} and 3.1 % (approximately 95 % confidence levels and $k = 2$), respectively, and the total radiation dose at the radiation point was 100 mGy [13, 14]. The extended uncertainties of the irradiation dose included measurement uncertainty of the ion chamber, electrometer, thermometer, barometer, beam uniformity and reproducibility of detector location. Table 1 shows the dose reading results of the laboratory mouse, 3-D mouse phantom, MCNP 3-D phantom, and MCNP simulation after the completion of the 100 mGy irradiation.

Because there was measurement uncertainty in all the experiments, the measurement uncertainty was evaluated more accurately in the glass dosimetry system using a small-volume element. In addition to the uncertainty of the ^{137}Cs radiation units, the elements of relative measurement uncertainty, based on the uncertainties of the dose measurement detector system, included uncertainty of the ion-chamber, ionization ammeter, barometer, thermometer, beam homogeneity, ion recombination, interpolation function, and position repeatability. Additionally, the uncertainty of the glass dosimetry system included the standard irradiation of glass dosimeters, reading repeatability, and the interpolation function of the dose-response curves [13, 14, 17, 18]. The relative combined uncertainty of the experimental dosimetry system was 6.2 % (approximately 95 % confidence levels and $k = 2$). All relative extended uncertainties are equal because of the uncertainty of the dose detector system and standard irradiated glass dosimeters with traceability. We obtained the radiation dose using the MCNP code with a relative error, directly obtained from the code, of less than 1 % [7].

Table 1 shows the dose assessment results for the laboratory mouse, 3-D mouse phantom, MCNP phantom, and MCNP simulation. A mouse apartment radiation system delivered a dose of 100 mGy to the heart position, and the tissue inside the mouse attenuated the photon. Therefore, the radiation dose that penetrated the heart was evaluated to be lower than 100 mGy. The brain, which was closer to the radiation source, received a radiation dose higher than 100 mGy. The abdomen, which required the radiation to penetrate deeper into the mouse, received a radiation dose of less than 100 mGy owing to radiation attenuation. Each assessed dose of the target organ was within uncertainty. The most uncertainty was the uncertainty of the measuring equipment and the uncertainty of the standard irradiated glass dosimeter.

Table 1. Results of the dose assessment of the inserted glass dosimeter in each target organ

Mouse model	Irradiated dose [mGy]				
	Brain	Heart	Lung (left)	Lung (right)	Abdominal
Laboratory mouse	108.5	89.7	94.9	92.5	83.6
3-D mouse phantom	106.5	90.2	95.9	95.7	86.0
MCNP 3-D phantom	108.8	93.6	96.5	99.1	81.9
MCNP simulation	106.0	92.5	96.9	97.5	87.9

In all dose assessment cases, the distance between the radiation source and heart position was set to 2 m, and 100 mGy was irradiated from this distance. The linear algebra-MCNP phantom shows a slightly higher dose value in the lungs, and the MCNP simulation shows a slightly higher dose value in the abdominal cavity. These differences are caused by the different geometric structures of the laboratory mouse, 3-D mouse phantom, MCNP 3-D phantom, and MCNP simulation.

The dose assessment results for each mouse model are shown in fig. 5. The results of all mouse models show a measured dose value higher than 100 mGy in the brain, where the distance between the radiation source and target organ was closer than the reference position, and the measured dose value, in all mouse models, decreased toward the abdominal cavity. In the case of the heart organ, it was wrapped in the lungs, which tended to be lower than the dose evaluated in the lungs.

CONCLUSSION

This study aimed to accurately measure the radiation doses that reach target organs-a process that is essential for ensuring the reliability of pre-experiments, which are required before evaluating the biological effects of radiation. The results from the laboratory mouse, 3-D mouse phantom, MCNP 3-D phantom, and MCNP simu-

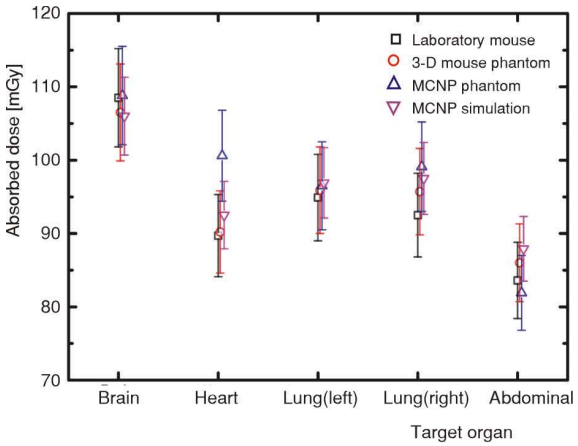

Figure 5. Comparison of dose assessment for laboratory mouse, 3-D mouse phantom, MCNP 3-D phantom, and MCNP simulation at center position

lation show that dose values higher than 100 mGy were measured in the brain, where the distance between the radiation source and target organ was closer than the reference position. The dose value decreased toward the abdomen in all cases. The uncertainties of final dosimetry include the dose detection system and dosimetry system. The measured dose evaluation values in the target organs of the laboratory mouse and 3-D mouse phantom differed by up to 3 %. Moreover, the measured dose values of a 3-D mouse phantom are within the measurement uncertainty for each target organ. This shows that the laboratory mouse may be replaced with the 3-D mouse phantom for dose evaluation of target organs in advance or in real-time. However, the 3-D mouse phantom does not reflect the movement of a living laboratory mouse. In the future, the movement of living laboratory mice will be evaluated and applied to dose assessment using a 3-D mouse phantom. Furthermore, in the future, the MCNP simulation will be directly compared with the manufactured 3-D mouse phantom using the DICOM file obtained through CT scanning. The MCNP simulations and phantoms in this study were representative of mice, but geometric simulations of detailed organs were not possible. Therefore, the geometry of linear algebra-based phantoms needs to be improved to voxel-based phantoms, and studies of MCNP representative phantoms development are also required for direct comparison with 3-D printed phantoms.

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AUTHORS' CONTRIBUTIONS

The idea for this study was initiated by Y.-R. Kang, W. S. Jo, C. G. Lee, and Y. U. Kye. Experiments, data collection, and statistical analysis were carried out by M. J. Bae, H. J. Jang, S. Mok, Y. U. Kye, H. J. Kim, and J. E. Lee. Y.-R. Kang supervised presented research and helped with its development that resulted in this paper. All the authors participated in the discussion of the presented results.

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РАЗВОЈ 3-D ШТАМПАНОГ ФАНТОМА МИША КАО ЗАМЕНЕ ЗА САДАШЊИ ЖИВОТИЊСКИ МОДЕЛ МИША

Процена дозе зрачења циљаних органа лабораторијског миша захтева да се стаклени дозиметар хируршки убаци на озрачено место. Међутим, прецизно уметање стакленог дозиметра на исту локацију код различитих мишева ретко се постиже, смањујући поузданост измерене дозе зрачења. Да би се решило ово ограничење, развијен је 3-D фантом миша коришћењем CT скенирања и технологије 3-D штампања. Доза зрачења циљаних органа процењена је коришћењем четири модела миша: лабораторијског миша, 3-D фантома миша, MCNP 3-D фантома и MCNP симулације. У свим експериментима, мозак, срце, плућа и абдомен зрачени су са 100 mGy измерене керме у ваздуху при јачини керме од 6 $mGyh^{-1}$. Стаклени дозиметар мале запремине убачен је у моделе миша да би се проценила доза зрачења, а поузданост система за очитавање стакленог дозиметра процењена је коришћењем криве доза-одзив. Утврђено је да се вредности дозе лабораторијског миша и 3-D штампаног фантома миша разликују до 3.3 %. Овај рад обезбеђује методу за прецизно мерење дозе зрачења на циљане органе, повећавајући поузданост припреме експеримената.

Кључне речи: стандардно озрачивање, дозиметрија са стаклом, 3-D фантом миша, Монте Карло симулација