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Development and characterization of a novel variable low-dose rate irradiator for in vivo mouse studies

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Abstract

Radiation exposure of humans generally results in low doses delivered at low dose-rate. Our limited knowledge of the biological effects of low dose radiation is mainly based on data from the atomic bomb long-term survivor study (LSS) cohort. However, the total doses and dose-rates in the LSS cohort are still higher than most environmental and occupational exposures in humans. Importantly, the dose-rate is a critical determinant of health risks stemming from radiation exposure. Understanding the shape of the dose-rate response curve for different biological outcomes is thus crucial for projecting the biological hazard from radiation in different environmental and man-made conditions. A significant barrier to performing low dose-rate studies is the difficulty in creating radiation source configurations compatible with long-term cellular or animal experiments. In this study the design and characterization of a large area, ¹²⁵I-based irradiator is described. The irradiator allows continuous long-term exposure of mice at variable dose-rates and can be sited in standard animal care facilities. The dose-rate is determined by the level of ¹²⁵I activity added to a large NaOH filled, rectangular phantom. The desired dose rate is maintained at essentially constant levels by weekly additions of ¹²⁵I to compensate for decay. Dosimetry results for long-term animal irradiation at targeted dose rates of 0.00021 and 0.0021 cGy min⁻¹ are presented.

INTRODUCTION

It has long been recognized that the biological consequences of irradiation depend not just on the dose delivered, but also on the rate of dose delivery. The magnitude of the dose-rate effect (DRE) can be very large. For instance, Bedford and Mitchell (Bedford and Mitchell 1973) report that for Chinese hamster ovary cells, toxicity is reduced by several orders of magnitude as the dose rate is lowered from roughly 106.7 cGy min⁻¹ to 0.04 cGy min⁻¹. Therefore, the effect of dose-rate on biological outcomes is taken into consideration when acutely generated radiobiological data are used to estimate biological effects of the same dose delivered chronically (BEIR 2006, Tubiana et al. 2006).

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Although there is a deep literature on the effects of high dose acutely delivered irradiation, much less is known about the effects of low dose-rate radiation. Interestingly, as the experimental dose-rate is lowered further and further, some investigators report an inverse dose-rate effect. The inverse dose-rate effect describes the observation that the magnitude of a biological response below a certain dose rate begins to increase as the dose-rate is further decreased (Rothkamm and Löbrich 2003, Sakai et al. 2003). Vilenchik and Knudson have analyzed published data dealing with several biological endpoints and find a range of dose-rates through which a minimum in radiation response is observed (Vilenchik and Knudson 2000). A parabolic response for several endpoints can be fit as a function of dose-rate. These endpoints include cell death, chromosomal translocations, human leukemogenesis and mutation (Vilenchik and Knudson 2000). The response curves tend to show a minimum in the dose-rate interval $0.03 - 1.0 \text{ cGy min}^{-1}$ ($1.8 - 60 \text{ cGy h}^{-1}$), the response being greater at both higher and lower dose-rates (Vilenchik and Knudson 2000). Remarkably, the dose-rate interval found to correlate with the least biological harm is approximately 10^5 times larger than the average background radiation dose rate in the US and 10^4 times larger than the background levels in high radiation areas of the world (Schauer and Linton 2009). This raises the questions as to why these biological systems might be responding most favorably at dose-rates so much greater than the largest dose-rates encountered in natural environments. Experimental evaluation of this incongruity is clearly warranted.

Understanding the shape of the dose-rate response curve for different biological outcomes is crucial for projecting the magnitude of radiological hazard stemming from different environmental and man-made conditions. A significant barrier to performing low dose-rate studies with low LET radiation is the difficulty in creating radiation source configurations compatible with long-term cellular or animal experiments. In this study the design and characterization of a large area, isotope-based irradiator capable of being sited in standard animal care facilities is described. The irradiator consists of three liquid-filled rectangular containers into which ^{125}I is added. The energy of the ^{125}I photons is high enough to ensure reasonably uniform penetration through mice housed in cages positioned directly above the irradiator, yet low enough that shielding is straightforward and minimal additional safety precautions are needed for the protection of animal care personnel. The details of irradiator construction, radiation dosimetry and practical use are reported.

MATERIALS AND METHODS

Irradiator

Nuclear Medicine flood phantoms (Biodex Medical Systems, Shirley, NY) are $71 \text{ cm} \times 52 \text{ cm} \times 3.2 \text{ cm}$ and are filled with 3.3 l 0.01 M NaOH into which varying activities of ^{125}I are added to achieve and maintain the desired dose-rate. Each phantom is placed in a custom-made aluminum tray ($59 \times 79 \times 8 \text{ cm}$), large enough to contain the entire 3.3 l of radioactive liquid in the event of phantom leakage. The aluminum tray containing the phantom is placed on a commercially-available wheeled plastic cart (Newell Rubbermaid Inc, Freeport, IL). Shielding consists of 5 mm lead sheets placed on the bottom and sides of the phantom to limit radiation exposure in all directions other than the top. A 5 mm thick PVC sheet with custom-made handles is placed under the lead-lined phantom to assist in lifting the phantom during addition of the radioisotope.

The plastic carts holding each phantom in its aluminum tray are designed to remain in place during all animal care work. Animals in cages are placed on a second moveable cart, which can be positioned so that the animals are directly above the source phantoms (Fig. 1a). This second cart is custom-built from 1.3 cm thick steel pipes with a surface made from 5 mm thick plexan to minimize photon attenuation between the source and the mice. The steel cart is fitted with wheels so that it can be easily pulled away from the radioactive source for

routine animal care procedures. At the end of animal husbandry, the steel cart is wheeled back into position according to positioning marks located on the room walls and on both carts, thus placing the animals inside the exposure area. A leaded acrylic shield (Atlantic Nuclear, Canton, MA) is suspended from the handle of the steel cart (Fig. 1b) providing both shielding of personnel and visual access to the animals.

Radiation source

Activity levels necessary to generate a given dose-rate at the mouse position were determined via radiation transport calculations using the Monte Carlo N Particle (MCNPX) code (Los Alamos, NM). The simulation model included the water-filled rectangular phantom, the 5 mm plexan surface of the steel cart and a 3.2 mm polymethylmethacrylate (PMMA) cage (Fig. 2a). Energy deposition was estimated in an 8 cm long, 2 cm diameter, tissue-equivalent cylinder representing a mouse. The mouse cylinder is positioned 1 cm above the cage bottom. Source photons were sampled from the ^{125}I spectrum (Firestone et al. 1999) and from locations evenly distributed inside the rectangular phantom. Energy deposition in the mouse, per starting photon, was converted to activity assuming 1.47 photons decay $^{-1}$ (NIST 2009).

^{125}I was purchased as solution in 0.1 ml 0.01M NaOH (MP Biomedicals, Irvine, CA). Given its 59.4 day half-life, regular additions of ^{125}I must be made to the phantom (8.5% week $^{-1}$) in order to maintain a constant dose-rate at the animal position for the duration of the experiment. Once each week a custom made lead sheet is placed over the top of the phantom (covering the only unshielded area) and the plastic cart holding each source is wheeled over to a radiochemical hood. The aluminum tray containing the phantom is placed in the hood. One edge is lifted and a wedge placed under the phantom (Fig. 1d) for easy supplementation of the isotope through a fill hole using a pipetman. Uniform mixing, by alternating lifts of each end of the phantom, was initially confirmed using dye.

Radiation safety

Area monitors are wall mounted and read monthly. Weekly surveys of ^{125}I contamination were performed by swipe test by the MIT Radiation Protection Office. Because iodine is a volatile radioisotope, iodine supplementation is performed in a radiochemical fume hood and a sodium-iodide meter is on site for immediate radiation exposure survey. Monthly thyroid scanning of ^{125}I handling personnel is performed using a thin crystal Scintillator NaI (TI) (Canberra Industries Inc, Meriden, CT) and Genie 2000 V3.0a software (Canberra Industries Inc, Meriden, CT).

Surface dose-rate

The photon dose-rate at the surface of the irradiator was measured using aluminum oxide (Al_2O_3) detectors in an optical stimulated luminescent (OSL) dosimetry system (Landauer Inc., Glenwood, IL) used for routine whole body radiation protection monitoring. These dosimeters consist of four individual Al_2O_3 ‘chips’, each of which is covered by a different absorber material. Comparison of the relative output from each of the differently-shielded chips with calibration data acquired from various pre-stored source spectra allows Landauer to convert the chip readings to an estimate of “surface dose” and “deep dose” (dose at a tissue depth of 1 cm), based on the radiation type that is predicted from the best fit when comparing the measured readings to the stored spectra from various sources.

Dosimeters were positioned on the plexan surface of each phantom and kept in position with velcro strips (Fig. 2b). Dosimeters were changed once weekly and sent to Landauer for analysis of radiation dose recordings. The dose-rate per cart was calculated by averaging weekly readings of all dosimeters per cart (Fig. 2c).

Dose-rate estimates at various depths within the mice

The dose-rate as a function of depth through a mouse located in cages placed above the source was examined in three ways. First, the MCNPX model described above was used to model energy deposition as a function of depth in the 2 cm diameter cylindrical mouse model (Fig. 2a). Second, the ratio of shallow and deep dose (1 cm depth) was estimated using OSL dosimeters provided by Landauer (Fig. 3a). Third, dose-rate as a function of depth within mice was measured using OSL chips (“Microdots”, Landauer Inc., Glenwood, IL) (Fig. 3c and 3d). For the in situ evaluation, three mice were humanely euthanized just prior to the experiment and six microdot dosimeters were implanted into each mouse. Dosimeters were removed from their plastic holders prior to placement in sacrificed animals, and after exposure the microdots were explanted, cleaned, returned to their plastic holders, and read using a desktop reader containing a light-emitting diode (“MicroStar”, Landauer Inc., Glenwood, IL).

RESULTS

Irradiator design

The primary objective of this work was to create an exposure apparatus that achieves constant and even irradiation for several mouse cages. ^{125}I was elected as the source of radiation because of its reasonably long half life and relatively low energy, which makes it possible to readily shield personnel from exposure (see below). To create a fairly uniform exposure across a large area, Nuclear Medicine flood phantoms were used; these phantoms are designed to safely contain radioactive liquid in a large area, shallow depth configuration. With this approach, a variable dose-rate irradiator system was created, in which these rectangular Nuclear Medicine flood phantoms are placed on a lower cart, with mouse cages placed above in a double cart configuration (Fig. 1a). The surface area of each flood phantom is sufficient for even irradiation of four mouse cages placed on the plexan shelf above. With three such irradiators and five mice per cage, a total of 60 animals can be irradiated simultaneously (Fig. 1b). The total production cost for one phantom, including material cost for carts and shielding as well as labor is approximately USD 1600. Once the irradiator is in place, the per diem isotope-cost per mouse depends on the dose-rate, but is 40 and 80 cents for dose-rates at $0.00021 \text{ cGy min}^{-1}$ and $0.0021 \text{ cGy min}^{-1}$, respectively.

Radiation safety

One of the most important aspects of the design of the irradiator is to create a configuration that provides relatively simple procedures for animal husbandry, while assuring safety for personnel who interact with the animals. In terms of husbandry, use of the large-area irradiators for long-term experimental use requires little additional training of animal care or veterinary personnel. The only difference to regular animal husbandry is that the animals are simply wheeled away from the phantom so that animal handling can be performed several feet away from the radiation source. Once pulled away from the phantom, animal husbandry is performed as usual. At the end of husbandry, the steel cart is repositioned in its original location (making use of positioning marks) over the radioactive source (Fig. 1b).

To reduce exposure to personnel, the flood phantoms are wrapped in lead sheets on all sides except the top. To reduce upper body exposure of personnel, a leaded acrylic shield is hung from the cart handle which, as can be seen in Fig. 1b, has been designed to accommodate a sufficiently large shield. The leaded acrylic shield blocks radiation while permitting safe viewing of the animals (without moving the cages away from the radioactive source), thus facilitating routine veterinary checks. With $462.5 \text{ MBq } ^{125}\text{I}$ in one phantom (for a targeted $0.00021 \text{ cGy min}^{-1}$ dose-rate to the mice; see below) and 4625 MBq in a second phantom (targeted dose-rate of $0.0021 \text{ cGy min}^{-1}$), the radiation exposure levels for personnel is

0.00083 cGy min⁻¹ when the animals are positioned above the source. When the cart is moved away from the source to perform animal husbandry, exposure to personnel is at background levels (0.00067 cGy min⁻¹). With these very low exposure rates, and given the short periods of time that personnel are located near the source, the dose to animal care personnel is substantially below levels of exposure for which extensive radiation training and body dosimetry are required.

In order to maintain a relatively constant dose rate, ¹²⁵I is supplemented each week. Due to its volatility, ¹²⁵I is handled in a radiochemical flow hood, which requires that the phantoms be moved from the carts to the hood. In addition to shielding that is constantly in place on all sides but the top of the phantom, additional lead shielding is placed on top of the phantom to reduce exposure during the supplementation procedure (see Materials and Methods).

All scientists and personnel handling ¹²⁵I are considered radiation workers and are equipped with OSL body and ring dosimeters worn during weekly isotope supplementation. However, with the lead sheet positioned on the top of the phantom, no radiation above background levels is detected at the personnel position. Similarly, thyroid radioactivity levels of experimenters were below the minimal detectable activity (~70 Bq) in 24 months of thyroid monitoring.

Uniformity of exposure and surface dosimetry

The variable low dose irradiator will be used to assess potential genotoxic effects of different very low dose-rates using an array of exquisitely sensitive methods to determine effects of ionizing radiation, such as changes in gene expression, chromosomal instability and DNA base damage. To initiate radiation dose-rate studies two very low dose-rates were chosen: 0.00021 cGy min⁻¹ and 0.0021 cGy min⁻¹, which are approximately equivalent to ~300X and 3000X background radiation levels. Monte Carlo estimates of absorbed dose in a tissue-equivalent cylindrical mouse predicted that 462.5 MBq ¹²⁵I in each phantom would deliver an absorbed dose of 0.00021 cGy min⁻¹ to a depth of 1 cm in the 2 cm diameter cylindrical mouse model and 4625 MBq would deliver an absorbed dose of 0.0021 cGy min⁻¹.

After filling the phantoms and adding the ¹²⁵I, careful dosimetry was performed to determine the actual dose-rate delivered at various positions above the source. Whole-body OSL dosimeters were positioned at the corners of each cage to determine the average dose delivered as well as the uniformity of exposure (Fig. 2b). We observed significant differences in the dose-rate depending on the position of the dosimeter, ranging from 0.00012 cGy min⁻¹ for a far corner and 0.00037 cGy min⁻¹ for a dosimeter placed in the middle of the phantom (Fig. 2b) at a targeted dose-rate of 0.00021 cGy min⁻¹. Nevertheless, the average dose-rate is 0.00017 cGy min⁻¹ ± 0.00002, consistent with Monte Carlo estimates. Importantly, given the symmetry of the phantom, all mice (one cage per quadrant above the phantom) are exposed to a similar radiation field. Although there is variation in the dose-rate across the bottom of the cage, it is expected that the dose-rate to the animals is more uniform because the mice spend time in different locations within the cage. Furthermore, cages are rotated each week in order to average out exposure in cases where animals prefer a certain position in the cage. The combination of mouse movement and cage rotation assures fairly consistent exposure, especially under conditions where animals are exposed for weeks or months.

Using the OSL dosimeters, radiation exposure is evaluated weekly. To estimate the dose-rate to the mice, weekly dose data from each of the nine dosimeters are averaged. Results obtained over a period of 42 weeks for an experiment designed to deliver an average dose-rate of 0.00021 cGy min⁻¹ and 0.0021 cGy min⁻¹ are shown in Fig. 2c. These data show

that exposure levels are maintained in a highly consistent fashion over a long period of time. In addition, the average dose delivered is consistent with the predicted dose-rate as determined by Monte Carlo simulation ($0.00017 \text{ cGy min}^{-1} \pm 0.00002$ and $0.0017 \text{ cGy min}^{-1} \pm 0.00021$, respectively).

Radiation penetration into mouse tissues

Although the mice irradiated with the variable dose-rate irradiators are only ~2 cm thick, the photons emitted by ^{125}I are low in energy and easily attenuated in tissue. It is therefore important to examine the dose delivered as a function of depth in the mouse. Accordingly, dose as a function of depth through a tissue-equivalent cylindrical volume (approximating a mouse) was modeled using MCNPX (Fig. 2a). In this model, the mouse was positioned in a cage on top of the irradiator and absorbed dose was estimated at various depths within the mouse. As can be seen from the plot shown in Fig. 3a, the dose at a depth of ~1.8 cm is estimated to be about half of the dose delivered to the surface of the animal. Also shown in Fig. 3a is the average “deep dose” estimated by Landauer using the whole body dosimeter data obtained from weekly irradiator dose measurements. The relative dose fall off with depth in the mouse as predicted by MCNPX calculation is approximately 70% of the surface dose. This is in excellent agreement with the Landauer estimate of dose at 1 cm.

To learn more about the actual dose delivered, six OSL Microdots were placed into each of several sacrificed mice. Dosimeters were placed subcutaneously, with two in the front and two in the back of the mouse. Two dosimeters were also placed inside the peritoneal cavity, at the sites of the pancreas and the spleen. Mice were placed on the bottom of the cage and the cage was positioned on the irradiator for three days prior to reading. The attenuation of the average dose rate at a depth of ~1.5 cm was remarkably close to that predicted by both Monte Carlo simulation and the OSL whole-body dosimeter readings (Fig. 3a). Analysis of specific regions showed that the dose rate delivered to the ventral side of the mouse was very close to the predicted dose rate of $0.00021 \text{ cGy min}^{-1}$ and $0.0021 \text{ cGy min}^{-1}$, whereas the dose-rate delivered to the dorsal side of the mouse was about 2-fold lower. The dose-rates measured at the position of the pancreas and the spleen showed intermediate values, as expected (Figures 3b and 3c). The uncertainty associated with the doses shown in Fig. 3b and 3c reflect the variation in surgical positioning and orienting the microdots within the mice. Taken together, these results show that the design of the irradiator successfully delivered the desired dose-rate close to the ventral surface of the mouse, and that attenuation causes ~40% reduction in the dose rate delivered to internal organs.

DISCUSSION

Radiation exposure of humans generally results in low doses delivered at low dose-rate. Our limited knowledge of the biological effects of low dose radiation is mainly based on data from the atomic bomb long-term survivor study (LSS) cohort. However, the total doses and dose-rates in the LSS cohort are still higher than most environmental and occupational exposures in humans (Preston et al. 2004). In addition, save tragic events such as the atomic bomb, it is impossible to design an epidemiological study that would address effects of very low dose and dose-rate exposures because the number of people that need to be included in the study to reach statistical significance is extremely high (Brenner et al. 2003). Therefore, experimental data in cells, and preferably in animals, are needed to determine radiobiological mechanisms and derive radioprotection guidelines from this knowledge. One obstacle to performing continuous low dose, low dose-rate radiation exposure studies is the need for a continuous low dose-rate irradiator.

For exposure of cells and/or animals to continuous low dose-rate radiation two general options exist: X-ray generators and radioisotopes. The main advantage of using an x-ray

generator for this purpose is that these devices can be temporarily turned off during access to the cells or animals thereby reducing radiation exposure to laboratory personnel. Disadvantages of using an x-ray tube include first, the potential problems created by round-the-clock operation leading to anode over-heating and second, the limited range of dose-rates that can be delivered with units typically encountered in radiobiology laboratories. A third disadvantage of standard x-ray machines is their incompatibility with use in a cell incubator. Most standard x-ray machines are too large for installation in even large cell incubators (although Evans et al describe results using an x-ray machine located in a walk-in incubator for low dose-rate studies (Evans et al. 1990)).

A more practical strategy is to make use of an isotope source. Isotope sources are “always on” so there is no concern regarding over-heating or malfunctioning of components from continual use. However, additional care must be taken when accessing cells or animals to minimize radiation exposure to personnel. The most common low-LET isotopic sources used are ^{60}Co (1.17 and 1.33 MeV photons) and ^{137}Cs (0.667 MeV photon). An important limitation of these sources is that the very penetrating nature of the radiations emitted requires specially shielded facilities or incubators. Several creative strategies for generating low dose rate irradiation conditions from ^{60}Co and ^{137}Cs have been deployed by various investigators. For instance, at the Gray Lab, cell-containing flasks are positioned within a water-filled glass tank which is then placed in front of a shielded 20 TBq ^{60}Co source (Mitchell et al. 2002). A similar strategy has been used by Ueno et al in Japan (Ueno et al. 1982). The water provides additional attenuation so that, depending on the position of the flask in the tank, the dose-rate received will vary. An interesting approach to irradiating animals was described by Howell et al. using mercury as attenuator for a ^{137}Cs source positioned on top of a radiation cabinet and animal cages placed on six shelves beneath the radiation source allowing simultaneous exposure of six mouse cages at different dose rates in a radiation cabinet (Howell et al. 1997). Another strategy, used primarily for animal studies, is to maintain an open source in a shielded facility with animal cages placed at various distances from the source. This strategy relies not on differential attenuation but on the $1/r^2$ fall-off in dose as a function of distance, r , from the source (Ullrich and Storer 1979, Sakai et al. 2003, Ishizaki et al. 2004, Tanaka et al. 2007). Wells and Bedford describe cell-irradiations using a ring of 12 ^{137}Cs sources positioned at the bottom of an incubator (Wells and Bedford 1983). Lead sheets are used to vary the dose-rate delivered to flasks on shelves above the ring.

Another advantage to use of an isotope source is the great flexibility in size and shape the apparatus can take. Collin et al use thorium-nitrate powder packed into bags and placed under animal cages (Collin et al. 2006). This provides dose-rates of 7 and 14 cGy y^{-1} . Yamamoto et al maintained mice on life-long tritiated water which allowed manipulation of the dose rate through variations of ^3H in the drinking water (Yamamoto et al. 1995, Yamamoto et al. 1998). Aird et al arranged a series of ^{125}I brachytherapy seeds under a cell culture dish (Aird et al. 2001). Partial rotation of the dish during cell irradiation led to dose uniformity at the cell position to within 23%. Given the 59.4 day half-life of ^{125}I the dose-rate at the cell position changed as a function of time, permitting investigation of the effects of a number of dose rates before the activity became too low. A similar strategy has been adopted by Elmore et al to examine the adaptive response following exposure to low dose-rate radiation (Elmore et al. 2008).

While the low photon energy of ^{125}I makes this isotope a good choice for straightforward radiation protection of personnel, the solid seed configuration and the short half-life limit the flexibility of experimental design since long-term studies of the effects of a constant dose-rate would not be possible. Use of a liquid ^{125}I source, as described in this work, overcomes this limitation and permits regular activity additions so that a targeted dose-rate can be

maintained indefinitely. Weekly ^{125}I supplementation leads to a dose-rate constant to within about 10% for several months, as shown in Fig. 2. It is noteworthy that in addition to their use for small animal studies, a modified version of the ^{125}I based irradiator would also be ideal for incubator-based cell irradiations using somewhat smaller-area phantoms.

Use of the isotope ^{125}I offers an additional advantage over strategies involving high-activity $^{137}\text{CsCl}$ -based irradiators in that ^{125}I , used in any practical amount in the configuration described here, will always remain a Category 5 radiation source (IAEA, 2005). On the other hand, the half-life, decay scheme, and physical form of $^{137}\text{CsCl}$ make large activities a security risk. High activity irradiators fall under IAEA Categories 1 and 2 and thus require strong measures for ensuring safety of the source; these measures add to the complexity, size, and cost of long-term low dose-rate experiments. While some of the Cs-based low dose-rate irradiations described above used lower activity sources, these would still be considered IAEA Category 3, leading to the requirement for controlled access to the source (IAEA, 1980).

^{125}I emits radiation at an energy level that can readily be shielded, and yet provides reasonable penetration. The low energy photons emitted by ^{125}I are easily shielded by thin sheets of lead or by leaded acrylic. However, these photons are still sufficiently penetrating through low Z material to deliver a fairly uniform dose distribution through the thickness of mice in cages located above the phantom. Importantly, the observed dose detected in the radiation set up presented in this study varies by about a factor of two throughout the thickness of a nine week old mouse.

CONCLUSION

The low dose-rate irradiator described here represents a simple and straightforward approach to generating continuous exposure conditions for large numbers of animals. There is considerable flexibility in targeted dose-rate which depends on the quantity of ^{125}I inserted into the phantom. This dose-rate can be maintained indefinitely, requiring only weekly additions of activity. Use of the irradiators requires no special facility since the ^{125}I photons are easily shielded. Similarly, no special training or monitoring of animal care workers is required given that animals can easily be moved away from the phantom source for animal husbandry. Thus, the system described here provides a highly feasible approach for long term low dose-rate studies in mice, facilitating studies of the effects of radiation exposure on molecular responses in vivo.

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Figure 1.

The variable low dose-rate irradiator consists of a plastic cart (PC), holding an aluminum tray (T) and flood phantom (P). The phantom is filled with radioactive liquid and serves as the radiation source. A steel cart (SC) holding the cages fits exactly above the plastic cart. A leaded acrylic sheet (A) mounted on the steel cart ensures radiation protection for experimenters and animal husbandry staff when handling the steel cart (a). When both carts are aligned according to the positioning marks (M), all animal cages are within the exposure area (b). The phantom (P) is encased in lead sheets (L) except for the top surface and placed on a phantom lifting device (LD) that allows easy lifting of the phantom during the weekly iodine supplementation (c). To supplement ^{125}I , the aluminum tray (T) and phantom are placed in a radiochemical fume hood, the phantom is lifted by handles of the lifting device (LD) and placed on a plastic wedge (W) to allow easy supplementation through a screw hole (arrow) using a pipetman (d).

Figure 2.

Using the MCNPX radiation transport code, energy deposition was calculated in a tissue equivalent cylinder (m) representing a mouse. The cylinder was positioned above a modeled cage bottom (b) and rectangular phantom (p) containing ^{125}I as radiation source (s). Blue indicates air (a). Nine LUXEL OSL dosimeters (arrowhead) were placed on the plexan surface above the phantom. Eight dosimeters are positioned along the edges of the exposure area and one is placed in the center (b). Dose-rates of 0.00021 min^{-1} and 0.0021 min^{-1} were calculated from the OSL dosimeters readings and kept constant over a period of 42 weeks (c).

Figure 3. MCNPX calculation of dose as a function of depth through the cylindrical mouse model with data normalized to the surface of the mouse (diamonds) and relative radiation dose measured by OSL dosimeters (square) (a). Dose-rates measured from microdot dosimeters implanted at the indicated positions within sacrificed mice at a targeted radiation source dose-rate of 0.00021 min^{-1} (b) and 0.0021 min^{-1} (c).