Technical note

Commissioning of the MultiRad 350 cell and small animal x-ray irradiation system

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ABSTRACT

Purpose: The main objective of this study was to commission a commercial x-ray irradiation system to be used for cell and small animal studies.
Materials and methods: Evaluated characteristics of an x-ray irradiator included dose linearity and dose repeatability with respect to time, x-ray beam profiles, light field to irradiation field agreement and absolute radiation dose. Radiochromic films, ionization chambers and radiophotoluminescence dosimeters were used for dosimetry and the maximum settings of the irradiator were applied.
Results: The dose was linear with time using several voltage settings and the dose repeatability with time was within 5% beyond 15 s of irradiation time. The x-ray beam profiles were acceptable, flatness being less than 4%. The light field to irradiation field agreement appeared to have a maximum difference of 0.5 cm; the irradiation field being closer to the irradiator's door than the light field.
Conclusions: The MultiRad 350 x-ray irradiation system can be used in a safe and controlled manner for irradiating cells and small animals. However, the user should be careful to verify the filter position prior the irradiation.

1. Introduction

Ionizing radiation is widely used for cell and small animal studies, e.g. in lowering mice's own immunity or to affect the cell growth [1]. Sealed radioactive sources are commonly used, but they require increased security measures and their use can be quite demanding [2]. Alternatives to radioisotope irradiators are self-shielded x-ray irradiators, which make it possible to perform cell and small animal irradiations in a safe and cost-effective manner [3–5].

There are no recommendations for the commissioning process of x-ray irradiators, and thus the aim here was to determine the beam characteristics, most importantly the dose delivery using absolute dosimetry methods. This study presents a commissioning process for the MultiRad 350 x-ray irradiation system, which is designed for irradiating biological objects, such as cells and small animals. To the best of our knowledge, this paper is the first to carry out research into the MultiRad 350 system. The study consists of four evaluated parts: dose linearity and dose repeatability with time, x-ray beam profiles, light field to irradiation field agreement and absolute radiation dose.

2. Materials and methods

2.1. MultiRad 350 x-ray irradiation system

The examinations of the present study were performed at the Institute of Biomedicine of Turku University (Turku, Finland). A fully-shielded, self-contained MultiRad 350 (Faxitron Bioptics, Tucson, AZ, USA) x-ray irradiation system (Fig. 1) uses metal ceramic x-ray tube capable of 350 kV maximum tube voltage (30–350 kV). Tube current can be changed between 0.1 and 30 mA, but for the maximum tube current of 350 kV it is fixed to 11.5 mA. The device has four different filters for beam hardening: 0.5 mm and 2.0 mm aluminum (Al), 0.3 mm copper (Cu) and a combination of tin-copper-aluminum (SnCuAl) filters. The last consists of 0.75 mm of Sn, 0.25 mm of Cu and 1.50 mm of Al. The MultiRad 350 has a motorized shelf as the specimen holder and it can be used to control the shelf-to-source distance in a range between 13 cm and 65 cm. The shelf has there is an integrated internal ionization chamber (IC) that can be used for dose control and daily QA check. In addition, the system is equipped with collimator jaws for limiting the x-ray beam size.

Fig. 1. Faxitron MultiRad 350 x-ray irradiation system. An adjustable rounded shelf is in the middle of hutch.
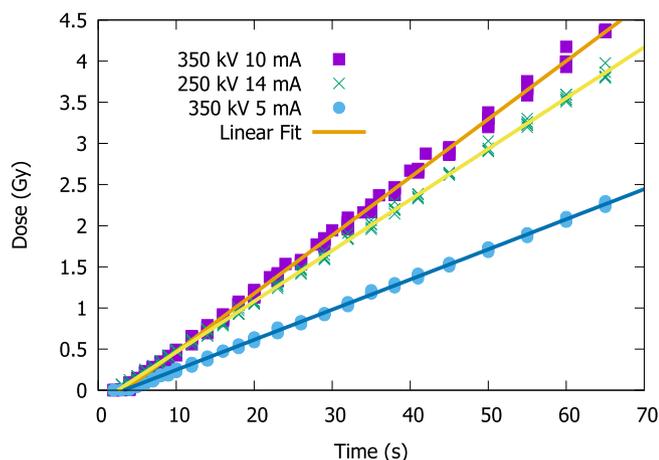

Fig. 2. Dose linearity of the x-ray beam with three setups: 350 kV and 10 mA, 250 kV and 14 mA, and 350 kV and 5 mA. Linear least squares fitting gives maximum deviation of 0.7% with respect to the measured points.
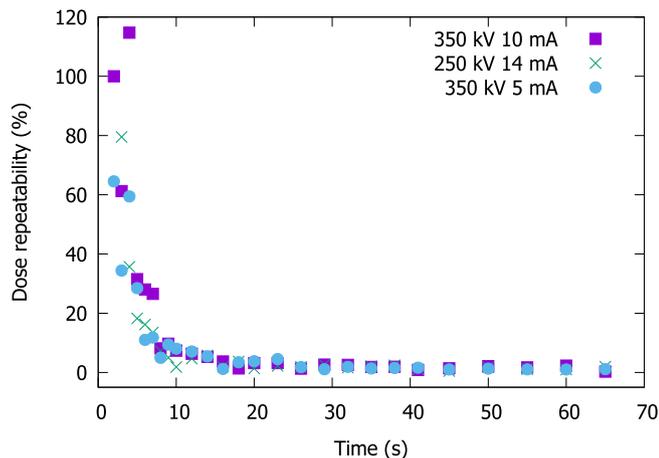

Fig. 3. Dose repeatability as a function of time with three different irradiation setups: 350 kV and 10 mA, 250 kV and 14 mA, and 350 kV and 5 mA. Worth noting is that the repeatability start to be constant after 15 s of irradiation.

2.2. Dose Ace GD-302M and GD-352M radiophotoluminescence dosimeters

One of the reasons for this study was to assess the use of a radio-photoluminescence (RPL) dosimetry system that was recently acquired by to the Department of Medical Physics at Turku University Hospital. RPL dosimeters, namely Dose Ace GD-302M and Dose Ace GD-352M (AGC Techno Glass Co., Shizuoka, Japan), were used; the only

difference being that the latter has a 1.0 mm tin filter in its capsule. The cylindrical RPL dosimeters are 1.5 mm in diameter and 12.0 mm in length. The effective atomic number of dosimeters is 12.04 and their density is 2.61 gm/cm^3 [6]. The GD-302 M can be operated at a dose range from 10 μGy to 100 Gy and the GD-352M from 10 μGy to 10 Gy. After irradiation and before reading, the dosimeters were pre-heated in an oven at 70 °C for half an hour. A glass dosimetry reader (Dose Ace FGD-1000, AGC Techno Glass Co., Shizuoka, Japan) was used to record the absorbed dose. After the reading procedure, the dosimeters were reset at 390 °C.

2.3. Dose linearity and dose repeatability with irradiation time

Dose linearity with respect to irradiation time was checked with the internal IC of MultiRad 350. Dose repeatability was determined by calculating the relative dose uncertainty per control point (specific irradiation time). The relative dose uncertainty is the ratio of the standard deviation to the average dose of each control point. Repeatability was studied using irradiation times from 2 to 60 s. The irradiations were performed with an 0.5 mm Al filter and using three different configurations of energy and current: 350 kV and 10 mA, 250 kV and 14 mA and 350 kV and 5 mA.

2.4. Beam profiles

The x-ray beam profiles were measured with radiochromic film (Gafchromic EBT3, Ashland, Wayne, NJ, USA). The film sheets were cut into four parts of $5 \times 25 \, \text{cm}^2$, which were irradiated separately on a 5.2 cm thick polymethyl methacrylate (PMMA) phantom to include full back-scattering. The field size, defined at 45 cm distance from the source, was set to $20 \times 20 \, \text{cm}^2$ and the irradiation was performed twice with each filter for both x and y directions using an irradiation configuration of 350 kV, 10 mA and 50 s. Before scanning, the films were stored for 24 ± 2 h in a fridge and protected from light [7]. The film digitization was then performed with an A4-size flatbed scanner (Epson Perfection V700 Photo, Seiko Epson Corporation, Suwa, Japan), which was used with an optical resolution of 150 pixels per inch (169 μm per pixel). Finally, the scanned images were saved in a tagged image file format (TIFF) and analyzed with analysis software (OmniPro – I'mRT, IBA Dosimetry GmbH, Schwarzenbruck, Germany). Profiles of the images were created with plotting software (gnuplot version 5.2, http://www.gnuplot.info/).

2.5. Light field to irradiation field agreement

Before irradiation, the x-ray beams were calibrated with the MultiRad 350's calibration software, which helps user calibrate the collimator jaws against the light field. The radiochromic film was set to the PMMA phantom and the light field was drawn by a marker pen on the film. The field size was set to $15 \times 15 \, \text{cm}^2$ and the used irradiation configuration was 350 kV, 10 mA and 50 s. Measurements were repeated with the field sizes of $10 \times 10 \, \text{cm}^2$ and $5 \times 5 \, \text{cm}^2$. After 24 h, the films were scanned and analyzed.

2.6. Absolute dose

Absolute dose measurements were carried out with RPL dosimeters (GD-302M and GD-352M), radiochromic film (EBT3) and a thimble IC (PTW30013, PTW-Freiburg GmbH, Freiburg, Germany). The absorbed dose was calculated from IC measurements according to the AAPM's dosimetry protocol TG-61 [8]:

$$D = M \, N_k P_{T,P} P_{Q,cham} \, P_{sheath} \left[\left(\frac{\mu_{en}}{\rho} \right)_{air}^{w} \right]_{water} \tag{1}$$

where M is the electrometer reading (current), N_k the air-kerma
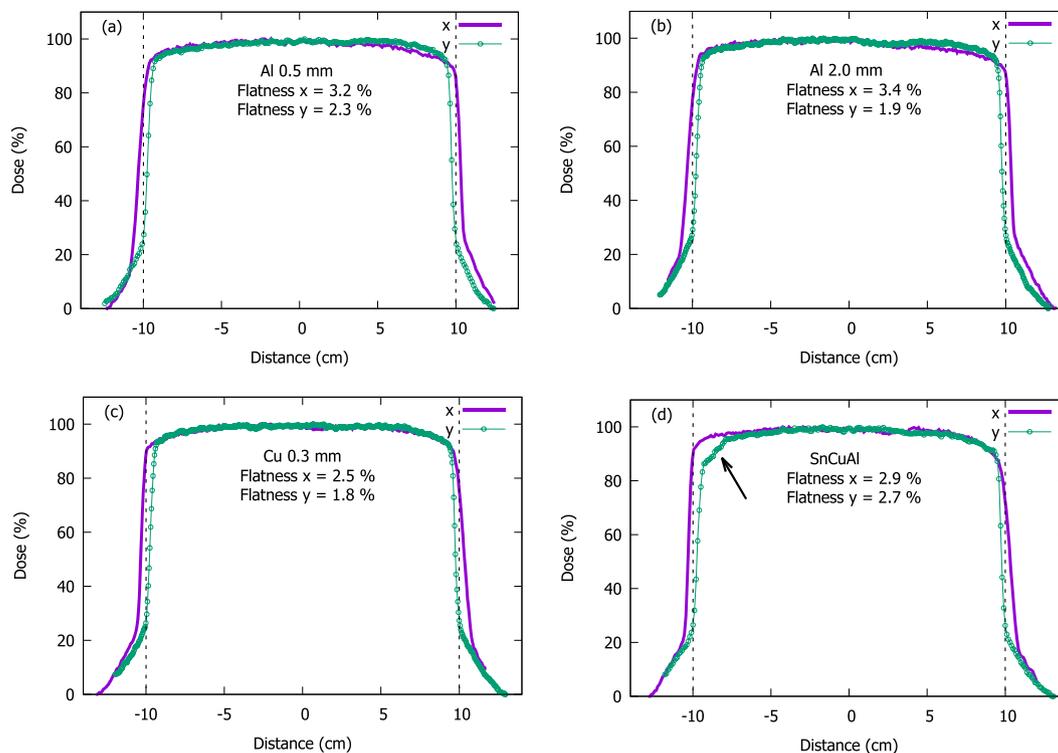
Fig. 4. Direction profiles x (purple) and y (green) of the irradiation field: (a) 0.5 mm Al, (b) 2.0 mm Al, (c) 0.3 mm Cu and (d) SnCuAl (0.75 mm of Sn, 0.25 mm of Cu, and 1.50 mm of Al). Black dashed lines represent a setup field. One may note the filter displacement, which is marked with an arrow in (d). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

calibration factor for BIPM 250 serie, $P_{T,P}$ the temperature and air pressure correction factor, $P_{Q,cham}$ the correction factor for chamber, P_{sheath} the correction factor for photon absorption and scattering in waterproofing sleeve and $[(\mu_{en}/\rho)_{air}^{w}]_{water}$ the water-to-air ratio of the mean mass energy-absorption coefficient. The N_k (an expanded uncertainty of 3% with a coverage factor of 2) was determined at the National Secondary Standard Dosimetry Laboratory (STUK, Helsinki, Finland). The $P_{Q,cham}$ is a correction for the change in beam quality between calibration and measurement. It also takes into account the effect of introducing a chamber air cavity and chamber stem in water at the measurement point. Tabulated values of $P_{Q,cham}$ and $[(\mu_{en}/\rho)_{air}^{w}]_{water}$ from the AAPM's TG-61 report were used in this study. The half-value layer (HVL) of x-rays emitted by the irradiator was 0.2 mm of Cu for 0.5 mm Al filter configurations and 4.0 mm of Cu for SnCuAl filter configurations [9]. The HVL for 0.5 mm Al filter was estimated from the HVL of the 2.0 mm Al filter [3]. The correction factors for HVL of 0.2 mm of Cu were: $P_{Q,cham} = 1.019$ and $[(\mu_{en}/\rho)_{air}^{w}]_{water} = 1.032$, while for HVL of 4.0 mm of Cu those were: $P_{Q,cham} = 1.004$ and $[(\mu_{en}/\rho)_{air}^{w}]_{water} = 1.101$, and the $P_{T,P}$ of 1.025 was used in both of the measurements. The P_{sheath} was 1 because the used IC was waterproof with an 0.335 mm thick PMMA coating. Studies were performed at a 45 cm distance from the focal spot of the x-ray source. In the AAPM's TG-61 report, the distance of 50 cm is used but the effect of this difference to the calculation factors is insignificant. The distance was chosen on the basis that users would have enough space to arrange the irradiated objects.

During measurements, the dosimeters were fixed in a small water phantom with a size of $28.0 \times 28.0 \times 9.5$ cm^3. The RPL dosimeters and radiochromic films were irradiated at depths of 0 cm, 2 cm and 5 cm. The tube voltage was set to 350 kV, the current to 10 mA, the time to 60 s and the field size to 10×10 cm^2. Measurements were executed with 0.5 mm Al and SnCuAl filters due to the fact that these will be the ones most frequently used by users. The IC measurements were conducted only at the depths of 2 cm and 5 cm. The dose at the 0 cm depth

was extrapolated from the dose at the 2 cm depth based on both the percent depth doses (PDD) curve of the MultiRad manual and the results from RPL and film measurements. The center of the IC's air cavity was placed at the depth of the measurement.

3. Results

3.1. Dose linearity and dose repeatability with irradiation time

Dose linearity and dose repeatability with respect to time at three different irradiation configurations are presented in Figs. 2 and 3. In Fig. 2, the linear least squares fitting the points gave a maximum error of 0.7%. Fitted lines cut the x-axis at 3 s, which is the timer correction. The size of timer correction is most likely due to the slow charging of the tube voltages. In Fig. 3, it can be noted that the dose repeatability with all the different configurations is almost constant after the irradiation of 15 s (relative dose uncertainty ≤5%).

3.2. Beam profiles

The x-ray beam profiles with different filtrations are presented in Fig. 4, where the size of an irradiation field appeared to be 20.7×19.5 cm^2 (x, y). The beam profile's flatness was calculated by the equation:

$$F = 100 \times \frac{(D_{max} - D_{min})}{(D_{max} + D_{min})} \qquad (2)$$

where D_{max} is the maximum dose and D_{min} is the minimum dose within the central 80% of the field [3]. Film scanning was always performed in the same way. The scanner's output of measured films was normalized by the film, which was irradiated to a constant dose using larger irradiation field than the size of the film. Thus, all the errors that can be found in the profiles of this particular film originate from the scanner.
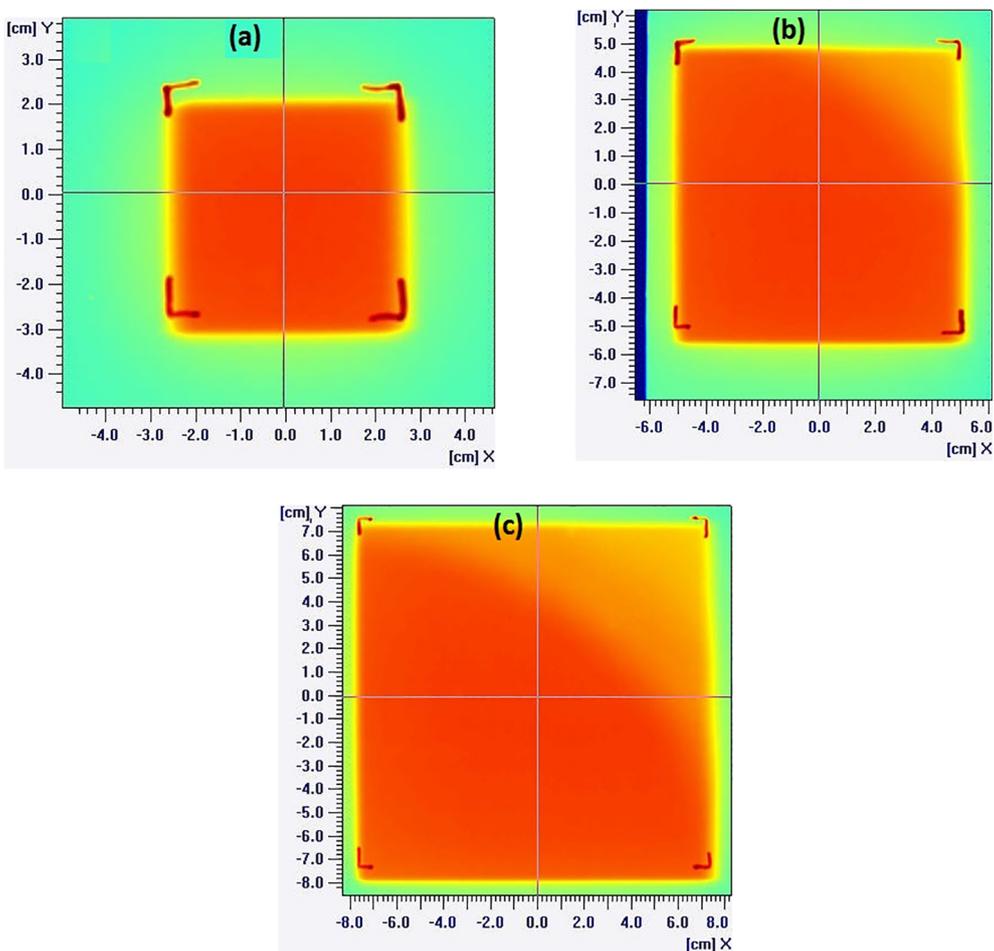
Fig. 5. Setup fields of (a) 5 × 5 cm², (b) 10 × 10 cm² and (c) 20 × 20 cm². The displacement in y direction between light field (corners) and irradiation field (square) can be clearly recognized. In the upper right corner of (b) and (c), the effect of filter displacement can be noticed.
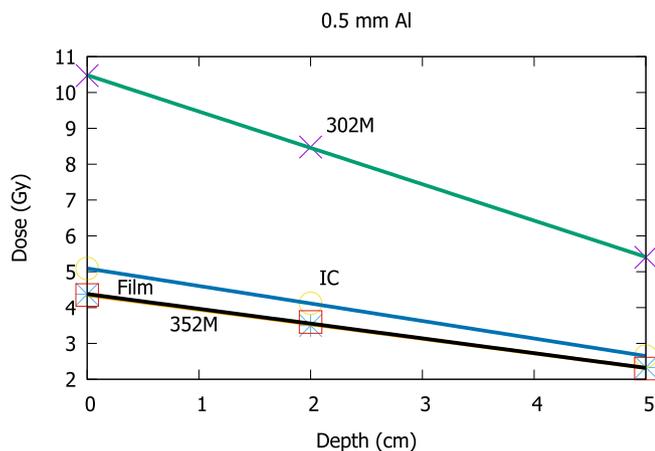

Fig. 6. Absorbed dose of the RPL, film and IC as a function of depth for 0.5 mm thick Al filter. The linear least squares fitting gives maximum deviation of 3.0% to measurement points.
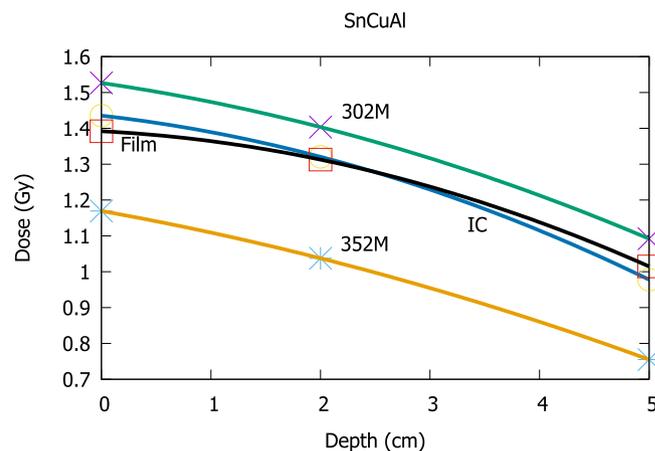

Fig. 7. Absorbed dose of the RPL, film and IC as a function of depth for SnCuAl filter consisting of 0.75 mm of Sn, 0.25 mm of Cu, and 1.50 mm of Al.

3.3. Light field to irradiation field agreement

The corresponding measurement results of light fields and irradiation fields are shown in Fig. 5. The corners of the light fields are marked with a pen in the figures. The maximum displacement between the fields is 0.5 cm; the irradiation field being closer to the irradiator's door than the light field.

3.4. Absolute dose

The dose measurement results with RPL dosimeters, radiochromic film and IC are shown in Figs. 6 and 7. The RPL dose represents an average dose of the two RPL dosimeters. The PDD curves of the RPL and film show that the dose at a depth of 20.0 mm is 81% of the dose at the surface for the 0.5 mm Al filter, while for the SnCuAl filter it is 92%.

4. Discussion

The results of this study show that the MultiRad 350 x-ray irradiation system can produce temporally linear and repeatable x-ray beam. After 15 s irradiations, including the timer correction of 3 s, the repeatability of the dose is acceptable with a maximum of 5% relative dose uncertainty. Repeatability is not affected by the irradiation settings, and it remains relatively stable in all measurements, the standard deviation being ± 0.07 Gy.

The beam profiles were acceptable and the calculated beam flatnesses were less than 4% with each filter used. Fig. 4 shows that with all the filters, 95% of the dose covers 80% of the field size, while 90% of the dose covers 95% of the field size. These results are very competitive compared with other similar studies with a $20 \times 20\,cm^2$ field [3–5]. A difference of about 1% between the areas of setting and the light fields was detected: although the beam size was set to $20.0 \times 20.0\,cm^2$, in reality it appeared to be $20.7 \times 19.5\,cm^2$. When light and irradiation fields were compared, the difference was notable: in the y direction, the light field was 0.5 cm closer to the door of the x-ray system than the irradiated field and this was not dependent on the field size. In addition, the size of the irradiation field was 12% larger than that of the light field. These errors need to be taken into account if small fields are used and if the irradiated object is placed close to the field edge. Small field irradiation sizes should be verified by measurements.

Results from the absolute dose measurements were coherent. With an 0.5 mm Al filtered x-ray beam, the dose increased 2-fold (max. 206%) with the GD-302 M dosimeters compared to the IC and it was almost 2.5 times (max. 241%) higher than that of the film (Fig. 6). The GD-352 M results were better, the maximum differences being 85% and 97% as compared to the IC and film, respectively. With the SnCuAl filter, these maximum differences for GD-302M and GD-352M were 112% and 77% in comparison to the IC and 110% and 74% in comparison to the film, respectively. The high doses measured with the GD-302M dosimeters in 0.5 mm Al filtered x-ray beam can be explained with their high energy response to low energy photons [10]. The GD-302M is designed for megavoltage beams used in radiotherapy. The SnCuAl filter cuts off lower energy photons resulting in a higher mean energy in the x-ray beam, and thus the results are more reliable with GD-302M. The GD-352M dosimeters are designed for the kilovoltage beams used in diagnostics. The included tin filter cuts off the lower energy components of the beam. For this reason, the GD-352M works better in the 0.5 mm Al filtered beam than in the SnCuAl filtered beam, and are more reliable than the GD-302M dosimeters in the 0.5 mm Al filtered beam. The GD-352M works fairly well with an 0.5 mm Al filter, but poor with SnCuAl filter. For the GD-302M, this performance works vice versa. More accurate measurements would need a calibration coefficient determination for both types of RPL dosimeters. Because the HVL value of 0.2 mm Cu was only an estimation, results were also calculated with an HVL of 0.5 mm Cu and 0.1 mm Cu in order to estimate possible error. These results gave a less than 2% deviation, thus it can be concluded that these results are sufficiently accurate for use in cell and small animal irradiations.

The Multirad 350 includes a computer with a Windows 7 (Microsoft Corp., Redmont, WA, USA) operating system. The control software contains detailed instructions for its use and includes a wide selection of irradiation options. However, the computer-controlled filter changer wheel of the collimator infrequently stopped spontaneously leaving the filter at its midway point. This is a severe fault, since the system still allows irradiation. This can be noticed in Fig. 4(d), 5(b) and 5(c). Since the filters' locations are not easy to check, the vendor recommends that the correct position be marked on the filter wheel.

5. Conclusions

It can be concluded that MultiRad 350 x-ray irradiation system is safe and suitable for irradiation of cells and small animals. The x-ray irradiation system can produce a radiation dose that is linear with time. The minimum acceptable irradiation time of 15 s has to be taken into account with doses less than1 Gy. It is also recommended that lower x-ray tube currents are utilized when doses of 1 Gy or less are used. Beam profile flatness is acceptable with all filters and the radiation dose is evenly distributed throughout the x-ray field. The results suggest that the irradiation system should not be used for exceptionally small targets before the light field is calibrated against the irradiation field. The absolute dose measurements of this study can be exploited for the planning of cell and small animal irradiations.

References

[1] Voza T, Kebaier C, Vanderberg JP. Intradermal immunization of mice with radiation-attenuated sporozoites of Plasmodium yoelii induces effective protective immunity. Malar. J. 2010;9:362.

[2] Ozbilgin MK, Aktas C, Uluer ET, Buyukuysal MC, Gareveran MS, Kurtman C. Influence of radiation exposure during radiotherapy. Evidence for the increase of Versican and Heparin-binding EGF-like growth factor concentrations. Anal. Quant. Cytopathol. Histpathol. 2016;38(2):126–32.

[3] Azimi R, Alaei P, Spezi E, Hui SK. Characterization of an orthovoltage biological irradiator used for radiobiological research. J. Radiat. Res. 2015;56(3):485–92.

[4] Bruno AC, Mazaro SJ, Amaral LL, Rego EM, Oliveira HF, Pavoni JF. Biological X-ray irradiator characterization for use with small animals and cells. Braz. J. Med. Biol. Res. 2017;50(3):1414–31.

[5] Kuess P, Bozsaky E, Hopfgartner J, Seifritz G, Dörr W, Georg D. Dosimetric challenges of small animal irradiation with a commercial X-ray unit. Z Med. Phys. 2014;24(4):363–72.

[6] Arakia F, Moribe N, Shimonobou T, Yamashita Y. Dosimetric properties of radio-photoluminescent glass rod detector in high-energy photon beams from a linear accelerator and Cyber-Knife. Med. Phys. 2004;31(7):1980–6.

[7] Casanova Borca V, Pasquino M, Russo G, Grosso P, Cante D, Sciacero P, et al. Dosimetric characterization and use of GAFCHROMIC EBT3 film for IMRT dose verification. J. Appl. Clin. Med. Phys. 2013;14(2):158–71.

[8] Ma CM, Coffey CW, DeWerd LA, Liu C, Nath R, Seltzer SM, et al. AAPM protocol for 40–300 kV x-ray beam dosimetry in radiotherapy and radiobiology. Med. Phys. 2001;28(6):868–93.

[9] MultiRad 350 user's manual. Faxitron Bioptics, LLC: Tucson, AZ, USA; 2015.

[10] Huang DYC, Hsu S-M. Radio-photoluminescence glass dosimeter (RPLGD). In: Gali-Muhtasib H, editor. Advances in Cancer Therapy. London: IntechOpen Limited; 2011. p. 553–68.