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Development of a shielding device for radiotherapy of breast cancer-bearing mice

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ABSTRACT

Breast cancer is the fifth most common cause of death worldwide. Currently, one of the standard treatments for breast cancer is radiation therapy (RT). On the other hand, mouse models have been used in pre-clinical studies for breast cancer RT, requiring dedicated shielding to exposure the breast region. In this work, we considered the values of the lead attenuation coefficient and the material tenth reducing layer for ^{60}Co gamma radiation and developed a lead shielding device for breast cancer-bearing mice to be exposed to localized breast RT. Five-kg of lead were heated to of 340ºC and inserted into an aluminum mold previously adjusted to the dimensions of the device. After solidification, the device was shaped into a cylinder with dimension of 14 x 15 x 7 cm (height x width x thickness, respectively). A round cut-out for breast exposure of 1 cm in diameter was made at 5 cm from the basis of the device. For shielding device validation, we performed calibrations to establish a dose of 10 Gy to the target volume. Fifteen $CaSO_4$:Dy thermoluminescent dosimeters were distributed inside the conical tube to mimic the mouse position inside the shielding. The shielding device was placed at a fixed distance of 10 cm from the target for optimal exposure time. After irradiation, the dosimeters were read using a thermoluminescent reader. According to our results, we were able to develop a body-shielding device that assured the required dose for RT of breast cancer in mice.

Keywords: **breast cancer, mice, ionizing radiation, lead shield, thermoluminescent dosimeters**

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1. INTRODUCTION

Breast cancer is a noncommunicable disease that constitutes an important public health concern, responsible for the fifth principal cause of cancer death worldwide [1]. Treatment is based on the type of breast cancer, its stage, and any other patient special condition. Frequently, it requires multimodality treatment comprising surgery, radiation therapy (or radiotherapy, RT), systemic treatment with chemotherapy, and/or hormone therapy [2].

RT involves the use of high-energy rays (e.g., X or γ rays) or particles to destroy tumor cells or delay their growth. For breast cancer, RT has been used as curative or palliative treatment after breast-conserving surgery or postmastectomy to diminish the risk of cancer relapse as well as if cancer has disseminated to other parts of the body [3].

RT can deliver energy in the breast through an external beam (i.e., the radiation comes from a source outside the body) or internal radiation (e.g., brachytherapy, whose radioactive sources are interstitially placed to the breast). External beam radiation is the most common type of RT for breast cancer. In this case, the radiation source focuses the radiation on the region affected by the tumor.

To advance breast cancer treatment, researches frequently use mice because their small size, low-cost housing and easy handling [4]. In addition, mice share many physiologic similarities with humans. However, local RT for small animals is not a simple task. Depending on radiation source, a physical barrier is necessary to deliver the dose in the target while sparing healthy tissues [5].

At the Nuclear and Energy Research Institute (IPEN-CNEN/SP, Brazil), there is a panoramic gamma ^{60}Co irradiator installed at the Radiation Technology Center. The irradiator is used mostly for research proposals and it is suitable to irradiate small animals. Thus, in this work we report the development of a lead-based body-shielding device for breast cancer-bearing mice to be exposed to a dose of 10 Gy to the target volume [6].

2. MATERIALS AND METHODS

Firstly, we chose lead to construct the whole body-shielding device because the material is cheap, malleable and commonly used to shield γ radiation. Five-kg of lead were heated to approximately 340 ºC during 10 min and posteriorly inserted into an aluminum mold. After lead solidification, the

device was molded into dimensions based on the mouse size and the necessary thickness to reduce the dose by a factor of approximately two tenth-value layer (TVL).

Fifteen $CaSO_4$:Dy thermoluminescent dosimeters (TLDs) produced at IPEN were distributed inside the conical tube to mimic the mouse position inside the device as described in Figure 1. The dosimeters were tablet shaped with mass of 42.2 mg and size 0.8 x 6.0 mm (thickness x diameter, respectively) and covered by a 1 mm-acrylic plate to maintain the electronic equilibrium [7]. The dosimeters were positioned vertically at 10 cm from the center of a panoramic gamma ^{60}CO irradiator (activity = 6.00 TBq and dose rate of 65.82 Gy/h). In the panoramic irradiator, the material to be irradiated orbits a high-intensity radiation source inside a shielded room. Two irradiations were carried out at two different moments. For each irradiation, we used two dosimeters per dose. $CaSO_4$:Dy dosimeters have an uncertainty of 5 % and the lower limit of detection is around 25 mGy [8]. The gamma radiation calibration curve was performed in the air with doses of 1, 4, 8, 10 and 12 Gy. For the thermal treatment of the TLDs, a Novus® model N1100 annealing oven was used and the $CaSO_4$:Dy samples were submitted to a pretreatment at 300°C for 3 h.

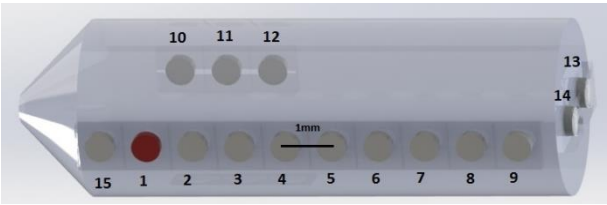

Figure 1: *Thermoluminescent dosimeters along the conical tube. The red region (dosimeter 1) refers to the location of the mouse breast. The distance between the dosimeter 1 and 10 (posterior to the breast) is around 3 cm. The dosimeters 13 and 14 represent the head region and the dosimeter 15 represents the tail region of the mouse.*

The mouse exposure was carried out using the same ^{60}Co irradiator as above mentioned. The target to be irradiated was also placed at 10 cm from the source as showed in Figure 2. The dose rate applied was 65.82 Gy/h with exposure time around 9 min to deliver 10 Gy to the target, i. e., the breast. The absorbed dose was measured only once due to the reproducibility of $CaSO_4$:Dy TLDs [8] and we used one TLD per position on the conic tube to mimic the mouse position. After irradiation,

the dosimeters readout procedure was carried out using a thermoluminescent system Harshaw 3500 (Thermo Scientific™ HARSHAW TLD™ Model 3500, USA).

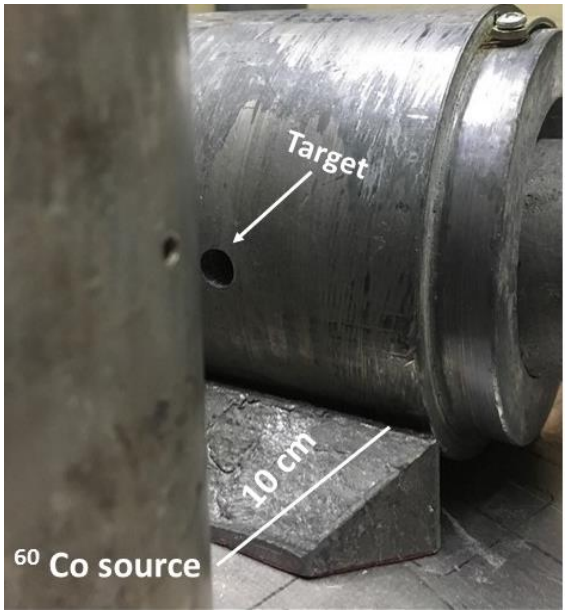

Figure 2: *Device positioned in the irradiator. A lead block was placed next to device to fix it.*

3. RESULTS AND DISCUSSION

The lead-based body-shielding device was designed to cover a conical tube of 3 cm in diameter where the mouse will be inserted and posteriorly irradiated. Thus, after molding, the device presented a hollow cylindrical shape with dimensions of 14 x 15 x 7 cm (height x width x thickness, respectively) and a round cut-out for breast exposure of 1 cm in diameter was made at 5 cm from the basis as showed in Figure 3. In fact, two lead TVLs for ^{60}Co correspond to a thickness of 8 cm of lead and an attenuation of a factor of 100 in relation to the dose that would exist at the point without the lead shield. Thus, the dose after our shielding (7 cm) should be a little higher than 1% of the existing dose without it [9].

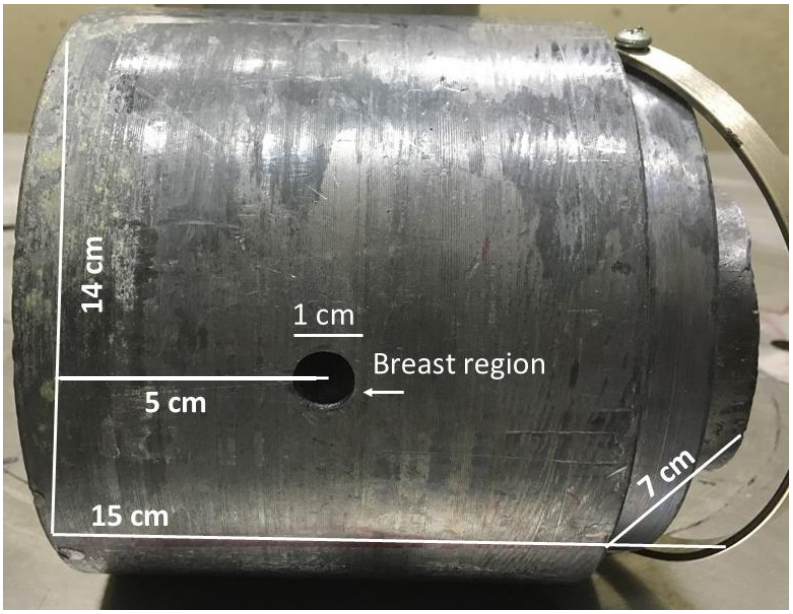

Figure 3: *Lead-based body-shielding device designed to exposure the breast region of mice to ^{60}Co irradiator.*

The calibration curve for $CaSO_4$:Dy TLDs is showed in Figure 4. We can observe that the thermoluminescent response increases linearly with the dose. This finding was expected since one of the advantages of TLDs is their linear response for a wide dose interval [10].

In fact, we used TLDs because their advantages, such as high sensitivity, which allows the use of small-sized dosimeters, low cost, easy handle and good reproducibility [8, 11]. Besides, IPEN produces $CaSO_4$:Dy TLDs for over 40 years.

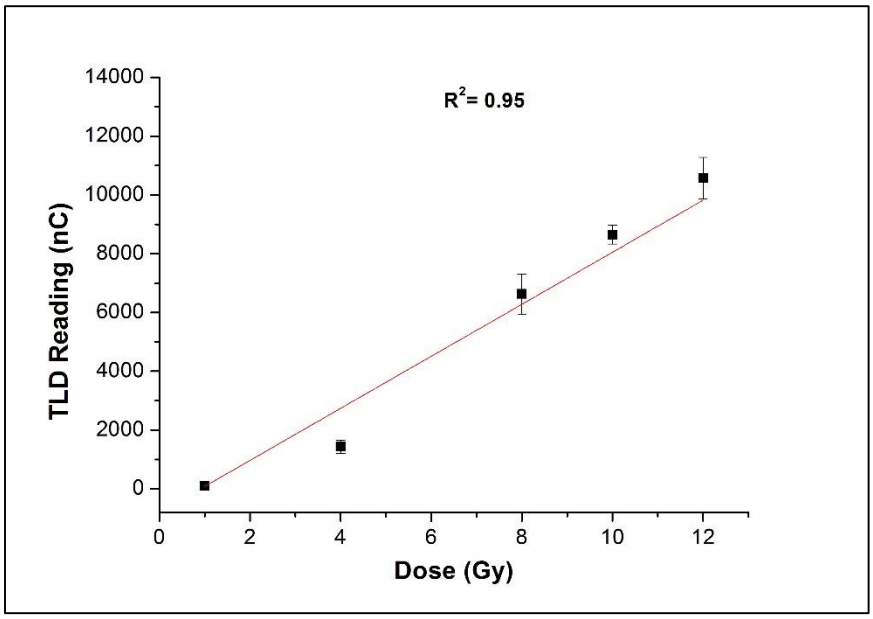

Figure 4: *Thermoluminescent response as a function of the dose in the air for the gamma radiation energy of ^{60}Co. TLD values (n=4 per dose) are presented as mean ± standard error of mean.*

The absorbed doses detected by TLDs are showed in the Table 1. We can observe that dosimeter 1 presents a response close to 10 Gy, which corresponds to the dose to be delivered to the breast area. For dosimeters placed away from the round cut-out, the measured dose decreases and dosimeters 3 to 9 present dose values lower than 1 Gy, i.e., non-significant values for RT of the mouse.

A dose of 7.5 Gy was detected by dosimeter 10, which is placed apart 3 cm from the orifice indicating a dose reduction of about 25%. This finding could be explained by the low attenuation of gamma radiation in the air and polypropylene [12]. Other dosimeters showed readings in the range of 1.5 and 5.3 Gy due to the scattered radiation [13]. In fact, dosimeters 2, 11 and 15 presented higher doses than dosimeters 12 and 13 due to their position next to the round cut-out.

Table 1: Absorbed dose values measured with $CaSO_4$:Dy thermoluminescent dosimeters.

Dosimeter	Dose (Gy)
1	9.8
2	3.0
3	<1.0
4	<1.0
5	<1.0
6	<1.0
7	<1.0
8	<1.0
9	<1.0
10	7.5
11	5.3
12	1.6
13	1.5
14	2.0
15	4.1

A few studies in literature have developed lead-shielding devices for preclinical assays involving small animals [5, 14-15]. Our results showed that the lead-based body-shielding device was able to attenuate close to 100% on the long axis of the conical tube, indicating a body equivalent dose below 1 Sv. This finding fits with those reported by Grasso and colleagues, who developed a shielding for gamma irradiation of a mouse intracranial glioma model [15].

4. CONCLUSIONS

In this study, we developed a lead-based shielding device that was able to attenuate approximately 100 % of the absorbed dose in the region of the mouse body. In addition, the round cut-out allowed a dose close to 10 Gy to the breast region. This device could be used in preclinical assays to advance research in breast cancer radiotherapy.

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