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Radiation Field Characterization for Cellular Irradiation: Application for Low Energy Beams

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ABSTRACT

The interaction of radiation with biological tissues may cause some damage. To quantify it, studying cells in vitro is one methodology for analyzing dose deposition in biological tissues because once exposed to radiation, different methods can quantify the biological damage. However, biological tissue culture exposure forms mostly employ high-energy beams (MeV). Thus, this study aims to characterize the radiation field from X-ray equipment using thermoluminescent dosimeters (TLD), to establish an in vitro irradiation protocol of breast cancer and glioblastoma cells for low energies. First, the central axis alignment test was performed to ensure the equipment followed the *Normativa* IN 90. Then the variation of radiation intensity was analyzed for a 5 x 5 cm² field at distances between 30 and 90 cm from the focal point to the detector. Subsequently, TLD immersed in breast cancer and glioblastoma cellular media were irradiated in a 106 kV and 71 mAs beam to evaluate the dose in cellular media. Simulations were performed with the PENELOPE code to compare with experimental results. The result of the central axis alignment showed that the equipment complies with the current *Normativ*a. The dose distributions for the evaluated distances were more homogeneous for the 40 cm distance, with a standard deviation of 1.7% and 0.9% of the distributions obtained with the TLD and simulation, respectively. Thus, the irradiation field for low energy beams was characterized for a 5 x 5 cm² field for 106 kV and 71 mAs beams at a DFS of 40 cm.

Keywords: **irradiation field, low energy beams, in vitro cells.**

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1. INTRODUCTION

The application of ionizing radiation to treat malignant tumors, among other diseases, has become a routine tool in medicine called radiotherapy. Initially, the risks of ionizing radiation were unknown; however, deleterious effects on irradiated healthy tissues started to be detected. Thus, with the advance in ionizing radiation, the need to define new magnitudes and units became necessary [1]. In 1925, the International Commission on Radiation Units and Measurements (ICRU) was created, with one of the objectives of defining magnitudes involving the use and quantification of ionizing radiation [2, 3].

According to the statistics of neoplasms occurrence from the National Cancer Institute (INCA), in the year 2022 - only in Brazil – 341.350 new cases of cancers were diagnosed in men and 362.730 in women. Among the types of cancers, breast cancer is responsible for 30.1% of new cases in women yearly. Glioblastoma is characterized by high lethality, corresponding to about 4.1% of cancer deaths in men in 2020 [4]. Breast cancer is the most common cancer among women worldwide, and glioblastoma is the most aggressive central nervous system cancer in adults. According to the literature [5], the neoplasms can be treated by surgery, chemotherapy, or radiotherapy, alone or through a combination of more than one modality, with radiotherapy being the most used method of treatment for being non-invasive and having high accuracy [6].

In vitro cell culture has allowed the analysis of radiation damage, such as growth, differentiation, and cell death, as well as the performing of genetic manipulations necessary for the knowledge of the structure and functions of genes [7]. The study of cells in vitro has a range of ramifications that can be explored, one of them being the characterization and quantification of cell damage from the interaction of biological tissue with external sources, such as ionizing radiation.

Most studies of cellular damage characterization and quantification use high-energy radiation beams, which have sufficient data for standardizing irradiation protocols. However, for low-energy beams, these protocols still need to be studied and analyzed [8]. Thus, this study aims to characterize the radiation field for low-energy beams for irradiation of in vitro breast cancer and glioblastoma cells.

2. MATERIALS AND METHODS

The Shimadzu mobile X-ray equipment, model MUX-10 - Mobileart ECO available in the Laboratory of Medical Physics of the Federal University of Health Sciences of Porto Alegre (UFCSPA), was used as a source of low-energy radiation beams for the development of this work, as well as for analysis of the deposited doses the solid-state dosimeter Black Piranha, RTI. Thermoluminescent dosimeters LiF: Mg, Ti (TLD-100) with dimensions of 3 x 3 x 1 mm^3, supplied by the Center for Instrumentation, Dosimetry, and Radioprotection (CIDRA). The TLDs were previously subjected to heat treatment; these were heated to 400°C for 60 minutes in an oven, followed by a 120-minute heating cycle at 100°C in an oven to eliminate any pre-existing signal [9]. Calibration is necessary to obtain a relationship between the quantity to be measured, usually the absorbed dose, and the reading provided by the TLD reader; this relationship is expressed through the calibration factor.

The detectors were exposed to radiation from a source of Cs-137, located in the CIDRA laboratory, with a dose of 8.08 mGy. The calibration factor (F) follows equation (1), which is the ratio between Kerma (mGy) and the system response (nC),

$$F = 8{,}08\ (mGy)/S\ (nC) \tag{1}$$

where S is the sensitivity of each detector in the reading equipment. Knowing the calibration factor for each detector gives the evaluated absorbed dose value:

$$D_{ab} = reading\ (nC)\ x\ F\ (mGy) \tag{2}$$

Reading measures, the light emitted when a TL detector is heated in a TL detector reader. When the energy that sensitized the detector is not the same as the calibration energy, an energy dependence factor of the detector must be considered, as in your case. The correction was made because the calibration energy of Cesium is 662 keV, and the one used in the experiment was approximately 30 keV. According to the TLD manufacturer, the correction is made in 25% [10].

It was necessary to characterize the radiation field to determine a protocol for irradiation at low energy. Thus, the mobile x-ray equipment quality control test was previously carried out by some co-authors of this work [11], as well as the homogeneity of its field. In addition, irradiation parameters were established as source-surface distance (SSD) from 30 cm to 90 cm - equally spaced every 10 cm - field size of 5x5 cm^2, irradiations were performed with 100 kV and 50 mAs current.

After carrying out the exhibitions, the data obtained experimentally were analyzed using Python's computational tool. Under the same conditions as the experimentally performed exposures, simulations were performed using the Monte Carlo simulation code PENELOPE V.08. [12] to verify the agreement between experimental and simulated data.

2.1. Quality control test of equipment

The X-ray beam central axis alignment test was performed and established according to the requirements of RDC 611, which determines health requirements for the organization and operation of diagnostic or interventional radiology services throughout the national territory [13].

Thus, the objective of this test was to evaluate the beam inclination using approximately 40 kV, 3 mAs, and a focus-detector distance of 100 cm; to carry out the test, the device for testing field size and the cylinder for beam alignment test were positioned above the detector, according to parameters stipulated by the current standard. However, the RDC 611 does not describe the test methodology, so we used the *Normativa IN 90* [14] guide as a basis.

2.2. Inverse Square Law

The Inverse Square Law (ISL) is a mathematical law that refers to the behavior of the measurement of the quantity proportional to the emission of an entity emitted isotropically by a point source, measured or estimated at different distances from the emitting source [15]. The size of the radiation field was calculated using a 5 x 5 cm^2 area, which included, for each exposure, three TLDs equally spaced at 1 cm from each other, arranged on the midline of the radiation field so that the anodic effect was as small as possible. As previously stated, the DFS exposures from 30 cm to 90 cm were performed with a 100 kV and 50 mAs beam. All exposures performed were reproduced three times to obtain statistics on the TLD analysis results, which were compared with the Black Piranha solid-state dosimeter (RTI Electronics) responses, calibrated for the voltages of 35 - 160 kVp and with an intrinsic uncertainty of 1.5%. Determinations of the inverse of the square of the distance following equation (3):

$$Y \alpha 1/d^2 \tag{3}$$

where 'Y' represents the radiation dose and 'd' is the distance between the object's source and surface.

2.3. Dose homogeneity in the radiation field

To analyze dose homogeneity in the radiation field, exposure data were collected in 5x5 cm² field configurations as used previously, but with 13 TLDs equally spaced 1 cm apart according to Figure 1, using a DFS of 30 cm, 40 cm, and 50 cm, Figure 2.

Figure 1: *Disposition of TLDs*

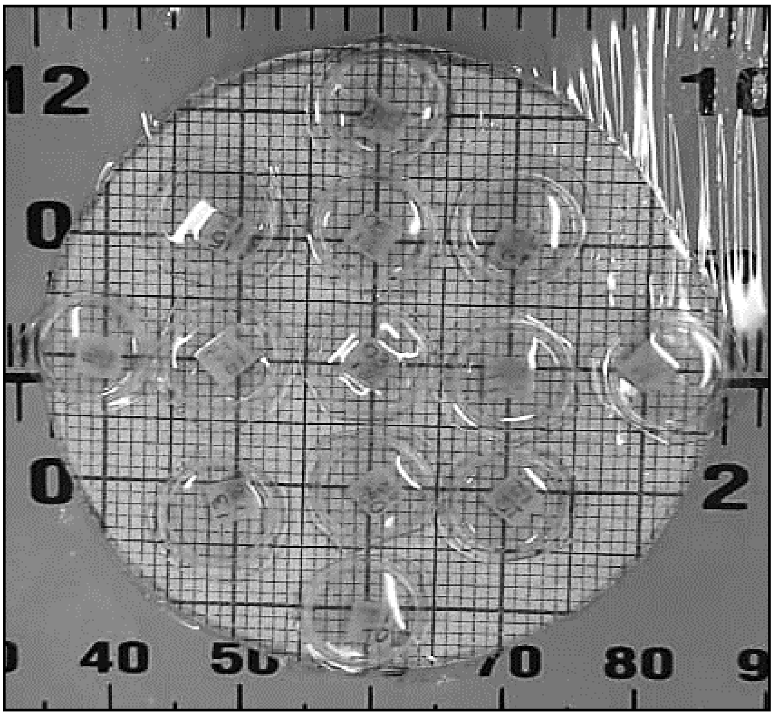


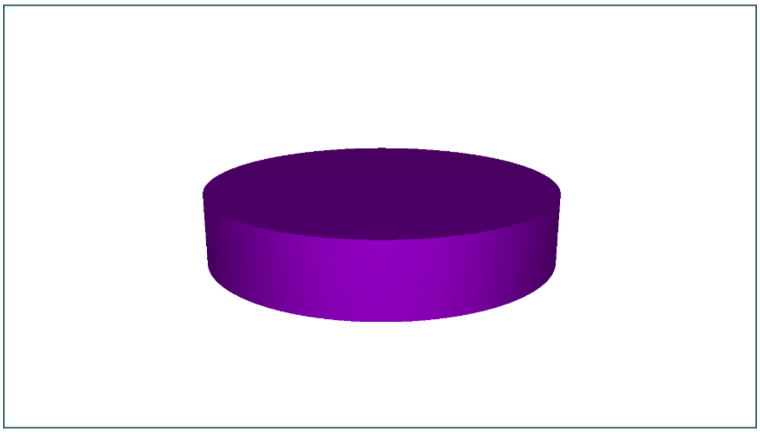
Figure 2: *TLDs exposure scheme*

Similarly, three exposures were made for each exposure condition of the dosimeter configurations. The data were analyzed using code developed in Python language, which made it possible to analyze the homogeneity of the irradiation field.

2.4. Monte Carlo simulation

To analyze the homogeneity of the radiation field, a simulation was performed using the Monte Carlo simulation code PENELOPE V.08. [12]. For this, a simulator object was built in the exact dimensions of the platelet, which was used as the basis for the configuration of the TLDs, with a radius of 2.5 cm and thickness of 1 cm, as shown in Figure 3.

Figure 3: *Geometry of the simulated object*



The simulation was performed with a 106 kV beam, 40 cm SSD, and 1x10^9 primary particles.

2.5. Immersion of TLDs in cell media

At this stage, TLDs will be immersed in breast and glioblastoma tumor cell media and then irradiated based on the protocol selected during the previous steps.

For irradiation of breast tumor cells and glioblastoma, the cell lines MCF-7 (breast adenocarcinoma) and U87 (glioblastoma) are used, both from ATCC (American Type Cell Culture). The cell lines are grown in RPMI medium with 20% fetal bovine serum and DMEM medium with 10% fetal bovine serum and maintained in a humidified atmosphere at 37°C with 5% CO2 (carbon dioxide gas).

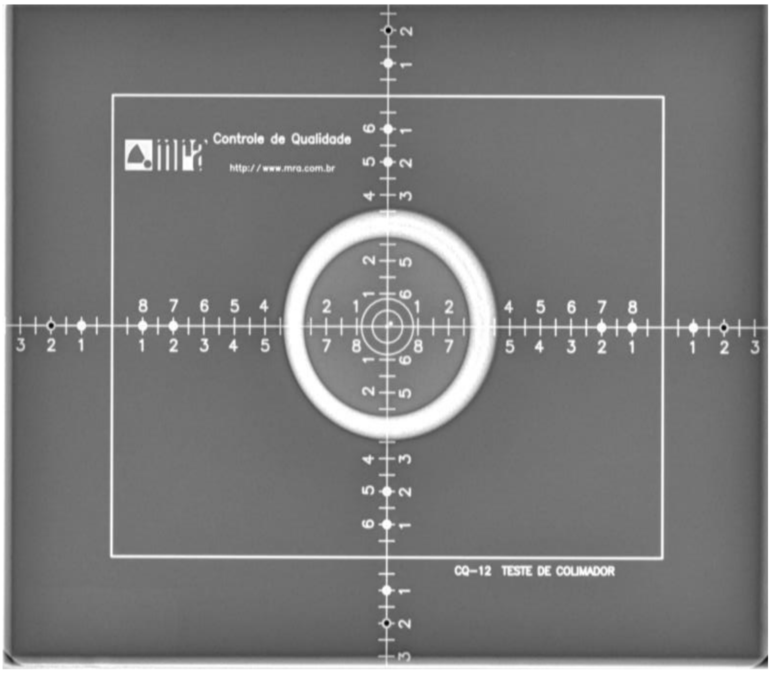
For this reason, the cell media used were RPMI and DMEM. Thus, the quantification of dose in TLDs immersed in cell media was performed to obtain irradiation conditions like those to be used for exposure of cell cultures. Thus, TLDs immersed in RPMI (breast cell medium) were exposed three times to the beam, and TLDs immersed in DMEM (glioblastoma cell medium) six times.

3. RESULTS

3.1. Quality control test of equipment

Figure 4 shows the result of the test performed to ensure the quality of the X-ray beam, which is established according to the RDC 611.

Figure 4: *Center axis alignment*

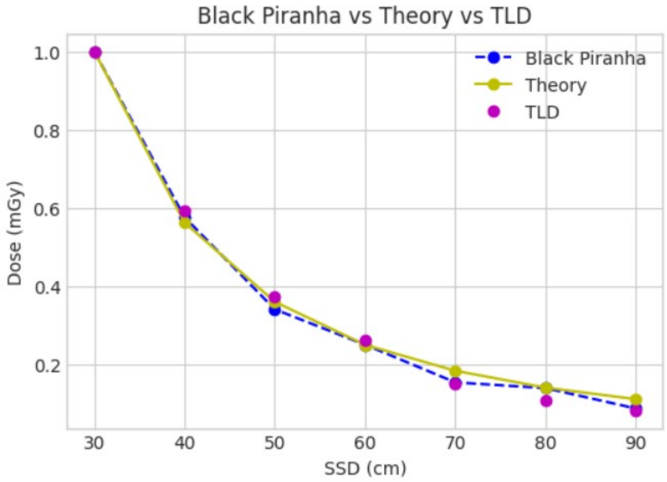


The ordinance of the RDC 611 establishes a tolerance of 3 degrees to the axis perpendicular to the receptor plane and 5 degrees for the restriction level of the equipment [13]. Since the RDC 611 does not establish how to perform the test, the *Normativa IN 90* [14] guide was adopted. Thus, according to the ordinance, the location of the image coming from the sphere on the top of the device for the beam alignment test must be within the smallest circle of the device for field size testing. In this way, the beam must have a tilt of fewer than 1.5 degrees and within the most extensive circle for a tilt of fewer than 3 degrees; the beam must be less than 3 degrees tilted [13]. The angle of an inclination concerning the beam's central axis was less than 1.5 degrees, as shown in Figure 4.

3.2. Inverse Square Law

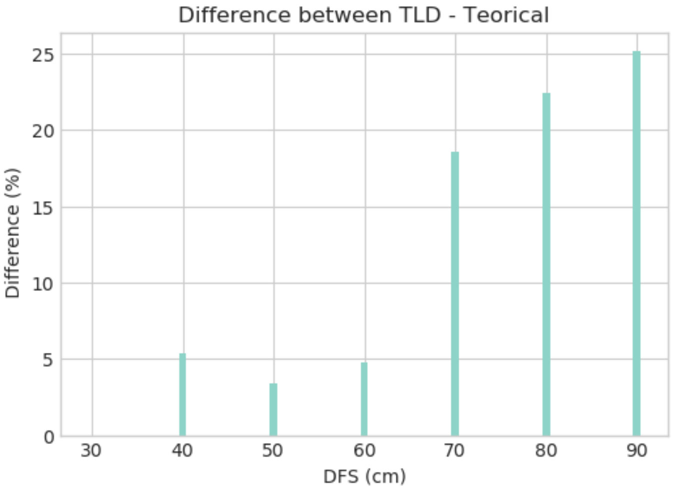
A comparison with ISL was necessary to verify the results obtained experimentally, as shown in Figure 5.

Figure 5: *Dose decay curve with theoretical and experimental data obtained with TLD and solid-state detector*



The dose data was obtained by reading the TLDs and the solid-state detector, Black piranha. As shown in Figure 5, the experimental and calculated data agree. Looking at Figure 6, we notice that for DFS values greater than 60 cm, the differences in percentage between the values measured with TDLs and theoretical are about three times greater than for DFS smaller than 60 cm.

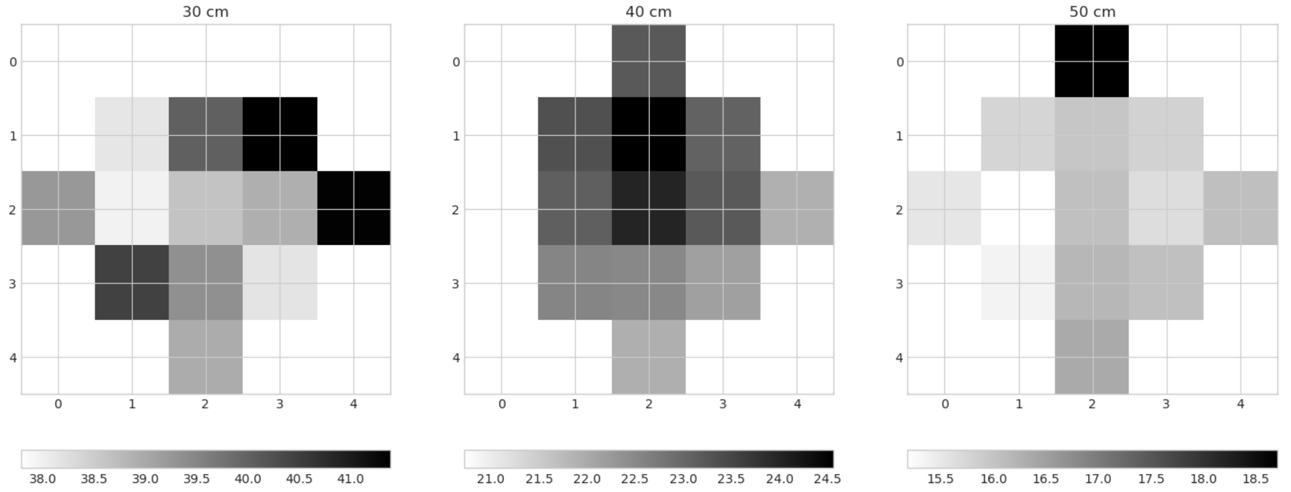
Figure 6: *Differences in percentage between values measured by the TLDs and theoretical values.*



3.3. Dose homogeneity in the radiation field

To characterize a radiation field, it is necessary to evaluate the homogeneity of the radiation field. According to Figure 7, a grayscale color scale was established to represent the deposited dose, with the darkest color representing the highest doses and the lighter colors representing the lowest doses, to standardize the presentation of the results.

Figure 7: *Configuration of TLDs to different distances of SSD*



The mean values of dose distribution, Mean reproducibility, and Standard deviation of the different SSDs are shown in Table 1 below.

Table 1: Statistics of the data found.

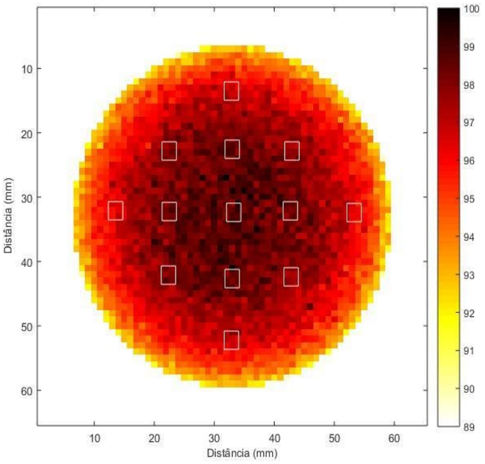
	SSD (cm)		
	30	**40**	**50**
Mean values of dose distribution (mGy)	38.93	21.44	14.49
Mean reproducibility (%)	17.47	9.38	27.03
Standard deviation (%)	3.1	1.42	4.67

As can be seen in Table 1, the TLD exposures at SSD of 30 cm obtained a mean value of the dose distribution of 38.93 mGy, mean reproducibility of 17.47 %, and standard deviation of 3.1 %. Equivalently, the dose distribution's surface source distance of 40 cm had a mean value of 21.44 mGy, mean reproducibility of 9.38 %, and a standard deviation of 1.42 %. For the TLDs exposed to SSD of 50 cm, the mean value of the dose distribution was 14.49 mGy, with mean reproducibility of 27.03 %, and a standard deviation of 4.67 %. As the field's homogeneity is inversely proportional to the standard deviation found in the exposures and we sought to find the SSD with the most homogeneous dose distribution, only SSD equal to 40cm was selected for the next steps.

3.4. Monte Carlo simulation

Figure 8 shows the dose distribution in the irradiated volume. According to the results obtained, the highest dose values are at the center of the geometry, and not at the edges due to the incidence of the point beam at the center of the object.

Figure 8: *Homogeneity of the simulated geometry field*



As the dose outside the geometry is not considered, the dose scale in Figure 8 is limited to values above 89 % to analyze the dose deposition in the region of interest. We considered 13 points at the exact locations where there would be TLDs, and the dose standard deviation of the image was around 0.90 %, within the selected regions.

3.5. Immersion of TLDs in cell media

In this step of the work, the dosimeter configurations immersed in RPMI (Figure 9) and DMEM (Figure 10) were irradiated with different doses to evaluate if there would be proportional damage to the number of exposures, thus verifying the radiosensitivity of each cell medium.

Figure 9: *Field homogeneity obtained by TLDs immersed in RPMI medium*

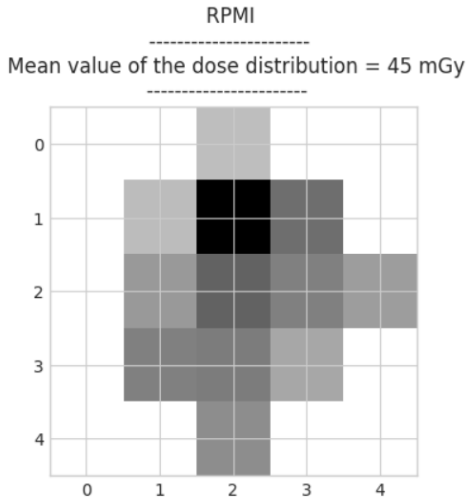
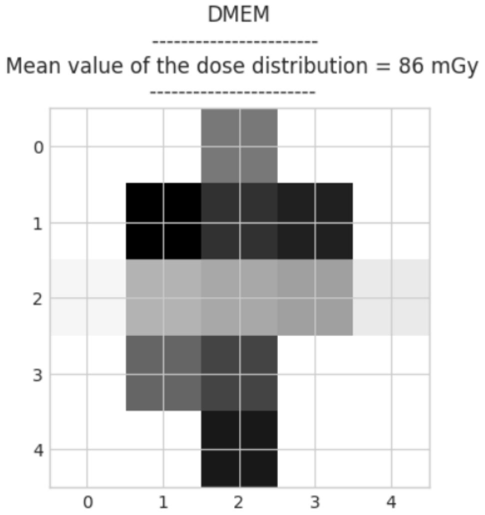


Figure 10: *Field homogeneity obtained by TLDs immersed in DEMEM medium*



As can be seen in Figure 9, the exposure obtained in the submerged configuration in RPMI had a mean value of the dose distribution of 45 mGy. However, in Figure 10, the exposure obtained in the submerged configuration in DMEM had a mean value of the dose distribution of 86 mGy.

As a result, lower dose deposition was obtained in the submerged configuration in RPMI than in DMEM as a function of the difference in the number of exposures. However, the doses were proportional to the number of exposures. Thus, we can conclude that the media do not influence the results, as the densities of the cell media used were similar.

4. DISCUSSION

The collimation system and central axis alignment test were performed to ensure that there was no deviation in the inclination of the beam, which resulted in a deviation of less than 1.5%, which ensured compliance with what is established by the legislation in force.

By exposing the thermoluminescent dosimeters and the solid-state dosimeter to the same exposure conditions, values were found to be close and in agreement with the law of the inverse of the square of the distance. Thus, validating the experimental results.

Looking for the most homogeneous radiation field configuration, the field homogeneity analysis was performed, and the most homogeneous result was obtained for the TLD configuration exposed with the 40 cm DFS, because it was the radiation field with the lowest standard deviation value found, with an average dose of 21.44 mGy. The proposal to immerse TLDs in cellular media and subject them to low-energy beams aims to analyze more reliably the reality of cell cultures in vitro exposed to low-energy clinical beams, such as dose values and field homogeneity. For this, only the 40 cm DFS was used because it was the one that obtained the best dose homogeneity in the previous phase of the work. Thirteen equally arranged TLDs were immersed in glioblastoma cell medium and exposed six times to 106 kV and 71 mAs beams, generating an average of 85.99 mGy of deposited dose. Equivalently, an equal configuration of TLDs was immersed in a breast cancer cell medium; however, being exposed 3 times to the same 106 kV and 71 mAs beam and obtaining an average deposited dose of 45.00 mGy.

The simulation was performed using the Monte Carlo code PENELOPE to compare the experimental results with the simulated ones. In this case, a standard deviation of 0.9% was obtained, which is lower than that recorded experimentally under the same conditions. This is because the simulation did not consider the existing anodic effect.

5. CONCLUSION

The main objective of the work was to characterize the irradiation field to obtain an irradiation protocol for in vitro breast cancer and glioblastoma cell cultures exposed to low-energy beams. For this purpose, it was necessary to characterize a small irradiation field for a low-energy beam.

The irradiation parameters selected for determining the irradiation protocol in DMEM and RPMI media were 40 cm between the irradiation source and the media surface, a voltage of 106 kV, and a current of 71 mAs. From the data presented, it was also possible to observe that the dose deposition in TLDs immersed in both media is proportional to the number of exposures, which assures us that the density of the cellular media used is similar and does not influence the irradiations. The simulation showed a radiation field with a standard deviation of 0.9%, smaller than the value found experimentally. This difference is due to the simulation program disregarding the existing anodic effect.

In future work, breast cancer and glioblastoma cell cultures will be irradiated with low-energy beams to analyze the damage caused by ionizing radiation and compared to the damage caused in the same cell cultures but exposed to high-energy beams to evaluate the possibility of treating superficial tumors with low energy beams.

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