Associação Brasileira de Energia Nuclear – ABEN
2019 International Nuclear Atlantic Conference - INAC 2019
Santos, SP, Brazil, October 21-25, 2019

Agência Brasileira do ISBN
ISBN 978-85-99141-08-3

END-WELD THICKNESS VARIATION EFFECTS ON DOSE RATE FOR A NEW Ir-192 BRACHYTHERAPY SOURCE

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ABSTRACT

Brachytherapy is a form of radiation therapy that uses small sealed sources close to the tumor to deliver a high dose to target while keeping dose on neighboring healthy tissues as low as possible. A wide variety of radionuclides and different sources are available for brachytherapy, each with his own unique geometry. The Laboratory of Sources Production for Radiotherapy (IPEN/CNEN) developed a new Ir-192 seed for eye tumor treatment that is currently under dosimetric definition. This work is part of a larger project that aims the full dosimetry of this new source, but rather than calculate the usual parameters proposed by the American Association of Physicists in Medicine, the specific contribution to the dose rate of a usually not considered factor was investigated under a statistical approach: end-weld thickness variation, which is important due to this source being welded by an in-house method. Its effects were investigated using the Monte Carlo radiation transport code MCNP4C and an in-house routine programmed with MATLAB® to analyze the data. Final results are presented as a mean value for dose rate at different points of interest and their associated standard deviations. The results are discussed based on the influence of said parameter on different points around the source.

1. INTRODUCTION

Cancer is a term that covers a wide range of different diseases which main symptom is an uncontrolled growth of cells and loss of apoptotic capacity. A complete understanding of cancer biology is yet to be reached, but is well established that it differs greatly across different populations for genetic and environmental particularities. Exposure to ionizing radiation and some chemicals, but also to tobacco, alcohol and even sunlight or processed food, are causes of risk that must be taken into account. [1]

The Brazilian National Institute of Cancer (INCA) estimates more than 630 thousand new cases of cancer in 2019 [2], being the second major mortality cause on the country (16.9 %, data from 2017), surpassed only by circulatory system diseases [3]. Amongst the different types of cancer, eye cancers are not prevalent, but of great interest once they have a high occurrence on children. In Brazil eye cancer represents 3 % of all cases of children cancer and enucleation (surgical remove of the eyeball) is still the main treatment, which incurs in complete vision loss for the affected eye and aesthetical problems to the patient. Ophthalmic brachytherapy is an alternative treatment that may preserve vision and yields better overall survival rates. [4,5,6]

Brachytherapy dose calculations rely on previous measurements of the dose rate around the source. These are usually done before the seed becomes commercially available, following a protocol for dosimetry. Although there are recent protocols that take into account inhomogeneities on patient's tissue, source self-attenuation and the finite dimensions of patient [7], the most commonly used is still the Task Group 43 Report (TG-43) from AAPM (American Association of Physicists in Medicine), published in 1995 and updated in 2004, also known as TG-43 U1 [8,9]. TG-43 U1 is widely used because it is easy to implement in clinical practice, relying on a water-based dosimetry that considers the patient and its surroundings to be an infinite homogeneous water medium.

The TG-43 U1 describes the dose at any point around the source through a set of parameters with different physical meanings, following a polar coordinate system centered on the geometrical center of the source. Dose rate to point of interest is described by Equation 1.

$$\dot{\boldsymbol{D}}(\boldsymbol{r},\boldsymbol{\theta}) = \boldsymbol{S_K} \cdot \boldsymbol{\Lambda} \cdot \frac{\boldsymbol{G_L}(\boldsymbol{r},\boldsymbol{\theta})}{\boldsymbol{G_L}(\boldsymbol{r_0},\boldsymbol{\theta_0})} \cdot \boldsymbol{g_L}(\boldsymbol{r}) \cdot \boldsymbol{F}(\boldsymbol{r},\boldsymbol{\theta}) \tag{1}$$

In Equation 1, the dose rate $\dot{D}$ depends on distance r from the source and angle θ counting from its longitudinal axis. The parameters on which it is decomposed are: air-kerma strength S_K and dose-rate constant Λ, that depend mainly on radionuclide used and unique seed characteristics; linear geometry factor G_L, that takes into account dose variation by geometry factors (photons spreading from source); radial dose function g_L, that describes dose fall-off in the transverse plane of the seed due to scattering and absorption; and anisotropy function F, which describes the angular variation of dose, present due to the fact that brachytherapy sources are usually elongated and cannot be considered a point-source. [9]

This protocol is considered a good approximation for brachytherapy, mainly because the soft tissue of human body is composed mostly of water, so it is a good material to consider in medium surrounding the seed for both its density and atomic composition. There are, however, some limitations pointed by newer protocols [7]. One topic usually not covered is the variation on the internal dimensions of seeds due to the inaccuracy in its production. Ideally, all sources should be equal to the one used during dosimetric characterization or their S_K should be measured for different seed batches to guarantee the validity of previous dosimetry calculations. It is also possible that effects due to this variation are negligible providing there is a criterion applied to prevent bad-shaped seeds to be used.

In Brazil, the eye cancer incidence on children encouraged the Radiotherapy Sources Production Laboratory of the Radiation Technology Center (CETER) at Nuclear and Energy Research Center (IPEN/CNEN-SP) to develop a new seed model with Ir-192 as radionuclide. Before it can be mass produced and benefit patients, it must pass through the dosimetric characterization described above. This work, however, does not aim the full dosimetry of the seed, but rather to estimate if the criteria for welding the tip of the seeds do affect the final dose rate relevantly. For this, data from the geometry of this source was gathered from their developers' thesis [10,11], and Monte Carlo simulations using MCNP4C code were analyzed under a statistical approach. Results are presented in the format of mean values for dose rate at specific points and their respective deviations.

2. MATERIALS AND METHODS

This work relies on simulations with MCNP4C, by Los Alamos National Laboratory. Output data reading was executed with in-house routines programmed with MATLAB® for such tasks. Simulations were executed under a personal computer with a 7th gen Intel® core i5 processor and 8 GB RAM. Total simulation time was approximately 42 hours.

2.1. Simulation Input Data

The seed was modeled after its nominal dimensions presented by their developers [10]. However, there is no such information regarding the end-weld dimensions, except it has the same radius of the capsule outer wall. Since the welding system used was developed specifically for use by the Radiotherapy Sources Production Laboratory of CETER, more details of it were found either under literature [11] or by direct measurement of the seeds. Some important topics arose:

- The welding process yields different results depending on which tip is being welded. In an initial stage of the seed production, the empty titanium tube that will become the capsule has one tip welded, resulting in an almost perfect spheroid with half its mass extending beyond the hollow section of the encapsulation tube and the other half within it. Then the Iridium-192 wire is accommodated inside the titanium tube, before the second tip is welded. Due to the pressure inside the tube, the second end-weld results in a different shape, with the outer part identical to the hemispheroid of the other tip, but the internal part being deformed into a slightly concave or plane shape. The plane shape was considered for this model, as shown in Figure 1.
- Even amongst the seeds selected by criteria like roundness, symmetry and damage of its welds, a considerable variation on the dimensions of it was found [11], thus reinforcing the need of a dosimetric analysis of it. The nominal length of the seed, 4.5 mm, has hemispheroidal tips with semidiameter of 0.25 mm on its longitudinal axis, but the variation on the welding may lead to lengths of up to 4.67 mm (on a batch of 70 samples analyzed). Since there is little deviation expected on the length of the outer capsule of the seed, this increase was attributed solely as variation on weld, and divided by two to be accounted on both tips.

The Iridium-192 core modeled also differs from literature because it was changed some point during the development of the seed. The surrounding medium was considered a 15 cm radius water sphere to assure ideal backscattering conditions. The final model used, as well as the material composition taken into account, are shown in Figure 1 and Table 1, respectively.

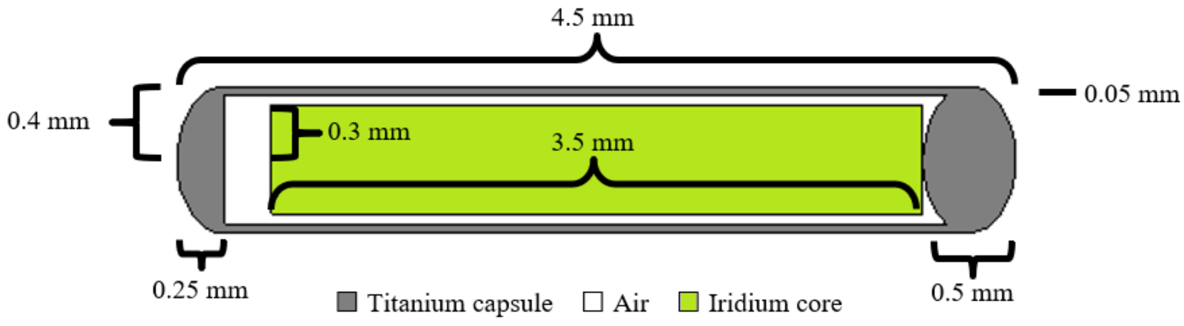

Figure 1: Iridium-192 seed model used

Table 1: Materials composition used for Monte Carlo simulation

Material	In model	Composition	Density
Iridium	Seed core	100 % Ir	22.56 g/cm³
Air[a]	Seed free-space	0.0124 % C 75.5268 % N 23.1781 % O 1.2827 % Ar	1.20479 x10^{-3} g/cm³
Titanium	Seed encapsulation	100 % Ti	4.54 g/cm³
Water	Surrounding medium (15 cm water sphere)	100 % H_2O	1 g/cm³

a. Dry air (near sea level) composition, taken from NIST STAR database. [12]

Once the titanium encapsulation shields all beta emitted from the core, only transport of photons was considered. Dose per photon was calculated using tally *F6 and considering electronic equilibrium to assume dose to be numerically equal to kerma. Results were analyzed to a total of 21 points of interest lying at seven different θ angles (from 0º to 180º, with a 30º step) and at three different r distances from the geometrical center of the source (0.5 cm, 1.0 cm, and 3.0 cm). Dose at these points are averaged over 1 mm³ cubes facing the center of the seed and centered at the point of interest, and also made of water, so there is no medium interface on tallying region (Figure 2). These points were chosen for the following reasons:

- Brachytherapy has a high dose gradient, therefore two small distances (0.5 mm and 1.0 mm) were used to assess for impact on dose near the source; also, dose at small distances are of interest in brachytherapy because the source is usually at contact with the tumor; in addition, although TG-43 protocol was not directly followed, the point at $r, \theta = 1\ cm\ , 90°$ is considered the reference point for it, thus is an interesting point to assess the dose at;
- The eye diameter is usually below 3 cm, so it was considered the farther distance of interest;
- Dose around the seed is taken into account on TG-43 protocol by calculating values for the anisotropy function $F(r, \theta)$. Values for F are of interest since they are affected not only by the overall shape of the seed, but are also heavily influenced by the end-welds at angles near 0º and 180º. Although TG-43 protocol was not followed directly in this work, the same coordinate system and methodology of accounting dose was considered, so a difference on dose at these angles should also be noted;
- Should the seed be symmetrical in relation to its transverse plane, results for supplementary angles would be expected to be identical, except by statistical uncertainty. This is not the case, however, as the difference on the first welded tip to the second may be significant, so angles up to 180º have to be considered.

Iridium-192 emission spectrum was taken from literature [13]. A total number of 2.5 x 10^7 particle-stories were simulated for each run, leading to a MCNP calculated type A uncertainty on dose no higher than 3 % for $r = 3\ cm$, 1 % for $r = 1\ cm$, and 0.5 % for $r = 0.5\ cm$, independently of θ. Dose by photon was converted to dose rate multiplying results by 10^{14} (conversion from jerks/g to cGy), by 2.2 (average number of photons by radioactive decay of Iridium-192), by 1.48 x 10^9 Bq (an approximated value for activity that can be achieved on these seeds), and by 60 (seconds per minute), leading to final results in units of cGy/min.

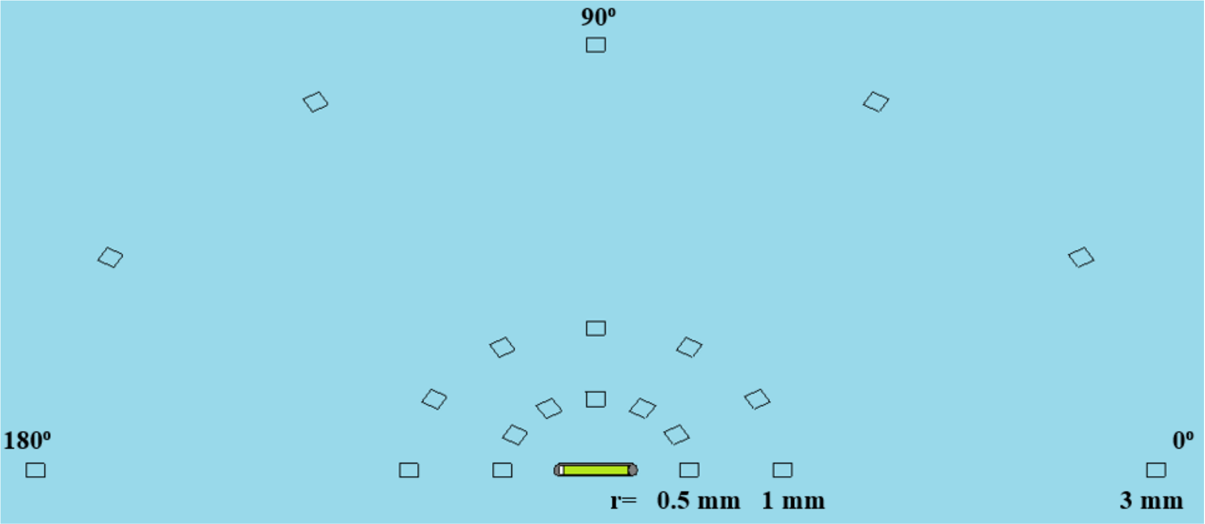

Figure 2: Tallying regions in relation to the seed

2.2. Variation of Parameters and Statistical Analysis

The statistical approach used in this work was based on Pantelis et al. [14] that suggests the values found to be taken into account in the full dosimetry by means of propagation of uncertainty. The effect of the variation of end-weld thickness was analyzed in this work. A total of 70 different simulations were ran, and the final result for dose at each point was calculated as the average of all 70 values at that point.

The data for end-weld thickness variation was taken from the welding process developer [11]. A batch of 70 seeds were already measured, so these lengths were used instead of randomly generated new values. The nominal value of $L = 4.5\ mm$ for seed length is not the actual mean value, but rather the minimum length. The maximum length measured in this batch was $L = 4.67\ mm$, the mean value was $L = 4.57 \pm 0.04\ mm$ and the mode is $L = 4.55\ mm$ $(n = 13/70)$. To account for the increase in the length on both tips, a parcel of 4.00 mm of the tube was subtracted from each value of L, and the result was divided by two, considering both end-welds to have always the same thickness of the longitudinal hemisphere (as an approximation). Two images of seeds modeled with different welds are shown in Figure 3.

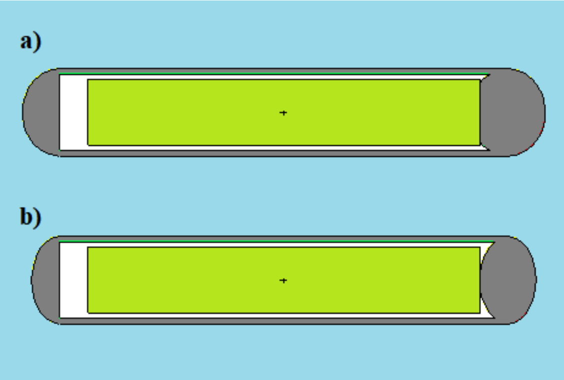

Figure 3: Two seeds modeled with different end-weld thickness a) 4.50 mm length seed; b) 4.67 mm length seed

The results were analyzed with MATLAB®. The two main aspects to be discussed are mean value for each point, which can represent a deviation from reference value, obtained with the nominal seed, and standard deviation from the sample, which indicates the expected variation of the dose with the variation of that parameter.

3. RESULTS AND DISCUSSIONS

Dose rate values for the reference seed model are shown in Table 2, while results averaged by the set of 70 seeds with varying weld thickness are shown in Table 3. It is important to note that uncertainty shown for the reference seed only depends on the Monte Carlo method, while the uncertainties on Table 3 refer only to standard deviation of the dose rate values averaged at that point, not propagating the uncertainty from each value. This would be the correct procedure to accurately describe the value at given point, but taking into account only the deviation within the set of seeds was the methodology considered in this work because its main goal is to analyze dispersion of data within this set.

Table 2: Calculated dose rate (cGy/min) and associated statistical uncertainty from reference seed model

	r = 0.5 cm	**r = 1.0 cm**	**r = 3.0 cm**
θ=0°	7.9779 ± 0.44 %	1.6840 ± 0.96 %	0.1929 ± 2.69 %
θ=30°	10.403 ± 0.38 %	2.4301 ± 0.79 %	0.2598 ± 2.32 %
θ=60°	10.197 ± 0.38 %	2.5428 ± 0.76 %	0.2862 ± 2.19 %
θ=90°	9.9472 ± 0.39 %	2.5849 ± 0.76 %	0.2942 ± 2.19 %
θ=120°	10.189 ± 0.38 %	2.5469 ± 0.76 %	0.2827 ± 2.22 %
θ=150°	10.314 ± 0.38 %	2.4145 ± 0.79 %	0.2708 ± 2.25 %
θ=180°	8.0886 ± 0.43 %	1.7143 ± 0.95 %	0.1925 ± 2.64 %

Table 3: Mean dose rates (cGy/min) and standard deviation from 70 sampled seed models with varying end-weld thicknesses, at 21 points of interest

	r = 0.5 cm	**r = 1.0 cm**	**r = 3.0 cm**
θ=0°	7.9678 ± 0.073 %	1.6826 ± 0.143 %	0.1931 ± 0.473 %
θ=30°	10.402 ± 0.018 %	2.4299 ± 0.032 %	0.2599 ± 0.188 %
θ=60°	10.197 ± 0.009 %	2.5411 ± 0.035 %	0.2867 ± 0.151 %
θ=90°	9.9477 ± 0.002 %	2.5845 ± 0.013 %	0.2942 ± 0.030 %
θ=120°	10.190 ± 0.002 %	2.5469 ± 0.005 %	0.2826 ± 0.023 %
θ=150°	10.313 ± 0.004 %	2.4148 ± 0.007 %	0.2708 ± 0.016 %
θ=180°	8.0806 ± 0.061 %	1.7124 ± 0.059 %	0.1924 ± 0.039 %

The overall results followed the expected behavior: a decrease on dose rates at angles near 0º and 180º; a decrease approximately proportional to the distance squared, since Iridium-192 has a high mean energy and attenuation does not play a major role at very small distances; and increasing uncertainty on farther distances and angles near 0º and 180º due to lower photon income.

Should the dose rate values calculated vary greatly, the dosimetry for this seed would be not totally reliable, and the standard deviation presented on Table 3 would have to be mapped for every point calculated and added to the overall uncertainty through propagation of uncertainty.

Another aspect that should be taken into account is the relative difference between these mean values and the reference ones. If the difference is negligible, then the dose rate for the reference case should follow the mean value of the distribution used, which means that only the augmented uncertainty should be considered. However, if they differ significantly, the reference model is probably failing to represent the real seed accurately. As seen in Table 4, the relative difference from reference case is shown to be irrelevant, so this is not the case.

Table 4: Relative difference between dose rate calculated with reference seed and mean dose rate calculated from 70 sampled seeds with varying end-weld thickness

	r = 0.5 cm	**r = 1.0 cm**	**r = 3.0 cm**
θ=0°	-0.090 %	-0.054 %	0.003 %
θ=30°	-0.022 %	-0.316 %	-0.267 %
θ=60°	-0.080 %	0.286 %	-0.254 %
θ=90°	0.039 %	0.222 %	-0.267 %
θ=120°	-0.006 %	0.056 %	0.530 %
θ=150°	0.081 %	0.306 %	0.027 %
θ=180°	-0.036 %	-0.081 %	0.128 %

Deviation in the end-weld thickness variation case is very small, below 0.1 % for most points and 0.2 % for all points, which shows good agreement. The mean values also deviate from reference values in less than 0.1 % for most points and 0.2% for all points, as shown in Table 4. This overall agreement and low standard deviation indicate that influence on final dose rate due to differences on the end-weld thickness is very low and statistically negligible, which is an important information on manufacturing the seed. It also shows that within the range of length L sampled nominal value of $L = 4.5\ mm$ can be used for dosimetric calculations even if it not corresponds to the actual mean value without incurring on relevant impact on the dose.

4. CONCLUSIONS

This work sought to analyze parameters relevant to dosimetry of a new brachytherapy seed model not taken into account on TG-43 U1 protocol, although the TG-43 U1 coordinate system was used, as well as its formalism of dose to water. One objective pursued was to prevent future inconsistencies when this protocol was applied for both experimental and Monte Carlo dosimetry, assessing the effects of a parameter not usually observed.

The end-weld thickness was considered as a possible source of error to the final dose, but within the range of observed seeds in one batch produced, this variation does not lead to any statistically significant change to final dose.

Since the mean value for dose rates obtained from a set of 70 seeds modeled following a real distribution of length values did agree to the dose rate calculated from reference case, it was considered that nominal value $L = 4.5\ cm$ is a good approximation to a real mean length value (that should be averaged over a larger number of samples).

Also, no great dispersion in dose rate mean values was observed, even close to the tips of the seed, so this deviation could be not taken into account when calculating the propagation of uncertainty on dose rate profile around the seed without great impact on final uncertainty.

This Brazilian seed model is under development by CETER (IPEN/CNEN-SP) aiming to meet a demand from hospitals for a cheaper ophthalmic brachytherapy seed, thus increasing the number of patients treated and reducing the number of enucleations, which brings several other problems to patients. Tracking these effects before the full dosimetry is undertaken is highly desirable, preventing unexpected inconsistencies that would be hard to correct following strictly the TG-43 U1 protocol. Further work on this subject shall consider other parameters, like movement of the core within the seed, outer tube thickness and composition of materials; also, reconsider the nominal seed model and, ultimately, realize the full TG-43 U1 protocol dosimetry considering all the effects previously observed. When considering multiple parameters, the impact on dose by each one shall be evaluated both individually and together since it is interesting to evaluate which ones are most relevant and should be taken care the most, but is also important to define the final impact on dose and its uncertainty due to the concurrence of all of them.

ACKNOWLEDGMENTS

The authors would like to thank CNEN, CNPq and CAPES for the scholarships and IAEA for funding fellowships that allowed the work to be made. The first author would also like to thank the Medical Physics group of the National and Kapodistrian University of Athens' Medical School, specially Ph.D. Panagiotis Papagiannis and Ph.D. Evangelos Pantelis, for the discussion on the subject.

This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – Brasil (CAPES) – Finance Code 001.

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