Comparative dosimetry of prostate brachytherapy with I-125 and Pd-103 seeds via SISCODES/MCNP*

Dosimetria comparativa de braquiterapia de próstata com sementes de I-125 e Pd-103 via SISCODES/MCNP

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Abstract **Objective:** The present paper is aimed at presenting a comparative dosimetric study of prostate brachytherapy with I-125 and Pd-103 seeds. **Materials and Methods:** A protocol for both implants with 148 seeds was simulated on a heterogeneous three-dimensional pelvic phantom by means of the SISCODES/MCNP5 codes. Dose-volume histograms on prostate, rectum and bladder, dose indexes D_{10}, D_{30}, D_{90}, $D_{0.5cc}$, D_{2cc} and D_{7cc}, and representations of the spatial dose distribution were evaluated. **Results:** For a D_{90} index equivalent to the prescription dose, the initial activity of each I-125 seed was calculated as 0.42 mCi and of Pd-103 as 0.94 mCi. The maximum dose on the uretra was 90% and 108% of the prescription dose for I-125 and Pd-103, respectively. The D_{2cc} for I-125 was 30 Gy on the rectum and 127 Gy on the bladder; for Pd-103 was 29 Gy on the rectum and 189 Gy on the bladder. The D_{10} on the pubic bone was 144 Gy for I-125 and 66 Gy for Pd-103. **Conclusion:** The results indicate that Pd-103 and I-125 implants could deposit the prescribed dose on the target volume. Among the findings of the present study, there is an excessive radiation exposure of the pelvic bones, particularly with the I-125 protocol.

Keywords: Radiotherapy; Dosimetry; Prostate cancer; Brachytherapy; SISCODES; MCNP.

Resumo **Objetivo:** O presente artigo visa apresentar um estudo dosimétrico comparativo de braquiterapia de próstata com sementes de I-125 e Pd-103. **Materiais e Métodos:** Um protocolo adotado para ambos os implantes com 148 sementes foi simulado em um fantoma tridimensional heterogêneo de pelve por meio dos códigos SISCODES/MCNP5. Histogramas dose-volume na próstata, bexiga e reto, índices de doses D_{10}, D_{30}, D_{90}, $D_{0,5cc}$, D_{2cc} e D_{7cc}, e representações de distribuição espacial de dose foram avaliados. **Resultados:** A atividade inicial de cada semente de I-125, para que D_{90} seja equivalente à dose de prescrição, foi calculada em 0,42 mCi, e de Pd-103, em 0,94 mCi. A dose máxima na uretra foi 90% e 108% da dose de prescrição para I-125 e Pd-103, respectivamente. A D_{2cc} para I-125 foi 30 Gy no reto e 127 Gy na bexiga, e para Pd-103 foi 29 Gy no reto e 189 Gy na bexiga. A D_{10} no osso do púbis foi 144 Gy para I-125 e 66 Gy para Pd-103. **Conclusão:** Os resultados indicam que os implantes de Pd-103 e I-125 puderam depositar a dose prescrita no volume alvo. Entre os achados, observou-se excessiva exposição de radiação nos ossos da pelve, principalmente no protocolo com I-125.

Unitermos: Radioterapia; Dosimetria; Câncer de próstata; Braquiterapia; SISCODES; MCNP.

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INTRODUCTION

Brachytherapy is a safe and effective treatment for localized prostate cancer[(1)]. Such technique utilizes sealed radioactive sources positioned adjacent to or in the interstitium of the cancerous tissue. As the absorbed dose is inversely proportional to the square of the distance from the emitting source, brachytherapy allows for the safe application of high absorbed doses at a determined target over a short period of time[(2)].

According to the space where brachytherapy is applied, it can be classified as follows: intracavitary brachytherapy, involving insertion of radiation sources into natural body cavities; interstitial brachytherapy, insertion of the radioactive sources into the target tissue; intraluminal or intravascular brachytherapy, where the radiation sources are placed in the lumen of the esophagus, bronchi or blood vessels; and superficial brachytherapy, as the source is directly positioned on the skin or mucosa of the area to be treated[(2)]. Also, it can be classified as temporary or permanent. On the report no.38 of the International Commission on Radiation Units (ICRU)[(3)], brachytherapy was classified, according to the dose rate, as low dose rate (LDR), medium dose rate (MDR) and high dose rate

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(HDR) for dose rates of 0.4 to 2 Gy.h^{-1}; 2 to 12 Gy.h^{-1}; and > 12 Gy.h^{-1}, respectively.

Interstitial brachytherapy with permanent implants of radioactive seeds is one of the methods utilized for treatment of prostate tumors, in general applied for neoplasms at T1 or T2 stages, with Gleason scores between 2 and 6, and serum PSA ≤ 10 ng. The indications for implants are mostly for small volumes, particularly at early stages of disease located within the prostatic capsule (T1B-T1C, T2A-T2B-T2C stages, and absence of metastasis and lymphatic compromise). Such technique may be associated with teletherapy, particularly in cases of patients considered as being at high risk[4]. Prostate brachytherapy primarily utilizes metal seeds of Iodine-125 (I-125) or, most recently, Palladium-103 (Pd-103)[5]. Seeds of I-125 and Pd-103 are constituted of material doped with radioactive isotope encapsulated in a titanium casing. The external dimensions of the seeds are 4.5 to 5 mm in length, and 0.8 mm in diameter[6,7]. Such seeds are represented on Figure 1.

I-125 is a radioactive isotope with a half-life of 60.1 days, emitting gamma rays some of which are internally converted into X-rays. The main photon emission energies are 27.20 keV, 27.47 keV and 30.97 keV, with the respective probabilities of 39.80%, 74.20% and 25.70%. On its turn, Pd-103 has a 17-day half-life and X-ray photon emission at the main energies of 20.07 keV, 20.22 keV and 22.71 keV, with probabilities of 19.83%, 37.55% and 11.88%, respectively[8]. Because of their lower energies, Pd-103 photons have a lower range in the tissue than those emitted by I-125. Thus, for a same distribution of seeds with equal activity, the spatial dose distribution obtained by Pd-103 theoretically tends to be less homogeneous that that obtained with I-125. On the other hand, and for the same reason, Pd-103 seeds will produce lower absorbed doses at longer distances, particularly in the surrounding healthy tissues. The Pd-103 dose rate as well as its relative biological effectiveness (RBE) is higher than that of I-125[9]. Thus, the prescription dose for Pb-103 seeds is lower than the recommended dose for I-125 seed implants, 125 and 144 Gy, respectively[10,11]. The value corresponding to 80% of the dose deposited by I-125 seeds is delivered in 140 days, while the Pd-103 seeds deliver such value in 39 days. This is due to the fact that Pd-103 seeds generate higher dose rate and, consequently, produce a greater biological effect, particularly on cancer strains with a high proliferation index.

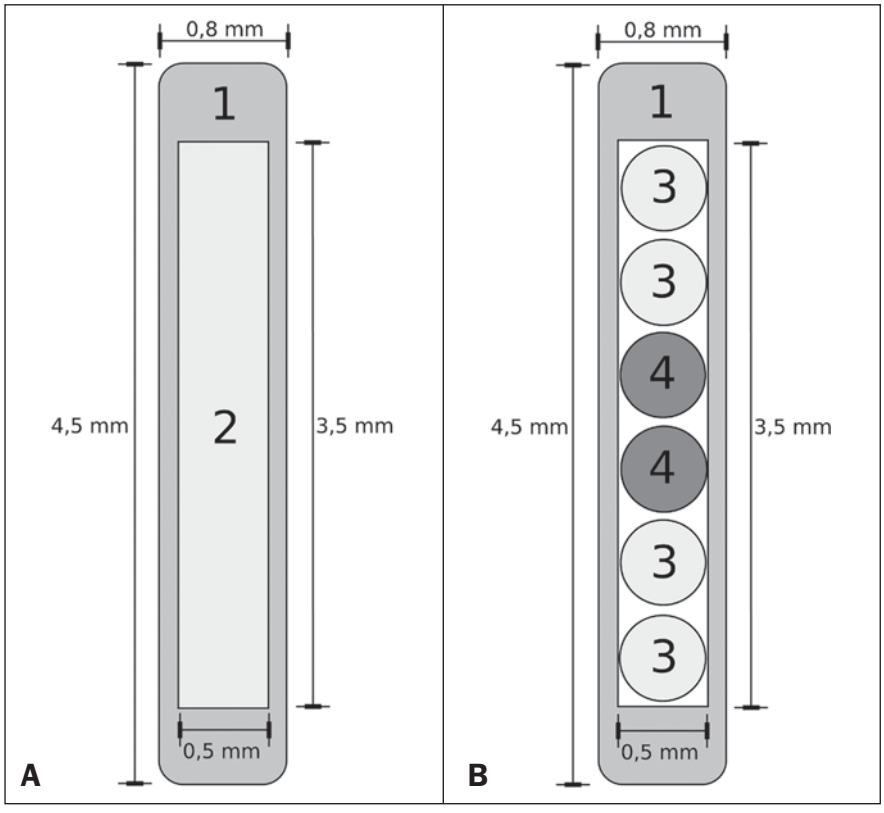

Figure 1. Diagram of I-125 (**A**) and Pd-103 (**B**) seeds. The seeds are composed of: 1 – titanium capsule; 2 – iodine oxide; 3 – Pd-103 doped polystyrene; 4 – Metal markers for the visualization of the seeds on X-ray images.

The number of seeds implanted in the prostate depends upon the following parameters: reference volume to be irradiated, individual seeds activity, adopted prescription dose, as well as the selected model of seeds spatial distribution[12]. The seeds are applied in an aligned pattern, by means of ultrasonography-guided insertion of needles containing a set of seeds. Such seeds are deployed on a one-by-one basis on the tissue, with a predetermined space between each other. The number and spatial distribution of the seeds are selected in such a manner to meet the prescription dose to the prostate, at the same time minimizing the dose delivered to adjacent tissues and structures. Obviously, there is a strong dependence between the management of the disease and the applied doses and also between applied doses and the arrangement of the seeds in the implant.

In order to measure the treatment effectiveness, as well as the possibility of adverse effects, reference or merit parameters related to absorbed dose, are established for comparison purposes. For example, the D_x parameter corresponds to the minimum dose value in x% of an irradiated volume. Such volume may refer to an organ or to a predefined volume of interest in the radiotherapy planning. On its turn, the D_{ycc} parameter corresponds to the minimum dose in the volume of y cm^3 containing the highest absorbed dose in an organ or volume of interest defined in the planning[13].

The Monte Carlo method is a mathematical technique applied in the reproduction of a statistical process. Such technique is particularly interesting in the resolution of complex problems which cannot be modeled by deterministic computational methods. The Monte Carlo N-Particle (MNCP) code applies such technique in the transport of nuclear particles, tracking each one of the many primary or secondary par-

ticles generated by a radioactive source, from the emission of such particles to some terminal event such as absorption, annihilation, escape from the system, among others[14]. The three dimensional simulation of the nuclear particle transport is aimed at eliminating the two dimensional planning deficiencies by means of an analytical method in homogeneous medium, constituting an important tool to improve the quality of radiotherapy procedures in oncology[15,16].

Computational methods have been highly relevant for dosimetric evaluation utilizing heterogeneous models[17–20]. The SISCODES (Computational System for Dosimetry by Neutrons and Photons by Stochastic Methods) is a tool for the construction of computational simulation objects and simulation of radiotherapy treatments by means of stochastic codes such as MCNP[21,22]. Such system allows the conversion of tomographic images into a voxel model. Based on a database including tissue chemical composition and nuclear data, SISCODES allows the association of nuclear and chemical data with the model of voxels by selection of the tissue of each voxel, as well as the positioning of brachytherapy and teletherapy sources. The system utilizes the MCNP for the simulation of nuclear particles transport in the model, consequently obtaining the absorbed dose. From the results, relevant dosimetry data are extracted and presented as spatial dose distribution and dose *versus* volume histogram (DVH)[21,22].

The present article is aimed at investigating the dosimetry in prostate permanent implants of I-125 and Pd-103 seeds, by means of DVHs, isodoses and reference parameters, such as D_x and D_{ycc}, with the purpose of performing comparisons between the two protocols.

MATERIALS AND METHODS

A protocol of permanent prostate implant of I-125 seeds was arbitrarily adopted. The same implant protocol was reproduced with Pd-103 seeds. The distribution and number of seeds were not altered between the protocols. The I-125 seeds were simply replaced by the Pd-103 ones.

For the simulation of nuclear particle transport, a voxels model of a male pelvis[23] was utilized, with voxels of 5 x 5 x 5 mm. In such a model, the prostate volume corresponds to approximately 40 cm^3. Figure 2 shows two sections of such a model. The seeds were positioned according to the *modified uniform distribution* proposed by Butler et al.[24], as shown on Figure 3. In total, 148 seeds were positioned in 24 applications, forming parallel lined-up segments in tangential direction to the pubic bones, on a spacing grid between segments of 1 cm, maintaining the seed spacing on a single segment of 6 mm between the centers of consecutive seeds.

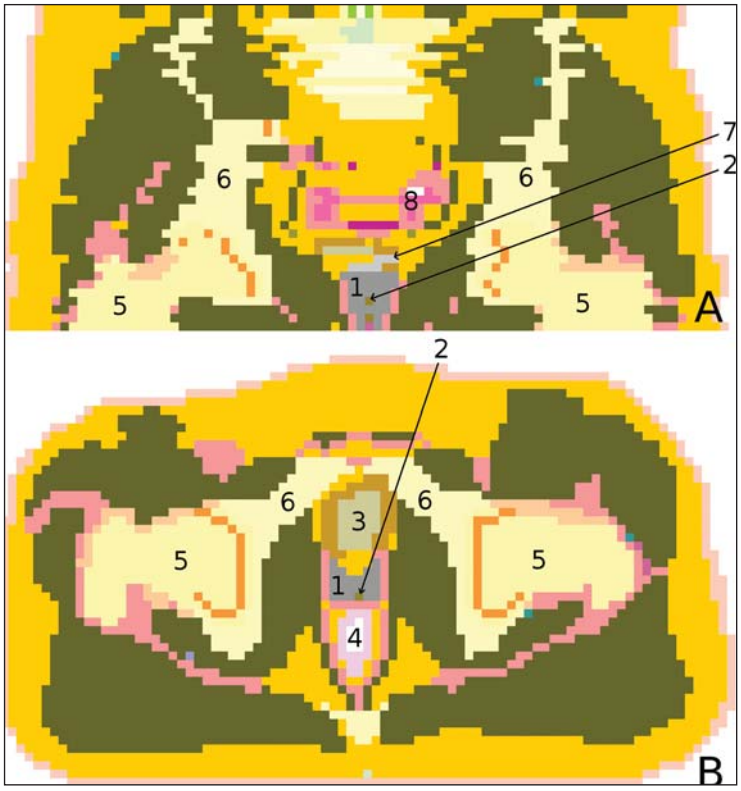

Figure 2. Frontal (**A**) and radial (**B**) sections of the voxel model, where the following anatomical structures can be observed: 1 –prostate; 2 – urethra; 3 – bladder; 4 – rectum; 5 – femur; 6 – iliac bones; 7 – seminal vesicle; 8 – colon.

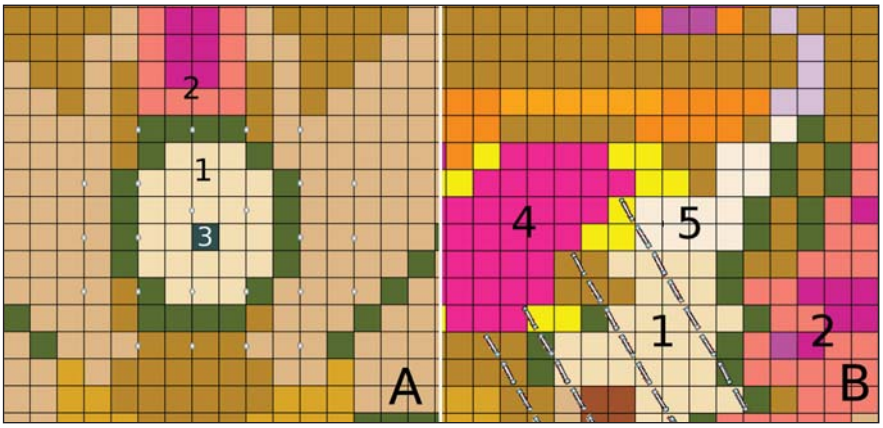

Figure 3. Section demonstrating the model with the seeds on the Z axis (**A**) (central view) and X axis (**B**) (sagittal view). The marked organs are the following: 1 – prostate; 2 – rectum; 3 – urethra; 4 – bladder; 5 – seminal vesicle.

Both seeds types were represented by a cylinder of radioactive material measuring 3.5 mm in length and 0.5 mm in diameter contained inside another titanium cylinder with 5 mm in length and 0.8 mm in diameter, as shown on Figure 4. The radioactive matrix adopted for the I-125 seed was iodine oxide, and for the palladium seed, polystyrene doped with Pd-103.

After simulation of each protocol with the MCNP (version 5.2), the results were imported by the SISCODES code. Then, the spatial dose distributions and DVHs of each procedure were generated. The initial activity of the seeds was calculated in order to obtain the prescription dose to the prostate recommended for each implant. The SISCODES code works as an interface for the MCNP code. The whole evaluation and simulation of nuclear particles transport is carried out by the MCNP code. Consequently, dosimetry is evaluated by MCNP. The SISCODES allows for the definition of the model and protocol to be simulated, and helps in the manipulation and presentation of the results as charts and histograms.

The particle transport code calculates the deposited energy per mass unit for each voxel, in $MeV.g^{-1}$ units per particle emitted by the source. Such value is converted into Gy ($J.kg^{-1}$) by particle unit emitted by the source. The emissions from the sources are evaluated as a function of activity (Bq = $transformations.s^{-1}$) multiplied by the photon production rate per transition unit. The results from such calculations generate the dose in Gy for each voxel. In the present case, one adopted the same activity for all seeds. The seed activity was calculated so that the prescribed doses (D90) were 144 and 125 Gy, respectively for I-125 and Pd-103. Thus, the activities were found in such a way to adjust D_{90} to the value equivalent to the prescribed dose in a clinical protocol.

With such activities, the absorbed doses were evaluated in the target regions as well as in the adjacent tissues, utilizing representation of isodoses regions and DVHs.

RESULTS

In order for the D_{90} to be equal to the recommended dose, the initial activity of each seed was calculated to be 0.42 mCi and 0.94 mCi, for I-125 and Pd-103, respectively. The resulting DVH for the prostate is shown on Figure 5A. Considering such activities and the adopted seeds spatial distribution, the maximum absorbed dose in the urethra was approximately 90% of the prescribed dose for I-125 and 108% of the prescribed dose for Pd-103. The D_{2cc} dose in the rectum was 30 Gy for I-125 and 29 Gy for Pd-103, as shown on the DVH represented at Figure 5B. The same dose (D_{2cc}) for the bladder was 127Gy for I-125 and 189 Gy for Pd-105 (Figure 5C). The

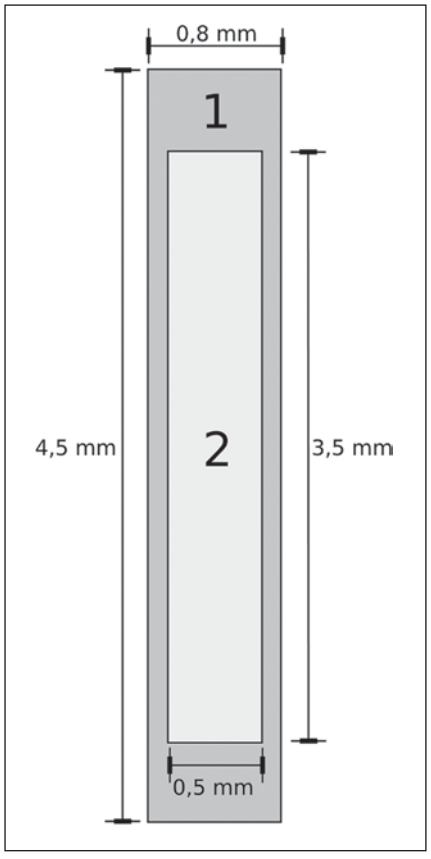

Figure 4. Model of the seed utilized at MCNP. The volume marked as 1 corresponds to the titanium capsule. The volume marked as 2 corresponds to the radioactive compound - iodine oxide or Pd-103 doped polystyrene.

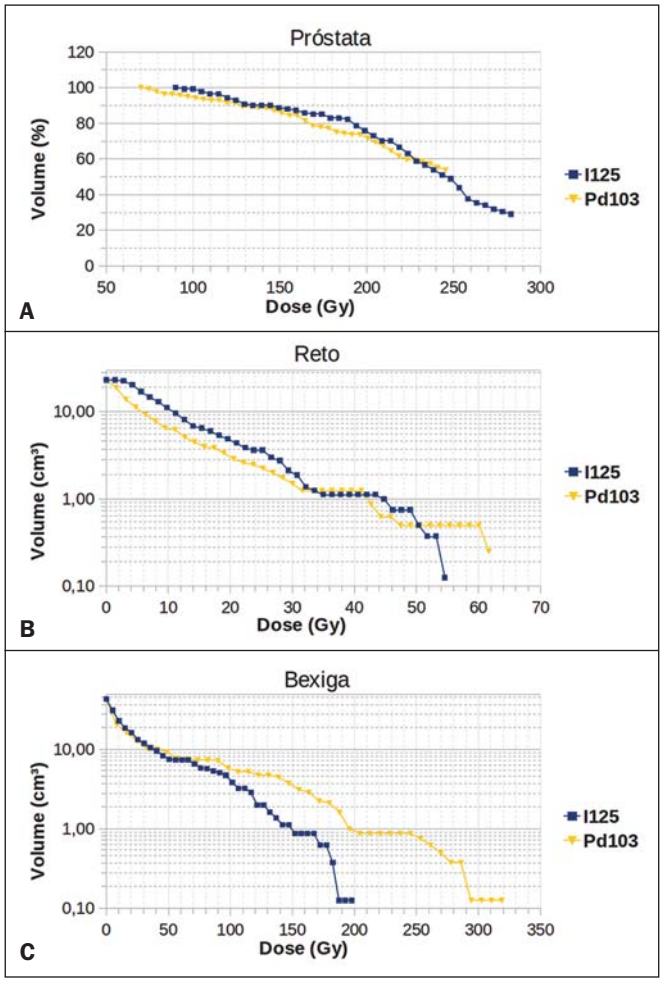

Figure 5. Dose volume histograms for the prostate, rectum and bladder.

pelvic bones presented high doses on the soft tissue-bone interface, particularly with the I-125 seeds. With I-125 seeds, the D10 value for the pubic bones was 144 Gy and for the iliac bones, the value was 2.7 Gy. The Pd-103 seeds presented a D10 value of 66 Gy for pubic bones, and 165 mGy for iliac bones. The differences in spatial dose distribution can be observed on the representation of spatial dose distribution shown on Figure 6.

Figure 6A shows high absorbed doses in the soft tissue-bone interface for the I-125 seed implants. However, such high absorbed doses were not observed for Pd-103 seed implants (Figure 6B).

The dose/volume ratios in the target volume (D_{90}) with the dose in the rectum (D_{2cc}) and in the bladder (D_{2cc}) for the I-125 seeds implant were 0.208 and 0.882 respectively, while for Pd-103, the ratios were 0.232 and 1.512 respectively. The D_{90}/D_{2cc} dose ratio in the bladder and rectum for the Pd-103 seeds was higher than the one obtained with the I-125 seeds.

DISCUSSION

The following effects were taken into consideration in the present simulations: self-absorption in the matrix and in the metal casing of the seeds; interseed attenuation; tissue heterogeneity, including high densities in bone regions and present empty spaces; boundary effect and proximity with external air. This fact differentiates the method in the present article from the analytical calculations utilized for dosimetry in brachytherapy recommended by the AAPP Task Group 43, which considers an infinite homogeneous water-equivalent medium[10].

The maximum absorbed dose in the urethra was below the threshold doses of the value $D_{10} < 150\%$ and $D_{30} < 130\%$ of the prescription dose with both seeds. The D_{2cc} doses in the rectum were significantly lower than the threshold dose limit 145 Gy[24].

The doses in the most irradiated volumes of the rectum, starting from $D_{0.5cc}$, as well as in the bladder starting from D_{7cc}, are higher with the Pd-103 seeds than with I-125 seeds. This can be explained by the lower range of the Pd-103 photons, so that the energy is deposited on a smaller volume, increasing the absorbed dose in the seed surroundings. If a Pd-103 seed is close to one of the vital organs, the dose to this organ will be high. On the other hand, with the I-125 seed, the spatial dose distribution is more ample, but tending towards lower dose values per volume.

Surprisingly, high doses in the order of 100% of the prescription dose were found in the interface between the pelvic bones and soft tissues. In such region, the doses from I-125 seeds are significantly higher than the doses from Pd-103 seeds, with D_{10} = 144 Gy and D_{10} = 66 Gy for I-125 and Pd-103, respectively. Such fact may also be explained by the greater range of I-125 photons, reaching the pelvic bones with higher intensity than those emitted by Pd-103. The effects of I-125 implants on such organs must be considered in clinical situations, requiring further investigation. It is important to observe that such effect is not observed in cases where the dosimetry is evaluated with analytical models and with homogeneous medium.

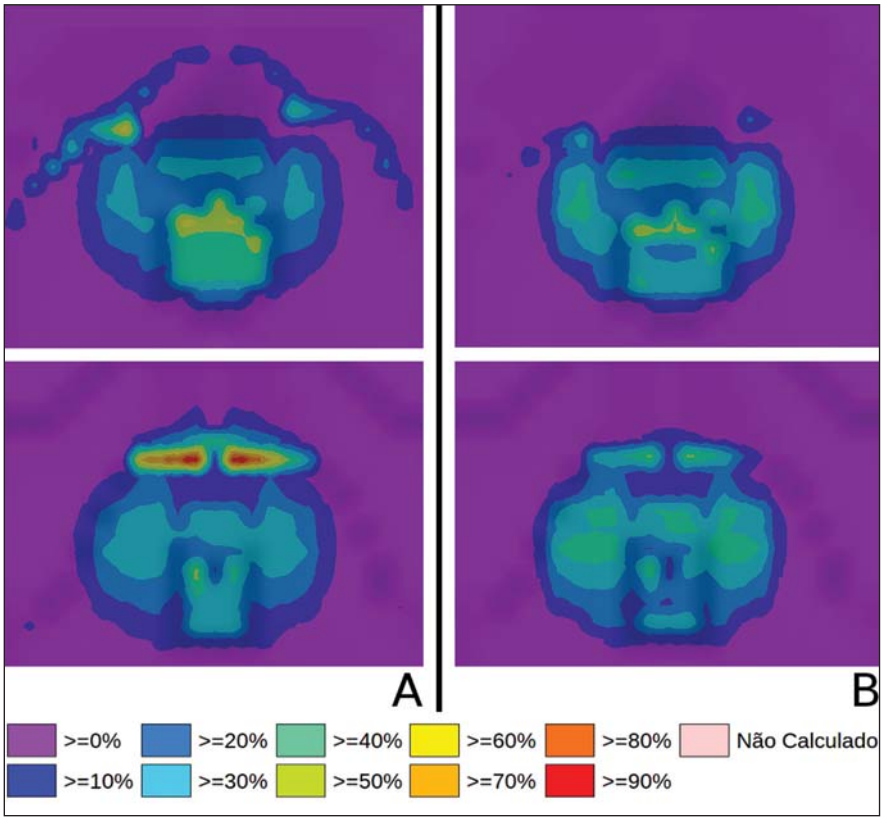

Figure 6. Spatial dose distribution in the prostate and surrounding tissues on two arbitrary axial views, for I-125 (**A**) and Pd-103 (**B**). The percentage on the caption refers to the maximum dose for each simulation. Observe the high doses in the soft tissue-bone interface, for the I-125 seeds, shown on the upper half of each image.

CONCLUSIONS

The Pd-103 and I-125 implants could deliver the prescription dose to the target volume. The Pd-103 implant is associated with a lower dose in pelvic bones, provided that the positioning of the seeds is carefully studied and that they are correctly positioned during the clinical protocol. The D_{2cc}/D_{90} dose ratio in the rectum was 11.5% higher for Pd-103 seeds. In the studied case, the Pd-103 implants deposited a higher dose in the rectum and bladder as compared to I-125 implants. The main finding of the present study was the high absorbed doses outside the target region in bone tissues adjacent to the prostate, particularly in the case of I-125 implants. The computational methods utilized in the present study can be useful in future comparative clinical evaluations of brachytherapy with I-125 and Pd-103 seeds implants, among other radioactive seeds, and can be later validated by means of experimental

trials simulating clinical protocols and dosimetry in realistic phantoms.

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