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Juste Vidal, BJ.; Miró Herrero, R.; Morató-Rafet, S.; Verdú Martín, GJ.; Peris, S. (2020). Prostate cancer Monte Carlo dose model with (177)Lutetium and (125)Iodine treatments. Radiation Physics and Chemistry. 174(108908):1-6. https://doi.org/10.1016/j.radphyschem.2020.108908

The final publication is available at

https://doi.org/10.1016/j.radphyschem.2020.108908

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Additional Information

Prostate cancer Monte Carlo dose model with ^{177}Lutetium and ^{125}Iodine treatments

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***Abstract*—Radiation Therapy Planning Systems (RTPS) presently operating in hospitals comprise algorithms founded on deterministic simplifications that do not correctly take into account electron lateral transport in the regions where there are variations in density, and as a consequence, erroneous dose estimations could be generated. According to this, the possibility of using the Monte Carlo (MC) method in radiation planning systems is proposed in this work, since this technique could affect positively on the patient treatment. The proposed methodology provides 3D dose results that are more accurate and considers the inhomogeneities density variations. This paper presents a MC simulation of two different prostate cancer treatments using the latest version of MCNP, v.6.1.1; brachytherapy with ^{125}I seeds and radiolabeled ^{177}Lu-PSMA. To that, a 3D model of the anatomy of a real anonymized patient is created from the segmentation of Computed Tomography (CT) images. Treatments over this 3D model is simulated and the dose given to the prostate and each surrounding organ is obtained for both treatments. Results have been verified with doses calculated by deterministic planning system used in hospital in the case of brachytherapy treatment, demonstrating the efficiency of MC method in the development of radiation cancer treatments, not only because of the results accuracy but also concerning the clinical affordable computing times.**

Keywords: Radiotherapy treatment planning, prostate cancer treatment, MCNP6, Monte Carlo, Brachytherapy, ^{125}I seeds, ^{177}Lu-PSMA

1. Introduction

Prostate cancer is the second most common primary tumor affecting men worldwide. Despite improvements in therapy over the past decades, this cancer tends to become highly aggressive in most patients over time, ultimately causing the death of more than 250000 men each year worldwide (Mydlo and Godec, 2018).

Calculation of absorbed dose distribution in a patient before treatment is one of the main steps in radiation therapy treatment planning. The accuracy of these planning systems is a stringent issue in brachytherapy or radionuclide treatment because of the high dose rates and prescribed dose per session. Thus, inaccuracies in dose distributions may lead to a higher dose to limiting normal tissue or lower target dose (NCCN, 2012).

Recent publication of Prostate Cancer Results Study Group (Skowronek, 2017; Grimm, 2012), states that brachytherapy is one of supreme curative options for prostate cancer. Normally, dose distributions for prostate brachytherapy treatments are estimated by analytical RTPS that use deterministic simplifications and the superposition principle of individual seed dose distributions to calculate the total dose distribution.

Moreover, dose distributions for brachytherapy treatments having significant material heterogeneities are not currently well-modeled using conventional RTPS since electron lateral transport is not well considered (Perez-Calatayud, 2014; ANS, 2017).

While numerous patients present with localized or lethargic disease, there are still a significant number of men that finally progress to advanced metastatic disease. In patients who fail primary treatment of curative intent (radical/partial prostatectomy or primary radiotherapy), radionuclide therapy has gained increasing importance for the treatment of metastatic prostate cancer. Recent published studies have raised the possibility of targeted radionuclide therapies such as ^{177}Lutetium-PSMA (prostate-specific membrane antigen) as a viable therapeutic option in men with metastatic prostate cancer (Emmett et al., 2017).

Before finding general use in the clinic, Monte Carlo simulation is an excellent tool to define the dosimetry of ^{177}Lu-PSMA, so as to enable administration of the optimal treatment activity, allowing tumor irradiation with the maximum absorbed dose without exceeding the recommended thresholds for critical organs.

The aim of this work is to demonstrate the possibility of establishing Monte Carlo as an accurate tool for planning technique in prostate clinical treatments where the conventional approach could be not acceptable, but also in promising experimental treatments where simulations could optimize the curative strategies. In this work, brachytherapy and ^{177}Lu-PSMA treatment doses are analyzed:

- Brachytherapy: Brachytherapy is a safe and effective treatment for localized prostate cancer. ^{125}Iodine low dose rate brachytherapy is an effective modality to administer a high dose to the prostate while minimizing toxicities for the adjacent organs at risk (Stock et al., 2006). Such technique utilizes sealed radioactive sources positioned adjacent to or in the interstitial 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.

- ^{177}Lu-prostate-specific membrane antigen (PSMA) radioligand therapy using inhibitors of PSMA is a novel and promising theragnostic concept (imaging diagnostics and targeted radionuclide therapy) of prostate cancer and its metastases (Fendler et al., 2017; Rahbar et al., 2018). ^{177}Lu is a therapeutic beta-emitter (E_{max} of 498.3 keV) radionuclide, useful for producing cytotoxicity in malignant tumors, but also a gamma-emitter ($E = 208$ keV), which makes its use for SPECT (single photon emission computed tomography) imaging possible. Radioligand therapy is started by intravenous application of ^{177}Lu-PSMA, either as a slow injection by hand or via an infusion pump. On the basis of clinical need and current evidence, the therapy is being implemented in a growing number of centers worldwide. ^{177}Lu-PSMA is not approved by the U.S. Food and Drug Administration or the European Medicines Agency, and thus formal criteria for patient inclusion have not been defined. Early clinical studies evaluating the safety and efficacy of Lu-PSMA therapy have demonstrated promising results with a significant proportion of men with metastatic prostate cancer, who have already failed other therapies, responding clinically well to Lu-PSMA (Virgolini et al., 2017; Baum et al., 2016). All patients that receive ^{177}Lu-PSMA treatment under compassionate use condition are informed about the experimental nature of the ^{177}Lu-PSMA therapy and are asked to give written informed consent. In most cases, this treatment only improves the patients quality of life and extends the life expectancy by a few months.

Calculation time has been always a limitation to the clinical access of Monte Carlo methods, but this project demonstrates that accurate dose values can be achieved with clinically viable rapidity in brachytherapy, because of the simplicity of the sources and patient's models, and the use of parallel computing. To achieve this objective, a 3D model has been created from CT images segmentation of the pelvis area of a real anonymized patient. This model was meshed and used to simulate the prostate brachytherapy treatment using the latest version of MCNP, v.6.1.1. Subsequently, dose results are

compared with doses of clinical RTPS in the case of brachytherapy treatment using deterministic methods, validating the MC methodology.

2. Methods and materials

2.1. CT images segmentation and 3D model creation

In this work, the segmentation objective is to create volumes from segmented slices and to export them in a recognized format by Abaqus/CAE to be meshed correctly (Dassault Systèmes, 2014). Different software allows CT images segmentation, but Materialise-Mimics (Materialise. Mimics Medical) has been selected because it contains the 3-Matic plugin that allows geometry exportation in ".step" format.

The segmentation procedure consists of delimiting the different organs of interest from all the CT slides based on gray-level information, i.e., consists of dividing the image into groups of pixels, so that each group is labeled as an independent structure. Segmentation aims to create volumes and 3-Matic exports those structures in a compatible format with Abaqus/CAE ".step" in order to be meshed.

Bones are segmented with an automatic tool, which allows the user to designate, with points, where are located and finally creating a new mask which will include all the pixels labeled as bone. Despite it, it is necessary to make posterior manual corrections (Cabrejas et al., 2012).

The soft organs segmented are the prostate (organ being treated) and the urethra and rectus (organs to protect), since they are of greater interest in this type of treatment. These volumes are segmented manually with the help of anatomical bibliography, as there is no automatic tool to differentiate them from the rest of soft tissue.

The last mask that is created is the one that contains all those parts that are within the CT image but have not been yet segmented. To that, a first mask that selects all the volumes it is created and subsequently all the other structures already segmented are removed using a tool that allows Boolean operations between masks.

Once all the parts are segmented, Mimics software is able to calculate a 3D volume from each of them, as shown below (Figure 1). This figure shows four different segmented volumes: prostate, urethra, bone and soft tissue.

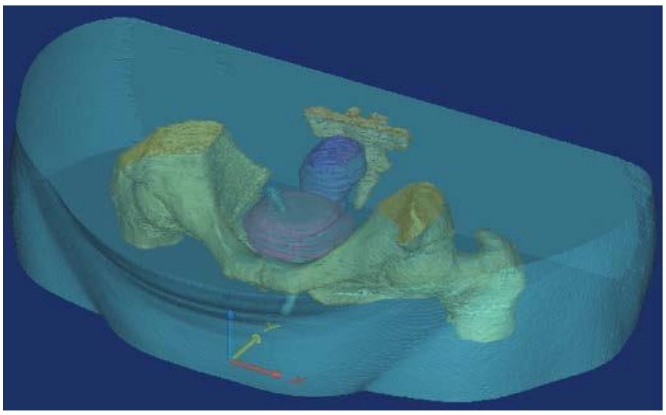

Figure 1. Patient pelvis 3D model separated into four different segmented volumes.

The 3D model is imported to the program *3-Matic* where the meshing process takes place, and the geometry is exported in ".step" format to be used by Abaqus software next. The meshing is performed to obtain the optimum size of the elements that compose it. The software 3-Matic allows geometry improvements to facilitate the size mesh selection by using the tools of anti-aliasing, gap-filling, wrapping, and automesh.

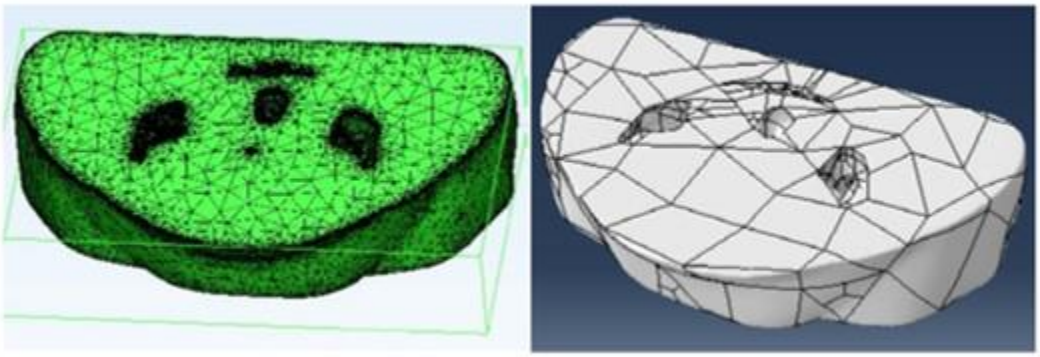

Figure 2. Visualization of a Meshed geometry part with 3-Matic (Left). Geometry imported in Abaqus/CAE in ".step" format (Right).

2.2. Mesh with Abaqus/CAE

It is necessary to use Abaqus/CAE software to generate the mesh geometry since it creates the mesh in ".inp" format, accepted by the MCNP6 software (Martz, 2017). This mesh will not work properly when performing the simulation if several parameters are not applied while using Abaqus.

The first step is to import all parts in ".step" format created with the software *Mimics*, as shown in Figure 2. When importing, the scaling option is used to achieve that the organs volumes have the same size as the real. Then, the meshes are generated. The type of mesh used in this work is unstructured mesh, i.e. those that use elements of different types or sizes, with the aim to modeling geometries more difficult and also use the optimal number of elements. In addition, within the mesh types accepted by MCNP6 (based on tetrahedrons, pentahedra or first and second order hexahedron) we used tetrahedrons of first order. In this case, the mesh is able to adjust the geometry calculations without such expensive as tetrahedrons of second order, where elements rather than straight faces and edges can be curvilinear. Finally, the file ".inp" is generated, where all the geometry information is stored.

The use of meshed geometries, presents the advantage of a higher accuracy in the geometry modelling which is reflected in an increased precision. Unstructured meshes enable the use of cells of different types and/or different size, allowing complex geometries and optimizing the number of cells used according to the needs. That is why, for the present work, we have used unstructured grids imported from Abaqus/CAE.

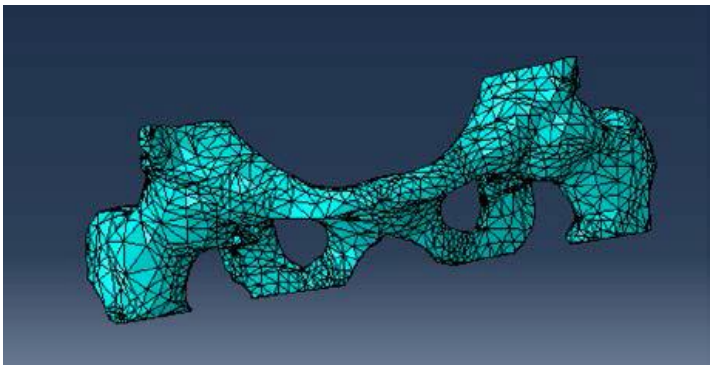

Figure 3. Meshed geometry part with Abaqus/CAE.

As shown in figure 3, the non-structured mesh elements are smaller in those areas where the geometry is more complex, and on the other hand are greatest in the areas of simpler geometry.

2.3. Sources location

The modelled geometry must include a source indicating particle type, location, source type and other characterization aspects. Energy spectra are obtained from Janis 4.0 (Nuclear Energy Agency, NEA) and contrasted with data from the NNDC (National Nuclear Data Center) and NCRP58 database (NCRP).
As this work analyzes two different cancer prostate treatments, each case contains a different source model.

2.3.1. Brachytherapy treatment

According to medical reports taken from the patient, for the treatment of a prostate tumor with brachytherapy, 71 cylindrical ^{125}I seeds were introduced to him.

To perform the simulation, it is necessary to locate each one of the seeds within the created 3D model. A medical document is available with the x, y, z coordinates of the 71 seeds. These coordinates must be transformed to the MC input coordinates.

Due to the type of treatment that is intended to simulate, sources are defined as punctual. The variables that are included in the definition of the source are: the type of particles (photons), the exact location of each seed and the energy and probability of emission of each of them, following a discrete energy distribution according to the ^{125}I disintegration (decays through the emission of a low-energy (35.49 keV) gamma rays and characteristic X-rays).

2.3.2. ^{177}Lu-PSMA treatment

The decay mode of the radionuclide ^{177}Lu presents a particular advantage for therapeutic dosimetry, as its beta emission provides tumor irradiation, while its gamma component allows uptake quantification by serial scintigraphy and SPECT. ^{177}Lu has two main photon energy peaks that could be used for imaging: one at 208 keV and one at 113 keV. The 208 keV peak has a higher incidence (10.4%) compared with that of 113 keV (6.8%).

Approximately 3.6 GBq of Lu-PSMA (Delker, 2015) is applied by a slow intravenous injection (30–60 sec) in a volume of 5 mL (diluted with 0.9% sterile sodium chloride solution), followed by a flush of sterile 0.9% sodium chloride. According Delker (Delker, 2015) the critical absorbed dose reported for tumor lesions (prostate when no radical prostatectomy has been undergone) range between 1.2 and 47.5 Gy (13.1 Gy/GBq) per cycle. Normally, a prostate Lu-PSMA treatment fractionates the patient administered activity in several independent sessions (cycles).

In this work, doses to surrounding prostate organs that are not estimated in the bibliography (rectum and urethra) have been calculated in the case of patients with no radical prostatectomy. To that, it has been assumed that the highest activity (0.12 GBq) is deposited the in prostate tumor, so the simulation includes a volumetric source corresponding to the prostate volume with this source activity. Due to the type of the intended simulated treatment, the source is defined as volumetric. A volumetric source uniformly distributed in prostate volume was included in the simulation using the VOLUMER command of MCNP6 (Figure 4).

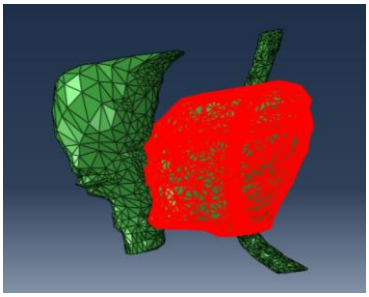

Figure 4. Location of source uniformly distributed in prostate volume adjacent to urethra and rectum.

2.4. Monte Carlo Simulation

The Monte Carlo code is based on an iterative statistical process to estimate random pathway transport and interactions of photons and electrons emitted by the sources in three dimensions, having the ability to record results of such interaction particles (tally).

The code used in this work is MCNP6.1.1 (Monte Carlo N-Particle) (MCNP6, 2014). Numerous input constraints are essential for an accurate simulation, including scattering and absorption behavior, medium materials characteristics and the number of simulated primary particles.

In general, Monte Carlo simulations are quite extensive compared with traditional treatment planning systems used in hospitals, since they consider tissue penetration depth, energy loss, bremsstrahlung photons and cross-fire dose with detail in heterogenous mediums and complex geometries.

To be able to perform the simulation it is necessary to create the input file in the correct MCNP format. Some important parts of this file is the definition of the "tallies". Three F4 type tallies are used, one for each entity where the received dose is studied. The F4 tally, provides flux in units of #/cm^2·s (by emitted particle), but flux-to-dose conversion multiplier factors are introduced to get average doses results. I.e., Gy/s received by each organ are obtained. The multiplying coefficients are the mass energy linear absorption coefficients (μ_{en}/ρ) (data obtained from NIST, National Institute of Standards and Technology) (National Institute of Standards and Technology). In addition, it is also implemented another factor that converts the MeV/g to J/kg ($1.60218 \cdot 10^{-10}$).

To simulate the received dose of prostate adjacent organs, MODE P, E has been activated to follow tracks of photons and electrons. In all cases, at least 1×10^8 initial particles of radionuclide sources were simulated to obtain uncertainties lower than 3% in all evaluated points. Those electron with energies lower than 1 keV were not tracked, but their energy was considered to be deposited locally.

To speed up the calculations without compromising the accuracy of the results, the MCNP6 (version 6.1.1) code has been parallelized in SENUBIO ISIRYM research group´s cluster Quasar using the MPI protocol with 32 processors.

3. Results

3.1.Conversion to absolute dose

3.1.1. Brachytherapy treatment

MCNP provide results of dose (Gy) per second and emitted particle. To convert this value to absolute dose, the procedure based on the Air Kerma Strength (*Sk*) is used. The *Sk* is a measure of the source intensity of brachytherapy, specified in terms of Kerma rate in air at a point along the transverse axis of the source in vacuum. This value is obtained by performing a simulation with specific characteristics. The unit of the *Sk* is U (cGy·cm^2·h^{-1}).

The type of seeds implanted in the analyzed patient is this work is the ^{125}I *SelectSeed*. *P. Karaiskos* et al. (Karaiskos et al., 2001) presented the dosimetric data of this seeds, including the value of *Sk* = $2.17 \cdot 10^{-8}$ (U/Bq). Once obtained the *Sk* and the simulation results $\dot{D}$, according to AAPM Report n.51 "Dosimetry of Interstitial Brachytherapy Sources" (AAPM Report n.51), these values are divided to obtain the dose rate constant, Λ. The dose rate constant is defined as the dose rate in water at a distance of 1 cm in the transverse axis of a source of 1 U in a water phantom. It is defined mathematically as:

$$\Lambda\left(\frac{cGy}{h \cdot U}\right) = \frac{\dot{D}\left(\frac{cGy}{Bq \cdot h}\right)}{Sk\left(\frac{U}{Bq}\right)} \qquad \text{(eq. 1)}$$

Before each particular implant, the physicist measures the value of *Sk* of seeds (Sk_{user}) with a calibrated ionization chamber. After that, to calculate the dose rate, the dose rate constant, Λ, is multiplied by Sk_{user}, offered in patient's documents (Nat, 1995).

$$\Lambda\left(\frac{Gy}{h \cdot U}\right) \cdot Sk_{user}(U) \quad \text{(eq. 2)}$$

The result is integrated over an infinite time (permanent implant) and multiplied by the number of seeds, obtaining finally the total dose by organ.

Figure 5 shows 3D distribution of absolute dose results and isodose curves inside the whole pelvis model.

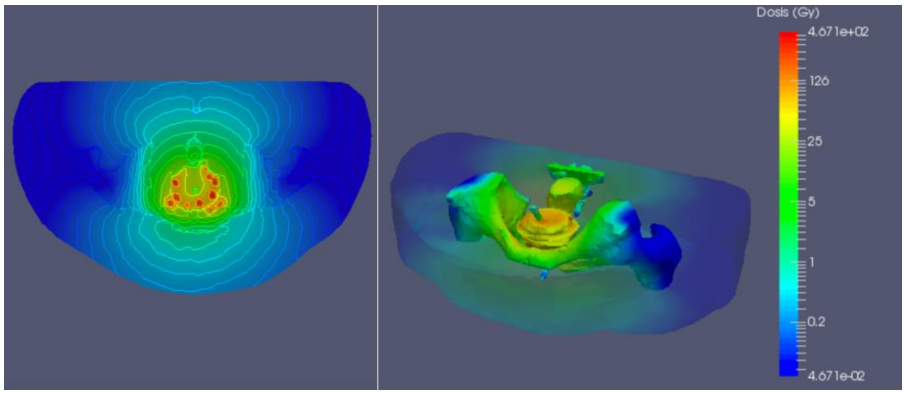

Figure 5. Isodose curves and 3D dose distribution calculated with MCNP6 inside the pelvis model.

3.1.2. ^{177}Lu-PSMA treatment

In this case, a metastasis prostate cancer patient with no radical prostatectomy bibliographic case has been followed. The absorbed doses from ^{177}Lu were calculated by multiplying the MCNP6 results by a conversion value derived from the total number of disintegrations per radioactivity unit (Bq), based on the experimental biokinetic results described in (Delker, 2015). Knowing that the absolute dose at prostate is 47.5 Gy (Delker, 2015) and obtaining MCNP results in dose rate $\left(\frac{Gy}{s \cdot part}\right)$, the activity (Bq) at prostate is calculated according:

$$\boldsymbol{Absolute\ dose\ (Gy) = dose\_rate}\left(\frac{\boldsymbol{Gy}}{\boldsymbol{s \cdot part}}\right) \cdot \frac{\boldsymbol{Bq}}{\boldsymbol{\lambda}}\boldsymbol{(part \cdot s)} \qquad \text{(eq. 3)}$$

Being λ the decay constant of ^{177}Lu (half live 6.65 days). According to this, the prostate initial activity for ^{177}Lu source at the implantation moment is 0.12 GBq, and this is the value used in this case to convert relative MCNP results in absolute dose. Moreover, results have considered that 3 cycles of radioligand therapy separated by eight weeks have been applied (Fendler, 2017), although some studies establish up to 6 cycles.

3.2. Results validation

(Delker, 2015) studied the critical absorbed dose for tumor lesions (i.e. prostate when partial prostatectomy was undertaken) vary among 1.2 and 47.5 Gy (13.1 Gy/GBq) per cycle. For this intention-

to-treat activity of 3.6 GBq (range 3.4 to 3.9 GBq), the average absorbed doses per cycle were 2.2±0.6 Gy for the kidneys (0.6Gy/GBq), 5.1±1.8 Gy for the salivary glands (1.4 Gy/GBq), 0.4±0.2 Gy for the liver (0.1 Gy/GBq), 0.4±0.1 Gy for the spleen (0.1 Gy/GBq), and 44±19mGy for the bone marrow (0.012Gy/GBq). Other authors (Scarpa, 2017) state high tumor doses for skeletal (3.4 ± 1.9 Gy/GBq), lymph node (2.6 ± 0.4 Gy/GBq) as well as liver (2.4 ± 0.8 Gy/GBq).

In this study, as explained, a flux tally associated to the conversion factors is applied to each organ, providing dose (Gy) per second and emitted particle received by each organ.

Organs at risk analyzed for a critical radiation dose are the prostate, rectum and urethra. The radiation estimated dose to these organs can be seen at Table 1. Applying the procedure explained in the previous section total doses can be obtained, as shown in the following table.

Table 1. Total dose received in each organ calculated by Monte Carlo simulation

Dose (Gy)	Prostate	Rectum	Urethra
^{125}I seeds	170.88	27.3	44.96
^{177}Lu-PSMA After 3 cycles applied	135	2.49	60.98
^{177}Lu-PSMA After 6 cycles applied	270	4.98	121.96

As Table 1 shows, dose received by organs are quite high values, which proves the acute side effects that these prostate treatments produce to the patient. In particular, the associated high doses to the organs (especially to urethra) after a common 6 cycles treatment with the lutetium therapy justifies that only patients with severe metastases and short life expectancy can receive this type of palliative treatment.

To validate calculations, brachytherapy results (^{125}I seeds) have been compared with a real patient's medical report, where the prostate dosage prescribed by the doctor was 160 Gy. I.e. 90% of prostate must receive at least this amount of dose. This means that the total of the prostate will receive a slightly higher dose value. Therefore, the result of 170.88 Gy is a fairly coherent and accurate value.

According to dose values calculated at the two organs of risk: urethra and rectum, the coincidence of the planning values with the results obtained by Monte Carlo is also accurate, with a percentage difference of 8%. Moreover, in the patient's medical report, the prostate dosage prescribed by the doctor was 160 Gy. I.e. 90% of prostate must receive at least this amount of dose. This means that the total of the prostate will receive a slightly higher dose value. Therefore, the result of 170,88 Gy is a fairly coherent and accurate value.

It is important to note that these adjacent organs receive a quite high dose despite being considered organs at risk and performing the treatment planning to its minimum irradiation.

The validation of the model with the previous described brachytherapy treatment, allows to assume the accuracy of the simulation. Based on this prior verification, and since the only difference between the two analyzed treatments is the source definition, it can be established that the results obtained with the ^{177}Lu-PSMA treatment are also correct.

3.3.Computation time

Computation time is a very important aspect when assessing the use of Monte Carlo in cancer treatments routines, in fact, the length of the simulation times remains the last major difficulty to translating the Monte Carlo method into clinical practice. While simulations are exceptional in accuracy to usually used analytical dose calculations, they involve considerably longer computation times. One of the purposes achieved in

this work has been to characterize a Monte Carlo model simplification to increase computation speed without compromising dosimetric precision.

On the one hand, several variance reduction techniques have been applied to improve the efficiency of the dose estimation, such as region importance splitting and transport cutoffs. But the greatest effort in reducing calculation times has been aimed at optimizing the geometric model. For this purpose, two geometries and their associated calculation times for obtaining accurate results have been studied. One of them includes the whole detailed region of the pelvis with each of the organs included. In the second simplified model, only the main volumes in which the doses are being studied are included: the prostate, rectum and urethra.

Moreover, to speed up the calculations without compromising the accuracy of the results, the MCNP6 (version 6.1.1) code has been parallelized in SENUBIO ISIRYM research group's cluster Quasar using the MPI protocol with 32 processors.

Table 2 shows the processing CPU time needed to simulate the two different geometry models. The first model includes in the simulation the complete segmented pelvis and the second model eliminates parts of the geometry just keeping the organs of interest. Results for both models were almost identical.

Table 2. Monte Carlo processing CPU time

Simulation	Number of processors	Computation time
The whole geometry model	31	16.13 hours
Prostate, rectum and urethra model	31	2.21 hours

The aim of simplifying the geometry model is to demonstrate the drastic reduction of simulation time while preserving dosimetric accuracy. Nowadays medical plans consider normally the segmentation of just these three organs since they are the ones intended to protect by setting dose limits.

Considering the clinical methods and creating a model with only those three bodies, the Monte Carlo method is an acceptable method offering accurate results and short computing times. If other parts of the anatomy were included, as done in this work, MC offers the possibility of obtaining the dose received in any area of the patient or entire structures such as bone tissue of the pelvis.

4. Conclusions

This study proves the precision of Monte Carlo dose distributions estimations for clinical use in traditional prostate brachytherapy treatments but also in novel therapeutic options such as radionuclide treatments. The principal benefits of Monte Carlo simulations are the competence to account for an inhomogeneous radioactivity distribution, induction of secondary particles, transitions between tissue types, and patient-specific organ and lesion geometries. For the latter, the use of meshed geometries to model and segment patients is the main novelty of this Monte Carlo study and presents the advantage of a higher accuracy in the geometry modeling, which is reflected in an increased absorbed dose estimation exactitude. Moreover, 3D dose distributions are easily obtained and allow to perform dose limitation in neoplastic areas decreasing in the adjacent organ at risk.

Results obtained from the MCNP6 simulation are consistent with doses prescriptions in the medical report analyzed for a ^{125}I seeds prostate treatment. Doses in prostate and surrounding organs at risk have been compared with doses prescribed and calculated using deterministic methods used at the hospital validating Monte Carlo simulation results, since percentual difference is below 8%.

Once the simulation was validated with the classic seed treatment, the generated Monte Carlo model allowed the study of doses in other prostate cancer treatments for more advanced cases that lead to metastasis. In particular, there is a targeted radionuclide therapy option with ^{177}Lu-PSMA that is still under experimentation and testing phase, for which this type of simulation allows to calculate the doses that the patient would receive accurately. Thus, we can conclude that the use of Monte Carlo simulations is a fundamental tool for the optimal implementation of new treatments.

Dose values obtained in organs demonstrate the severe side effects that these prostate treatments produce to the patient. In particular, lutetium therapy is a promising treatment, but the associated high doses given to the organs (especially urethra) reveals that this treatment is only given to patients with severe metastases and short life expectancy.

Monte Carlo computing times is an important issue regarding the implementation of this method in the treatments planning routines. As more complex is the model developed and the physics considered in particles transport, the needed time for the simulation can be increased significantly. In this case, a balance between accurate results and simulation time has been achieved applying several variance reduction techniques and considering just the important anatomical structures for this prostate study. The required simulation time for obtaining precise and detailed results with the presented methodology is around two hours, which is acceptable for clinical practice. Nevertheless, the computer speed will not pose a problem in the next future, due to the great advances of the new processors and parallel computing capacities.

This work has proved that the accuracy and efficiency of the parallel Monte Carlo dose calculation methodology both for well proven brachytherapy treatments and for new promising treatments such as ^{177}Lu-PSMA, making particles simulation tools attractive for clinical applications.

ACKNOWLEDGMENT

The authors wish to thank the *Hospital Universitari i Politècnic la Fe de València* for the given information and all its kind support in this work.

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