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Original paper

3D Monte Carlo dosimetry of intraoperative electron radiation therapy (IOERT)

Husein Alhamada[a,b,*], Stephane Simon[a,b], Catherine Philippson[b], Christophe Vandekerkhove[b], Younes Jourani[b], Nicolas Pauly[a], Dirk VanGestel[b], Nick Reynaert[a,b]

[a] Nuclear Metrology, Ecole Polytechnique, Université Libre de Bruxelles, Bruxelles, Belgium
[b] Radiothérapy Department, Institut Jules Bordet, Bruxelles, Belgium

A B S T R A C T

Purpose: This paper studies the feasibility of using Monte Carlo (MC) for treatment planning of intraoperative electron radiation therapy (IOERT) procedure to get 3D dose by using patient's CT images.
Methods: The IOERT treatment planning was performed using the following successive steps:
I) The Mobetron 1000® machine was modelled with the EGSnrc MC codes. II) The MC model was validated with measurements of percentage depth doses and profiles for three energies (12, 9, 6) MeV. III) CT images were imported as DICOM files. IV) Contouring of the planning target volume (PTV) and the organs at risk was done by the radiation oncologist. V) The medical physicist with the radiation oncologist, had chosen the same parameters of IOERT procedures like energy, applicator (type, size) and using or not bolus. VI) Finally, dose calculation and analysis of 3D maps was carried out.
Results: The tuning process of the MC model provides good results, as the maximum value of the root mean square deviation (RMSD) was less than 3% between the MC simulated PDDs and the measured PDDs. The contouring and dose analysis review were easy to conduct for the classical treatment planning system. The radiation oncologist had many tools for dose analysis such as DVH and color wash for all the slides. Summation of the 3D dose of IOERT with other radiotherapy plans is possible and helpful for total dose estimation. Archiving and documentation is as good as treatment planning system (TPS).
Conclusions: The method displayed in this paper provides a step forward for IOERT Dosimetry and allows to obtain accurate dosimetry of treated volumes.

1. Introduction

Intraoperative electron radiation therapy (IOERT) is the deposition of high doses to the potential residual tumor cells during the surgical intervention. Direct vision of the treated area, limitation of the dose deposition to the target and sparing healthy organs present IOERT as a favorite technique [1,2]. IOERT has been in clinical use more than 45 years, and it has showed increasing interest since 2000 when a dedicated mobile accelerator become available in operation rooms [3,4].

IOERT is a complex technique and it is considered to be challenging for many reasons:

A. Uniform global standardizations have not yet been adopted and there are many guidelines and protocols that provided by AAPM and IAEA [5,6]. The global protocols have common aspects like depth and dose prescription but on other hands they do not agree for other points like considering tissue heterogeneities, shielding disk material and target volume.
B. Shortage of the treatment planning systems (TPS) for IOERT is a main obstacle. The variety of the anatomy of the patient's candidates and the variety of the tumor locations and sizes impose the necessity to have 3D dosimetry. Determination of the best parameters of IOERT procedures for real patients depends on the 3D dosimetry of the treated area which in turn presupposes using a TPS [7].
C. IOERT procedures require good organization and cooperation of the multidisciplinary team (the radiation oncologist, the medical physicist, the surgeon, the anesthetist, the nurses, etc.), whereas there is no information system that supports the IOERT procedure [8].
D. Documentation of the IOERT procedure is poor. The documentation and the archiving of IOERT dosimetry are done by filling a form with IOERT parameters in most of the centers. This is a vital step, especially when the patient should have a complementary radiotherapy session to the same organ [9].

Many algorithms are reported for dose calculation of electron external radiotherapy such as pencil beam (PB) and Macro MC (MMC) [10,11]. The dose algorithms have fast calculation time, but they have limited accuracy for many reasons such as the electron transport in low-density regions. The calculation algorithms face challenges in the buildup dosimetry. The dose calculation in a heterogeneous media

* Corresponding author at: Nuclear Metrology, Ecole Polytechnique, Université Libre de Bruxelles, Bruxelles, Belgium.
E-mail address: Husein.alhamada@ulb.ac.be (H. Alhamada).

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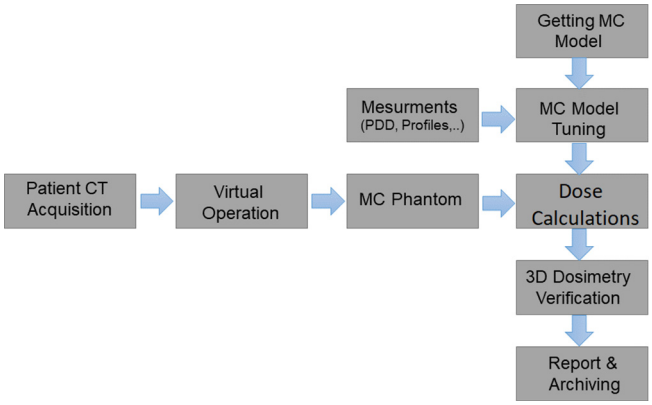

Fig. 1. Diagram research methodology for 3D IOERT patient dosimetry.

depends on the used algorithm, in which the absorption and the scattering of the beam are not equal. Monte Carlo (MC) is a golden tool of dose calculation, and it is highly demanded in clinical use for routine dose calculations [12,13]. MC computational time has been reduced to acceptable levels of clinical usage due to the tremendous developments of computer processors and improvements in MC codes.

The aim of our research is thus to develop an independent 3D dosimetry system for IOERT by using Monte Carlo, which includes a surgical simulation, 3D dose verification tools, and improve archiving duties of IOERT. This study applied post-operation by using the same IOERT parameters (Applicator size, position of the applicator, energy, …).

2. Material and Methods

Proposed methodology of this study composes of some steps as illustrated in Fig. 1. Getting a valid MC model of Mobetron 1000 machine is the first step which requires three steps: beam modeling, phantom Measurements and tuning of MC model. 3D dosimetry planning of IOERT patient involves the following steps: contouring of target and organs at risk, virtual operation, dose calculation, 3D Dosimetry verification and finally Reporting and archiving.

2.1. Beam modeling

Mobetron 1000® (IntraOp Medical, Inc., Santa Clara, CA) is a mobile linear accelerator specifically designed for the operation room. The Mobetron 1000 produces high-energy electron beams (12, 9, 6, 4 MeV) that deliver a uniform dose to a surgically exposed target in a single fraction. The dose rate of 10 Gy/min will ultimately allow to deliver a large single dose in a limited amount of time. The gantry can be rotated ± 45° in the transverse plane, ± 30° in the radial plane and moved in a horizontal plane ± 5 cm. There are 3 types of applicators available with Mobetron 1000 which have different end type angles (0° "flat", 15° or 30°). The flat applicator diameter ranges from 3 cm to 10 cm in 1 cm increments, whereas the beveled applicators have diameters of 3, 4, 5 and 6 cm. The gantry design includes a beam stopper under operation bed, so which reduce shielding requirements on the walls of the standard operating room. The Mobetron 1000 has a soft-docking system with its applicator, where there is no hard connection between the head of the Mobetron 1000 and the applicator. The accelerator head is aligned with the applicator by using the laser/mirror system [14–16].

The accelerator head was modelled using the EGSnrc/BEAMnrc package with the data of the manufacturing company without any simplifications that could affect MC simulations results [17]. The head components modelled were: 1 – Electron source, 2 – Scattering foil, 3 – Primary Collimator, 4 – Ion monitor chamber, 5 – Secondary collimator, and 6 – Applicator. Setup of Measurements and MC simulation is illustrated in Fig. 2, where the applicator touch the water surface and the ion chamber inside the water phantom for PDDs and Profile measurement.

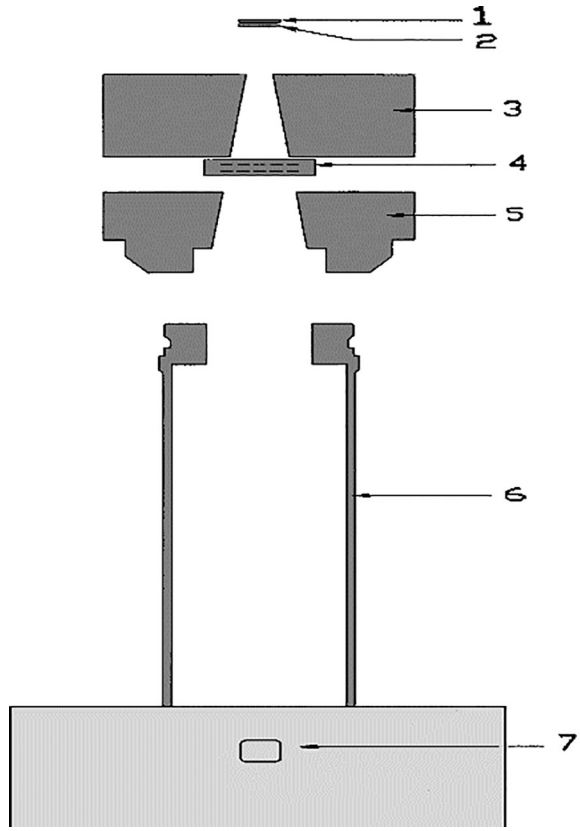

Fig. 2. Schematic overview of the model of Mobetron 1000 geometry which include: 1 – Electron source, 2 – Scattering foil, 3 – Primary Collimator, 4 – Ion monitor chamber, 5 – Secondary collimator, 6 – Applicator which it was in contact with the water surface, 7 – Moving ion-chamber inside the water phantom.

2.2. Tuning of MC model

The measurements and the simulations were performed with the same setup when the applicator was in contact with the water surface as it is illustrated in Fig. 2. PDD measurements were performed with a plane parallel ionization chamber, the "Roos chamber" (PTW, Freiburg, Germany). The ionometric data was corrected for relative air to water stopping-power ratio variation with energy and for ion recombination. The profile measurements were done with the Diode-E chamber (PTW, Freiburg, Germany) [18].

The dose distribution was calculated with the DOSXYZnrc code. For all the simulations of this study, the water phantom had a 20 cm^3 cube size and consisted of H2O521ICRU material with 1 mm^3 voxel size. The transport and particles production threshold energy for electrons were set to 521 KeV (ECUT, AE) which refers to the total energy of the electron (including electron rest mass) and to 10 KeV for photons (PCUT, AP).

The Module 9 of DOSXYZnrc was used to minimize the calculation time and to avoid using a big phase-space file. Module 9 of DOSXYZnrc launches calculation of BEAMnrc and DOSXYZnrc simultaneously, so the electrons generated at initial electron source traverse through all machine parts and calculate deposited energy in a water phantom or within patient phantom. The deposited dose at the water phantom comes from the particles (photon, electron or positron), which exit from the applicator. MC statistical uncertainty was less than 1% at PDD max

point. Without using any variance reduction techniques, the calculation time took roughly 10 h per simulation by using a dedicated cluster (2.9 GHz/64 cores/128 Gb RAM). For all the simulations, PRESTA-II (electron transport algorithm) was used [17].

The MC model tuning process includes matching the MC simulation results with standard measurements by finding the right properties of the initial electron source. The properties of the initial electron beam are the energy spectrum and the full width at half maximum (FWHM) of the Gaussian source. In the literature, it is noted that the common way for the tuning process for conventional accelerators is to iteratively change the values of the mean energy and FWHM [19,20]. Using approach of Laccarino et al. [21], the tuning approach was done by calculating PDDs using mono-energetic electrons ranging from 1 MeV up to 13 MeV with a step of 0.5 MeV. The weight factor was calculated by Eq. (1) for each mono-energy value and optimized in order to minimize the square difference of simulated and measured PDD.

$$\text{Min} \sum_i \left\| \sum_j D_j^c(Z_i) * W_j - d^m(Z_i) \right\|^2 \quad (1)$$

$D_j^c(Z_i)$ is the MC calculated PDD for mono- energy (j), $d^m(Z_i)$ is the measured PDD and W_j (≥ 0) is the weight of energy (j) in the spectrum to get the minimum difference between MC and measured values.

2.3. IOERT patients dosimetry

After having a valid MC model of Mobetron 1000, a breast patient is presented to clarify the steps of 3D dosimetry of IOERT patient.

2.3.1. The contouring

The treatment planning dosimetry uses a standard information format for all involved systems. DICOM is currently being used in many medical specialties including radiotherapy [22]. DICOM modalities were used in our study with the following objectives: RT image, RT structure, RT plan, RT dose, and RT treatment summary record.

The co-registration of multi images modalities such as MRI, CT, and PET enhances the visibility of the tumor. CT images were used for dose calculation since they consider the heterogeneity of various organs. A calibration curve of CT images should be done before using them for dose calculation. The CT calibration curve of our CT machine was done by using Catphan phantom where ranges of Hounsfield Units (HU) are assigned to specific material densities. All the CT images were imported in the Eclipse™ Treatment Planning System (Varian Medical Systems Palo Alto, CA, USA) [23].

Contouring is an essential step in radiotherapy planning. The radiation oncologist, along with a medical physicist, draws the borders of the target and the organs at risk such as the heart, lungs, and ribs in the region of interest using Eclipse™ tools like contrast and brightness. Using the same IOERT parameters which was done in the operation room, the medical physicist chooses energy, the size and type of applicator (0°, 15°, 30°), the bolus thickness and the two layers of the shielding disk.

The contouring process should simulate the real operation setup, in other words, the contouring of the applicator tip should touch the target (beneath the skin) and the shielding disk is directly above the pectoral muscles for breast patients. The manual segmentation process is a mandatory step to merge the applicator, bolus and the shielding disk with the CT images of the patient. Many measurement tools are available with Eclipse™ such as distance, angle, and volume of the tumor, so the medical physicist can choose the positions of the applicator, bolus and the shielding disk according to the tumor position in the three views (XY, XZ, YZ) as it is illustrated in Fig. 4. The user can do the contouring by using any treatment planning system of classical external radiotherapy or any open source system.

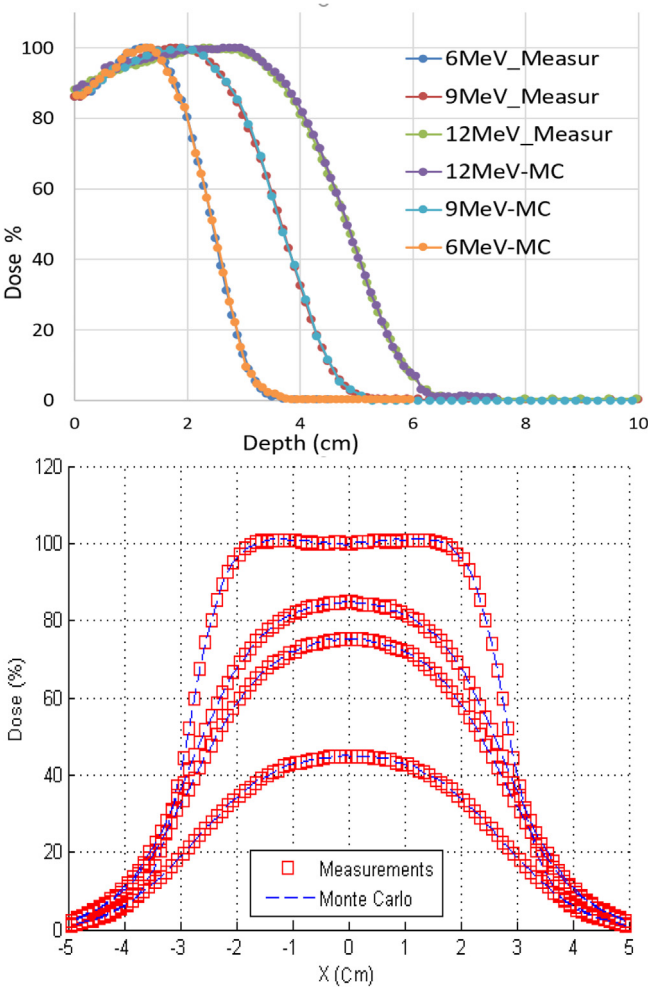

Fig. 3. MC and measurements comparison: Up: PDDs of 12, 9 and 6 MeV for 5.5 cm diameter of flat applicator. Down: Profile for electron beam energy 12 Mev /5.5 cm diameter of flat applicator at 27, 39, 43 and 50 mm depths.

2.3.2. Virtual operation

A homemade C++ code was used to change the CT Hounsfield Units values of some voxels composing some contours. The new HU for the voxels inside the contours will be as follows: 3200 for the Steel, 3100 for the Aluminum and 3000 for the PMMA. Changing the HU of CT images of the patient is necessary to get accurate dosimetry of IOERT and it is preferable to use new numbers outside the range of original HU CT which is −1024–1976 for our CT. The new HU numbers of the bolus (PMMA), the upper layer of the shielding (Aluminum) and the second layer of the shielding (Steel) have been chosen to be outside the range of the HU numbers of patient CT to convert only the contoured volume to a specific material.

After finishing the contouring and changing the HU numbers of the CT images, the CTCREATE code was used to convert the CT images of the patient to a phantom which was used for the MC dose calculation. For each used material in MC phantom, there are two lines of input in CTCREATE code. The first of these lines is the name of the material which must be identical to a material in EGSnrc material library (PEGS4). The second line specifies the maximum HU number for the material and its density range. Every voxel is assigned to a material depending on its HU number and the density is then calculated using a linear interpolation between the material's density limits [24]. Table 1 illustrates the materials and their densities for the phantom that was used for the MC calculation. The size of the voxel in MC patient phantom is customized. The larger the voxels size in the MC patient phantom, the lower the calculation time. Generally, electrons do not

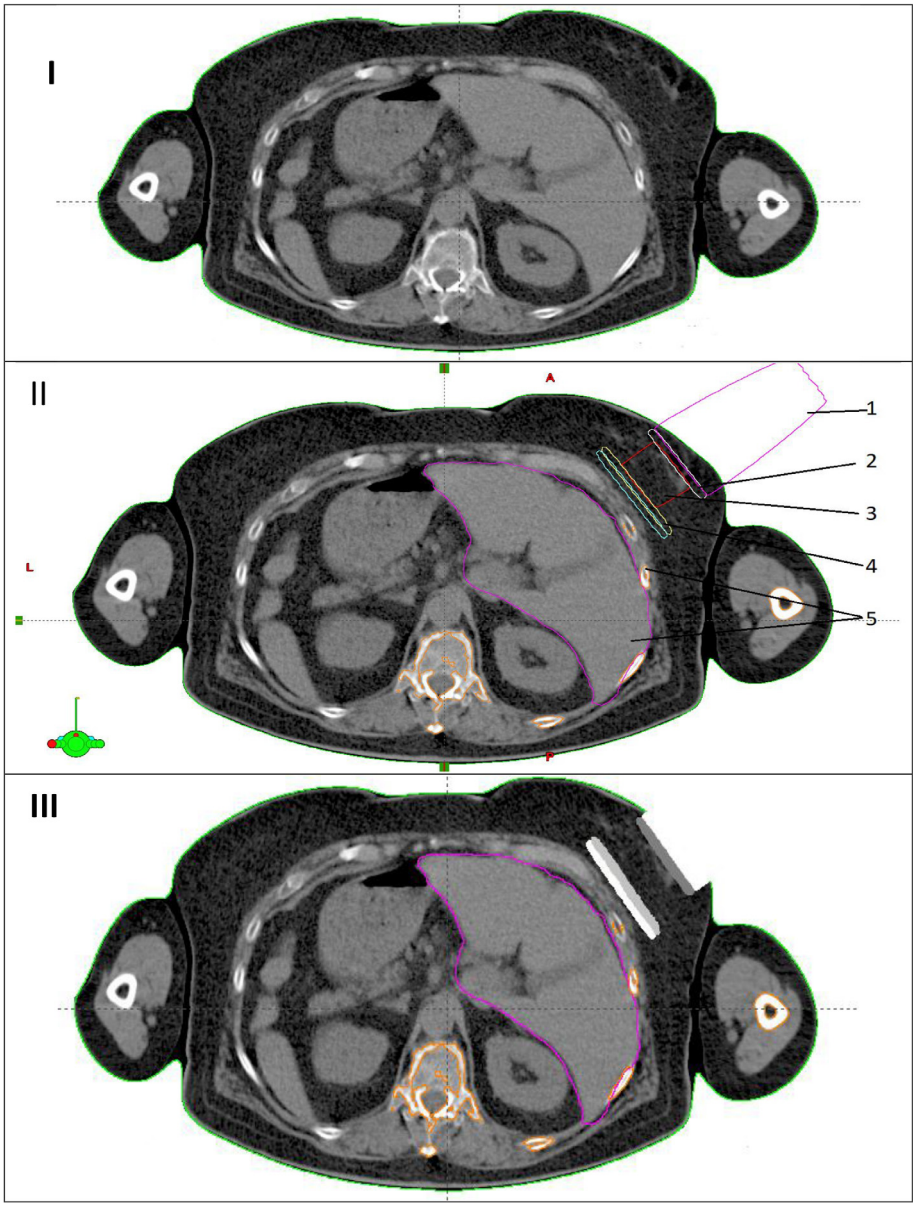

Fig. 4. I) original CT image. II) Contouring using Eclipse™: 1-The applicator, 2-Bolus (1 cm),3-Target to irradiate, 4-two layers of shielding disk, 5- organs at risk. III) CT image after the virtual operation.

Table 1
Converting parameters of CT images of the patient to a MC phantom.

HU	MC Material Name	Density (g/cm^3)	Materials
−1024–974	Air521ICRU	0.001–0.044	Air cavities inside the applicator
−974 − 100	Lung521ICRU	0.044–0.302	Lung tissue
−100–180	Tissue521ICRU	0.302–1.101	Muscles and fat
180–1976	Bone521ICRU	1.101–2.088	Bones
3000	PMMA521ICRU	1.17	Bolus / PMMA
3100	AL521ICRU	2.7	Upper shielding disk/ Aluminum
3200	Steel521ICRU	7.8	Lower shielding disk/Steel

move far from the place where they are generated compared to the photon size, so just the region of interest is converted to a CT patient phantom instead of converted full patient CT.

2.3.3. Dose calculation

The voxel dimensions were chosen as $2.5 \times 2.5 \times 2.5$ mm according to AAPM TG-105 [25]. The region of interest was just $20 \times 20 \times 20$ cm^3 of the CT patient phantom, as considering the entire CT is not useful. The time of calculation depends on many parameters like the energy, applicator size and voxel dimensions. However, MC statistical uncertainty is 1% inside the PTV for all our calculations.

MC of absorbed dose calculations was done with the DOSXYZnrc code. The deposited energy in the patient phantom is a result of the initial electrons and its secondary radiation particles (electrons, positrons, and photons). The angles of machine rotation are determined according to coordinates of the isocenter point the CT of the patient. Particles production and cut threshold energies for electron photons were set as the same values of the tuning of the MC Model. At the end of the dose calculation of MC, we obtain the 3ddose file. The normalization of the MC dose was done according to the work of Popescu et al. [26]. As there are no moving jaws in the Mobetron 1000, the backscattered component to the chamber is ignored. A homemade C++ code was used to convert the .3ddose file (MC output) to a RTdose (DICOM) file and to calculate the absolute dose according to Eq. (2).

$$D_{abs}^{MC} = D_{cal}^{MC} * MU * \frac{D_{Ref}^{Meas}}{D_{Ref}^{MC}} \quad (2)$$

with $\boldsymbol{D_{abs}^{MC}}$: the absolute dose (Gy); $\boldsymbol{D_{cal}^{MC}}$: the MC raw dose (Gy/particle incident on target), MU: the number of monitor unit, $\boldsymbol{D_{Ref}^{Meas}}$: the measured dose / MU for reference conditions (Gy/MU), $\boldsymbol{D_{Ref}^{MC}}$ (Gy/particle): the MC raw dose for reference conditions (with reference conditions: 10 cm flat applicator, source to surface distance = 54 cm, depth = 1.4 cm).

2.3.4. 3D plan evaluation

3D dose visualization could be done using DOSXYZ_SHOW, Eclipse™ or any open source software that uses DICOM images. Many tools (zoom, density, color wash) can help for dose verification on DOSXYZ_SHOW using egsphant and 3ddose files. A homemade C++ code was used to convert the 3ddose file to a DICOM (RT does) file in which the 3D dose was showed by using Eclipse™. The 90% isodose value is normalized to be the prescribed dose for example “21 or 9 Gy”. Eclipse™ enables the radiation oncologist to verify the 3D absolute dose, 3D relative dose distributions and the dose volume histogram (DVH) for the target and for the organs at risk.

2.3.5. Reporting and archiving

Patients’ data archiving is mandatory for security and late treatments duties [27]. Most of IOERT centers archive simple calculation documents and some photos during the IOERT operation for each patient, they do not have DICOM Images or 3D dosimetry files. At the end of this study, all archiving and reporting steps are developed to the level of the classical radiotherapy, which include personal information of the patient, CT/PET/MRI images, DVH, snapshots of one or many slides of the dose map, and the names of the IOERT team with their signatures for legal reasons. If the patient needs another radiotherapy treatment in the same location after few years, a physicist can calculate dose sum with IOERT dose, biologically effective dose should be considered, and radiation oncologist can thus avoid overdose for the same treated organs.

3. Results

3.1. Measurements and tuning process

It was found that the spectrum of the initial electron source that its MC simulation best matched our measurements has a mean energy of (12.43, 10, 6.75) MeV for (12, 9, 6) MeV nominal energies with a FWHM of 0.2 cm of Gaussian source in the MC model.

The value of the root mean square deviation (RMSD) is about 1.8% with a 1% uncertainty value in the region of calculation. The Monte Carlo model is well tuned also with 9 and 6 MeV as it illustrates in Fig. 3. PDDs of Monte Carlo for 5.5 cm flat applicator with 12, 9 and 6 MeV are illustrated with measured data in Figure (3-UP) whereas Figure (3-Down) illustrates the profiles of 5.5 applicator for 12 MeV at 27, 39, 43 and 50 mm depths in a water phantom. The Monte Carlo model is not tuned for nominal energy (4 MeV) as it is not used clinically in our center.

3.2. Contouring and virtual operation

Contouring of the target which is always under the applicator and above the shielding disk, the organs at risk, the applicator, the bolus and the shielding disk were done by using the contouring section of Eclipse™. The fusion process includes manual moving and rotating of the applicator, bolus and two layers of the shielding disk on the CT images on XY, YZ and XZ planes.

We have studied 20 cases using 6, 9 or 12 MeV energies with various applicator types and diameters like 5, 5.5 or 6 cm in deferent positions. The bolus with various diameters was simulated if it was deemed necessary according to the anatomy of the patient. The shielding disk (4 mm Al + 4 mm Steel) was simulated, when it was possible according to the position of the treated volume. The shielding disk is inserted exactly above the pectoral muscles for the breast patients. A 90% isodose line should cover the target volume, and according to the thickness of the target, the radiation oncologist and the medical physicist choose the energy and thickness of the bolus. The material of the PMMA bolus was simulated, if it was necessary to have good coverage of the target.

A good alignment between the applicator and the shielding disk was considered for all the patients. The same patient setup for CT and for the IOERT operation was assumed. In our study we have considered that the patient body consists of only seven materials with different densities.

The virtual operation mimic real patient setup before irradiation so the shielding disk took place of the tissue above pectoral muscles. The tissues above bolus and that one which bolus took its place in Fig. 4 were removed after the virtual operation, the oncologist suppose these tissues were cut off during surgery or they were pulled out of radiation path. Fig. 4-I shows a slide of CT image of a candidate patient for IOERT in left breast. Fig. 4-II illustrates the contouring step of organs at risk, the applicator and shielding disk. Fig. 4-III illustrates CT image after virtual operation, so CT images ready to use them for MC calculation.

3.3. 3D plan evaluation

IOERT parameters should achieve well coverage of the target volume and well protection for the organs at risk. Fig. 5 illustrates the isodose lines, DVH, relative dose and absolute dose. The used applicator type, applicator diameter and energy are suitable for this patient. The medical physicist can check if the shielding disk material and its position are good enough to protect the other organs. Fig. 5-A shows absolute and relative dosimetry over coronal CT images that can be verified by scrolling up and down (like any external radiotherapy treatment). DVH is illustrated in Fig. 5-B the PTV is covered with 90% of prescribed dose and well protection of the liver and bones. Applicator and shielding disk positions in 3D patient body is illustrated in Fig. 5-D whereas patient and contouring of sagittal view is illustrated in Fig. 5-C.

4. Discussion

creating MC model of the machine, validation MC model (getting same results of measurements), converting patient DICOM images to MC phantom and finally dose calculation are general successive steps of our methodology for 3D MC dosimetry which applicable for any IOERT machine. Proposed methodology is applicable for all IOERT patients such as breast, rectal, and retroperitoneal sarcoma and it is indispensable especially when it is not possible to use a shielding disk to protect the sensitive organs like the spinal cord during IOERT irradiation of sarcomas patients. 3D dosimetry of IOERT is a crucial step to have successful clinical results, it is necessary for patients who do not have enough surrounding tissue, so they have a difficult target position to treat or if the patient has artificial implant in the organs at risk like pacemaker, which the surgeon cannot see it during breast operation.

QA procedures of IOERT machine are done daily, monthly and annually but there is no end to end test for patient treatment plan. This methodology can be used as 3D dosimetry of IOERT patient or as an independent QA of treatment plan if the user has IOERT TPS.

The possibility to do a real time in the operation room or post treatment dosimetry planning depends on CT acquisition time if it has done inside the operation room or after the IOERT operation. IOERT post planning is possible by using CT images after going out from operation room with IOERT operation parameters which was already done. Post planning is more real comparing to pre-planning as the anatomy of the tumor bed probably will change during the surgery. The optimal scenario of IOERT 3D dosimetry calculation requires acquiring CT images during the operation after removing of the tumor, but this is

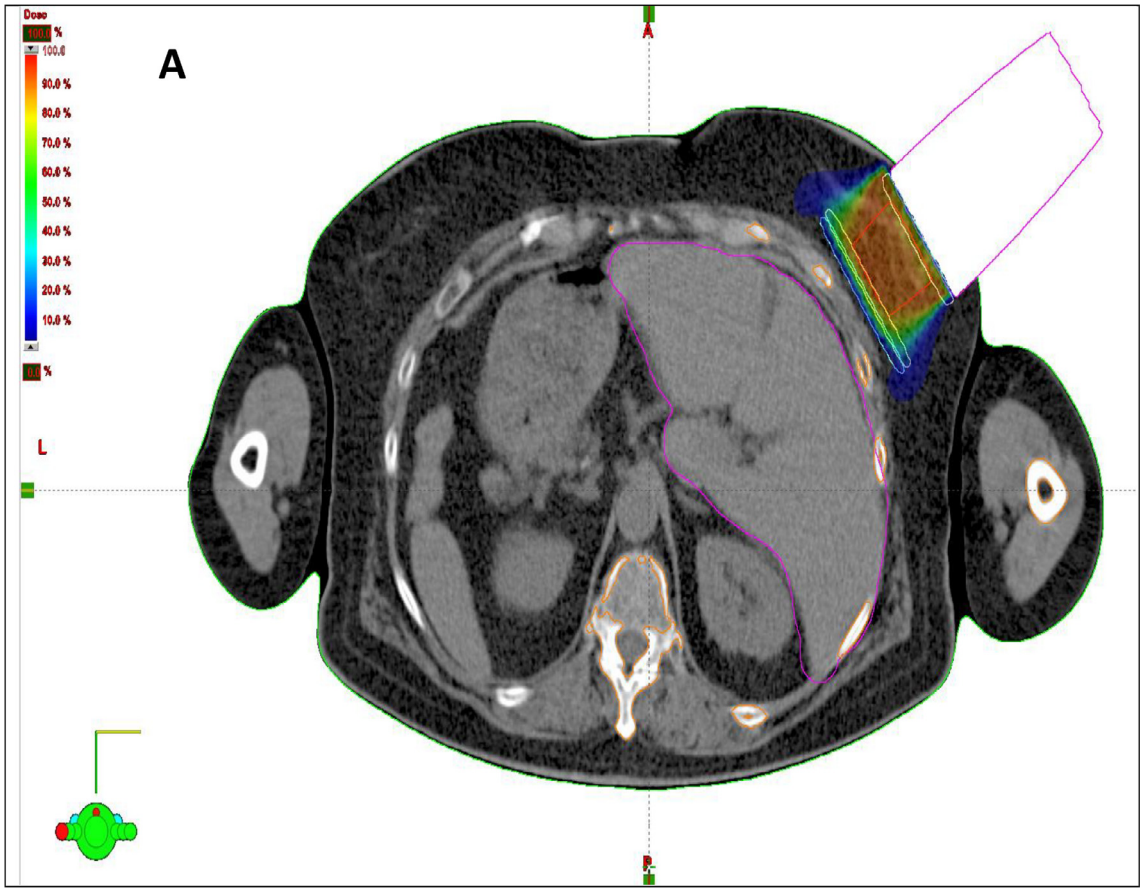

Fig. 5. 3D IOERT patient dosimetry results: A) coronal dose, B) Dose volume Histogram (DVH), C) Dosimetry on sagittal plan, D) 3D position of the applicator with patient body.

will be available only next year in our clinic.

IOERT preplanning could be a good estimation of IOERT operation parameters (energy, applicator type, applicator position, MU,…). It is possible to have difference patient's setup between CT images before IOERT and during the real operation.

MC dose calculation time could be minimized without affecting MC accuracy by: I) using variance reduction techniques, II) using a phase space file at the end of the applicator, III) using a big voxel size [25]. Conventional TPSs enable the user to calculate the dose by using HU/relative electron density curve "dose to water", whereas for our MC study provides an accurate 3D dose to variable materials as a "dose to medium".

The objective of virtual operation procedure is to change the material within some volumes to a specific material with a specific density. As the irradiation is performed after remove the tumor, inserting new structures and modifying CT images are vital to have accurate dosimetry. IOERT pre-planning could be a good opportunity for planning for minimally invasive surgery. Using flat tabletop CT instead of concave one and using markers as reference for the coordinates system during CT images acquisition could help the surgeon to achieve minimal invasive surgery and aids in choosing the best entrance angle.

A commercial IOERT TPS which uses two dose calculation algorithms Pencil Beam and MC dose planning method (DPM) algorithms is available for certain IOERT machines [28]. IOERT TPS and proposed methodology enables the user to do forward dosimetry planning and not inverse planning. IOERT TPS and proposed methodology have same results for 3D patient dosimetry, but our methodology enables the user to do non-standard IOERT treatment. Using special applicator or beam shaper device are not possible with IORT TPS [28–31]. Alhamada et al. and Kamomae et al. have proposed new shielding disks and tungsten paper for organ at risk protection [32,33]. 3D Dosimetry impact verification of using these new materials is possible only with our methodology whereas a limited materials list is available in IOERT TPS. Total dose sum from IOERT treatment and any other radiotherapy treatment "boost" is very helpful for total overdose avoidance which can be done by IOERT TPS or our methodology. Documentation of IOERT dosimetry plan of our methodology is same as documentation of linear accelerator dosimetry procedures. IOERT records of this study includes CT images, 3D dose and IOERT irradiation parameters (applicator diameter, applicator type, energy, shielding disk position, thickness of bolus,…).

The calculated dose in organs at risk according to our study could be verified by in vivo measurements using MOSFET and GAFROMIC films according to Petoukhova et al. or Costa et al. [34,35]. Our study was performed with 4 different materials for the anatomy of the patient and 3 materials for shielding disk and bolus, but any material can be used and verify its dosimetry impact for clinical usage. Mechanical limitations of Mobetron 1000 machine with the operation table should be considered during MC simulation. The 4 MeV energy has not been modelled as we do not use it in clinical routine.

Automatic irradiation according to real time dosimetry plan inside the operation room could be available with the next generation of IOERT machines by using CT or cone beam CT CBCT images.

5. Conclusion

3D, Real and precise dosimetry of IOERT is not available in most of IOERT centers as they have not TPS dedicated to IOERT. This study has proved the feasibility of doing post-operation dosimetry of IOERT patients. The presented methodology is applicable to any IOERT machine

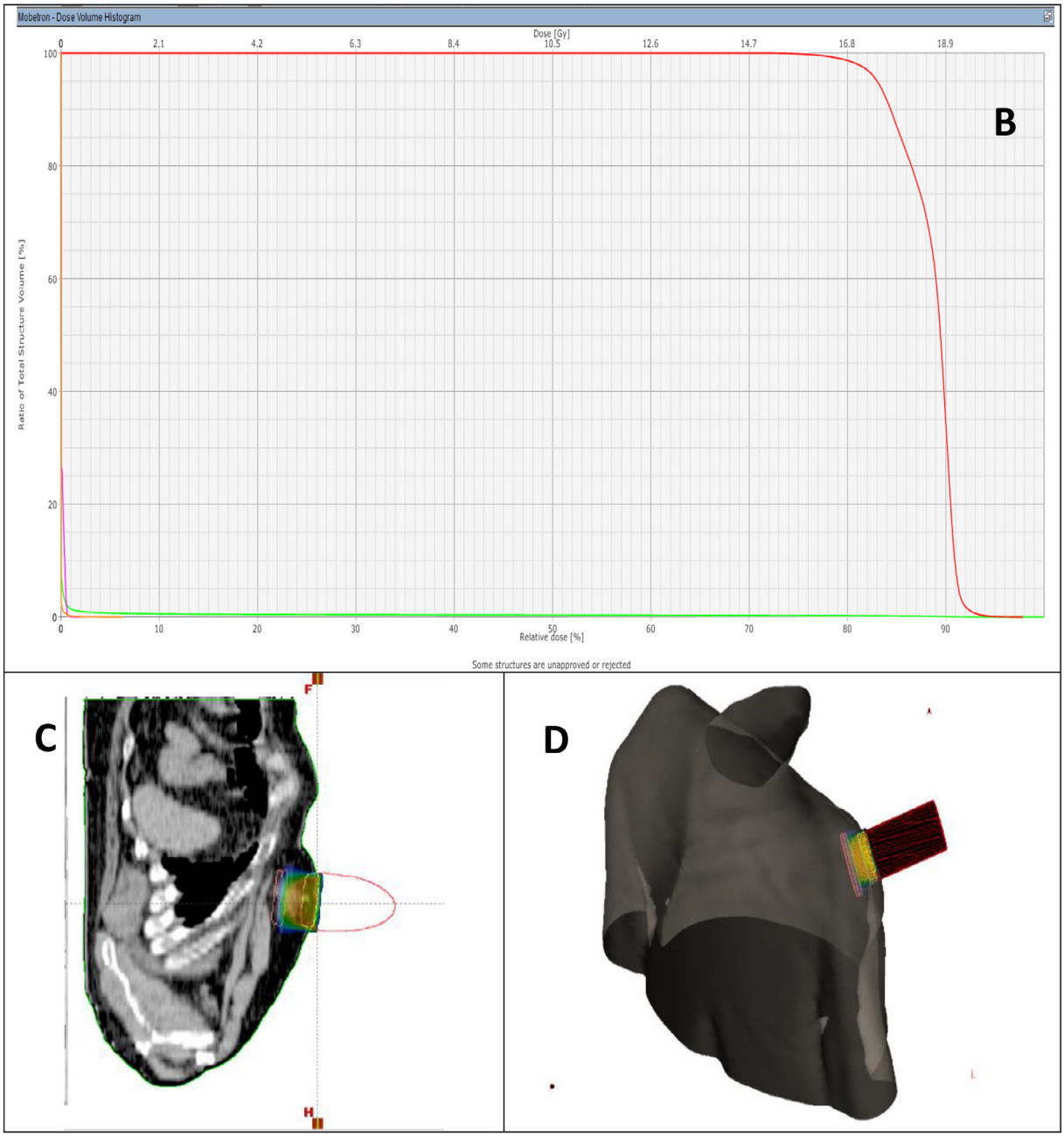

Fig. 5. (*continued*)

and it is not unique to Mobetron 1000 Machine. The presented methodology improves safety by providing a simulation of IOERT parameters as required in the report of TG-72 of the AAPM.

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