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# An Innovative Tool for Intraoperative Electron Beam Radiotherapy Simulation and Planning: Description and Initial Evaluation by Radiation Oncologists

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**Summary**

The lack of specific treatment planning tools limits the spread of Intraoperative Electron Radiation Therapy. An innovative simulation and planning tool is presented. Applicator positioning, isodose curves, and dose volume histograms can be estimated for previously segmented regions to treat/protect. Evaluation by three radiation oncologists on 15 patients showed high parameter agreement in nine cases, demonstrating the possibilities in cases involving different anatomical locations, and

**Purpose:** Intraoperative electron beam radiation therapy (IOERT) involves a modified strategy of conventional radiation therapy and surgery. The lack of specific planning tools limits the spread of this technique. The purpose of the present study is to describe a new simulation and planning tool and its initial evaluation by clinical users.

**Methods and Materials:** The tool works on a preoperative computed tomography scan. A physician contours regions to be treated and protected and simulates applicator positioning, calculating isodoses and the corresponding dose−volume histograms depending on the selected electron energy. Three radiation oncologists evaluated data from 15 IOERT patients, including different tumor locations. Segmentation masks, applicator positions, and treatment parameters were compared.

**Results:** High parameter agreement was found in the following cases: three breast and three rectal cancer, retroperitoneal sarcoma, and rectal and ovary monotopic recurrences. All radiation oncologists performed similar segmentations of tumors and high risk areas. The average applicator position difference was 1.2 ± 0.95 cm. The remaining cancer sites showed higher deviations because of differences in the criteria for segmenting high risk areas (one rectal, one pancreas) and different surgical access simulated (two rectal, one Ewing sarcoma).

**Conclusions:** The results show that this new tool can be used to simulate IOERT cases involving different anatomic locations, and that preplanning has to be carried out with specialized surgical input.

**Keywords:** Intraoperative electron beam radiation therapy, Intraoperative radiotherapy, Treatment planning, Treatment simulation, Electrons

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identifying the importance of specialized surgical input in the preplanning process.

## Introduction

Intraoperative radiation therapy (IOERT) refers to the delivery of radiation to the postresected tumor bed, or to an unresected tumor, during the surgical procedure (1). The technique enables the precise application of a high radiation dose to the target area while minimizing exposure to surroundings tissues, which are displaced or shielded during the procedure (2). However, running an IOERT program involves several aspects from the institutional point of view because it is necessary to organize structural and human resources. Conventional or mobile linear accelerators are used for IOERT. A multidisciplinary group of surgeons, anesthetists, medical physicists, radiation oncologists (ROs), and technical and nursing staff have to be involved. The two main actors are the surgeon and the RO, and both must provide their knowledge and experience in the decision making process, identifying the high risk areas and mobilizing noninvolved dose sensitive organs. Finally, the RO will define the treatment volume, prescribe the dose, and report the results (3).

Although treatment planning is a necessary step in external radiotherapy, the corresponding procedure has not been available in IOERT up to now. There are several reasons for this: most organs at risk are displaced or protected during surgery, the electron beam presents a very high dose gradient (4), and the treatment volume is directly visualized by the surgeon and the RO. Although all these circumstances support IOERT practice, this does not mean that treatment planning is not desirable. In current clinical practice, all necessary parameters such as applicator diameter, bevel angle, position, and electron beam energy are decided by the RO in real time, with high dependence on accumulated expertise (5). This also means that postsurgical follow up cannot include objective variables such as volume coverage for target and healthy tissue; consequently, local tumor control and toxicity are not completely documented.

Although there are several treatment planning tools for brachytherapy that work on imaging studies (6), no such developments have been available for IOERT. The first proposal on IOERT simulation was reported by our own research group (7). The underlying idea was that simulating the IOERT procedure was feasible by displaying the virtual position of the applicator superimposed on the patient's computed tomography (CT) or magnetic resonance image. With this approach, the treatment parameters could be predefined depending on the patient's anatomy, and the RO could improve the preoperative planning for the procedure. This initial proposal was later implemented and improved, becoming the so called Radiance IOERT simulation and planning tool (GMV Aerospace and Defence, Madrid, Spain). Development of the system has brought together industrial and academic partners: Hospital General Universitario Gregorio Marañón (HGUGM) and Consorcio Hospitalario Provincial de Castellón (HPC). The simulation and planning process is performed in several steps: segmentation, applicator positioning using CT images, and parameter selection (applicator diameter, bevel angle, and electron beam energy) by optimizing the dose−volume histograms on the regions. The results of the process can be stored in a single file, allowing for comparison of different procedures. The main features and advantages of this approach will be presented in this article, together with an initial evaluation in clinical cases by three ROs.

## Methods and Materials

The system allows IOERT simulation and planning, giving the user support in the different steps of this workflow. A CT image of the patient including the tumor location is acquired before IOERT. The user navigates through the axial, sagittal, and coronal sections, and also with a three dimensional (3D) volume rendering (Fig. 1). The rendering engine takes advantage of the graphics process unit capabilities, providing real time updates when the rendering parameters are modified. The steps followed to simulate and plan the IOERT are described below. The RO can interact with the surgeon to define several aspects of the procedure.

### Image segmentation

The RO performs the segmentation on axial, coronal, or sagittal sections, and these contours can be combined into a single 3D region of interest. This contouring process is slightly different from the one performed in external radiotherapy. First, the tumor is not the target volume, because it might be resected during surgery, but it must be segmented for correct placement of the IOERT applicator. At the same time, only the organs at risk that could not be displaced and manipulated during the surgical process should be taken into account. Finally, the planning treatment volume (PTV) is the region surrounding the tumor (residual or tumor bed) that is considered to have a high risk for relapse, or the tumor itself for unresectable cases. Tumor location, the patient's clinical history, and radiologic reports are factors to consider when contouring the PTV. Regions that are not expected to be present during surgery can be hidden from the two dimensional and 3D display (virtual surgery effect). The result will be the definition of a series of regions of interest (Fig. 2), with their corresponding labels, which will be the basis for the following steps.

### Surgical frame definition

With this optional tool, the RO defines the expected anatomic regional access (*e.g.,* lateral, anterior, perineal) and dimensions of the surgical incision. This feature improves the representation of the procedure in the 3D volume rendering and at the same time limits the possible movements of the IOERT applicator in the next steps (navigation effect), resembling the physical geometric limitations of the real procedure (Fig. 3).

### Definition of applicator parameters

With the organs at risk, target areas, and surgical procedure defined, the user can now decide on the applicator best adapted for the desired treatment and also the proper position and orientation related to the patient's anatomy and limited by the surgical frame.

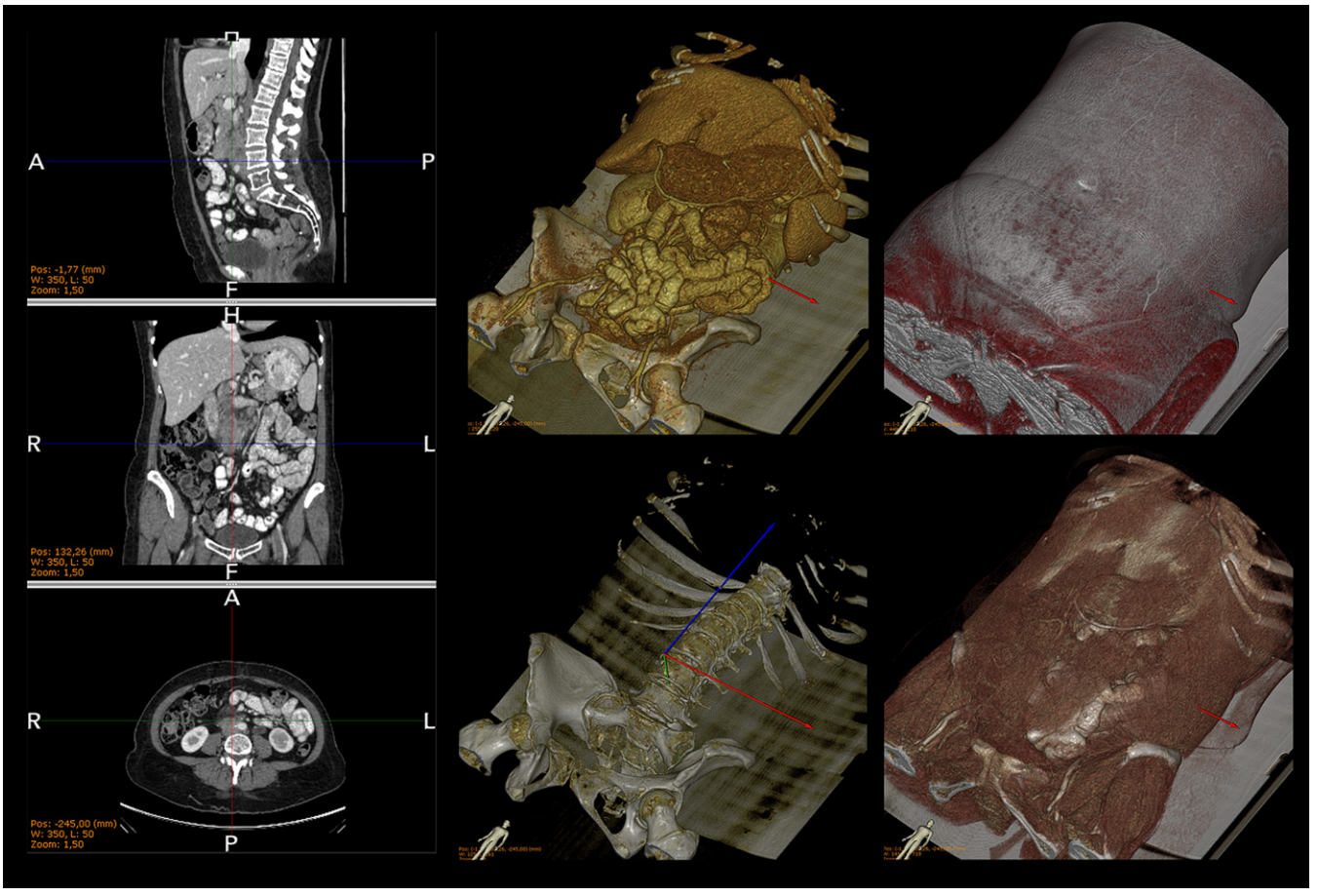


**Fig. 1.** Computed tomography of the abdomen demonstrating three dimensional rendering capabilities in the Radiance system with different color and opacity tables.

The user can modify the applicator parameters (diameter, bevel angle, position, and orientation) depending on several factors: size of the treatment target (high risk area), anatomic structures that could act as physical bounds to the movement, or candidate areas to be protected (Fig. 4).

## Simulation of final treatment parameters

The final step is the selection of the electron beam treatment energy. Every time an energy value is selected, the corresponding dose–volume histograms of all the regions of interest are plotted. The user searches for the best possible coverage for the high risk area combined with a clinically acceptable dose to organs and normal tissues within the PTV. To improve the result, the previ ously defined applicator parameters may be slightly modified. Visual representation of isodose curves on two dimensional and 3D views over the treatment area and related tissues is also valuable for this final step. The resulting values that maximize treatment effectiveness can be stored in a single file. This feature allows comparison of several simulations between users or even alternative approaches from the same user (Fig. 5).

## Possible uses

The system is meant to be used in the three phases of IOERT procedure:

### Preplanning

Several treatment or surgical alternatives can be assessed before surgery. Because there is no time limit in this simulation, the RO can improve the preparation for the real procedure.

### Intraplanning

Treatment parameters can be updated from the preplanning simulation during the IOERT procedure to assess the impact of the intrasurgical modifications. Availability of intraoperative CT would be best suited for this step.

### Postplanning

Postsurgical control CT studies combined with the simulation tool enable better patient follow up and also assessment of correlations for late normal tissue toxicity and topographic characteristics of cancer control or relapse.

## System evaluation in clinical cases by different clinical users

The IOERT planning system was evaluated to determine whether the proposed tools and workflow fulfill the needs of an RO when preplanning these types of procedures. Three ROs took part in this study: one of them (RO1) has had more than 20 years of experience in IOERT working at HGUGM, and the other two

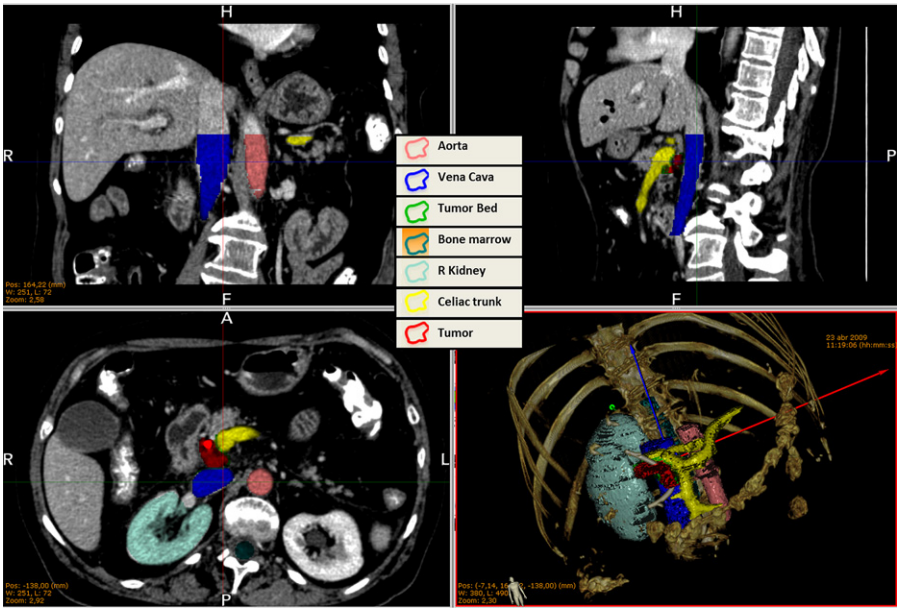


**Fig. 2.** Segmentation result for a patient with resectable pancreatic cancer. Healthy tissues have been contoured to potentially protect them during intraoperative electron beam radiotherapy. Tumor and high risk area (tumor bed) are identified to guide applicator positioning.

(RO2 and RO3) started the IOERT program in HPC 4 years ago. This difference in clinical experience and site is expected to provide clues about the ability of the system to account for the needs of dissimilar user profiles. Less experienced users will be confronted with cases that they have never seen in their clinical practice, and their results will demonstrate the capability of the Radiance system to improve their abilities in these situations. Thirty six cases were retrieved at HGUGM over a 1 year period. From this group, 15 cases were selected in such a way that the most representative IOERT anatomic locations were included: breast cancer (3 cases), rectal primary cancer (6 cases), retroperitoneal sarcoma (1 case), resectable pancreatic cancer (1 case), rectal monotopic recurrence (2 cases), ovary monotopic recurrence (1 case), and Ewing sarcoma (1 case). The described method was completely independent of the standard clinical treatment of the patients. In each of these 15 cases, every RO performed the simulation process after accessing the patient's clinical history, including all relevant image studies, to prepare for the procedure, although in our test setting there was no dia logue with the surgeon responsible for every procedure. The stepwise procedure for every patient followed the steps described in the previous sections.

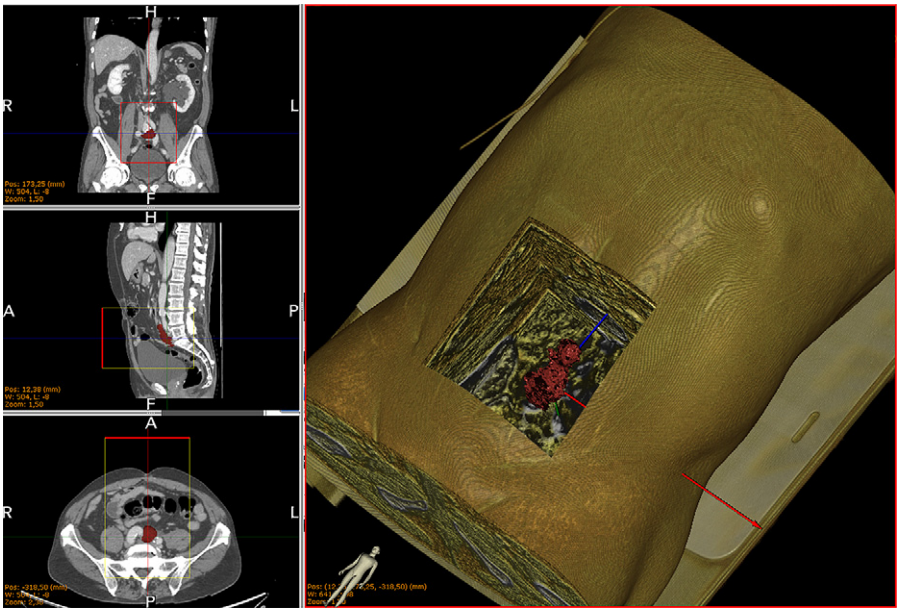

**Fig. 3.** Surgical frame drawn on a patient with rectal monotopic recurrent cancer. Red and yellow lines indicate anterior and lateral limits of the frame.

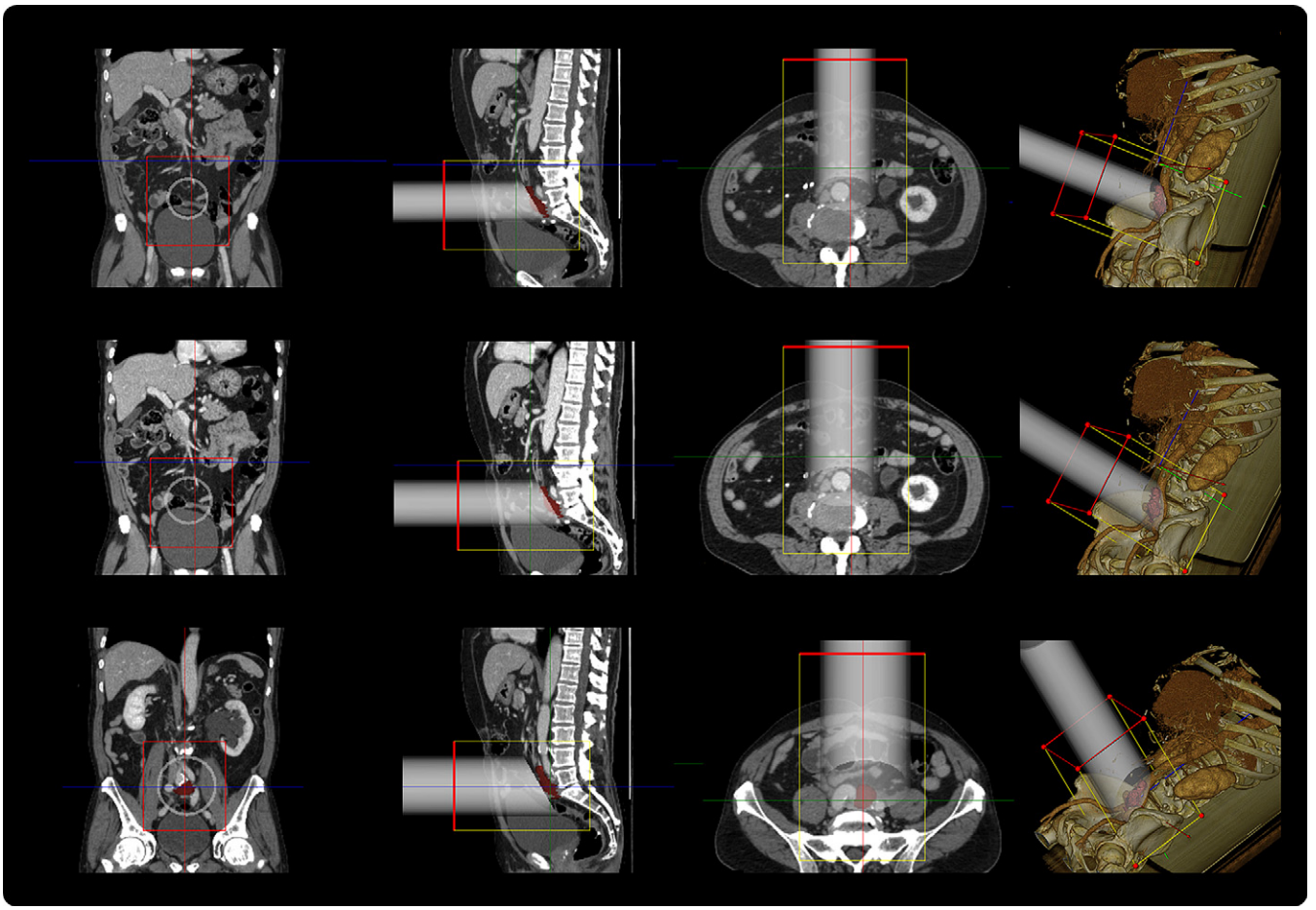

**Fig. 4.** Alternative applicator selection for the patient with rectal recurrent cancer shown in Fig. 3 (30° bevel angle in all cases). Top to bottom: 70 cm, 80 cm, and 100 cm.

After all ROs had performed the preplans on the 15 cases, the resulting files were compared. Agreement between users was evaluated for the following aspects: segmentation regions (qualitatively), treatment parameters (considering agreement when parameters were the same or within one step of difference) and applicator position. The results for RO1 were used as a reference because this user is the most experienced in IOERT. Applicator position difference between two plans was calculated as the Euclidian distance between the coordinate positions that corresponded to the center of the bevels. Perfect agreement was not expected for all the cases. The aim of this study was to evaluate the contribution of the Radiance treatment planning system to the IOERT preplanning step, and also the confidence with which less experienced users could approach new cases using such a system.

All users had the same treatment parameters available: bevel angle (0°, 30°, and 45°), diameter (3, 4, 5, 6, 7, 8, 9, 10, 12, and 15 cm) and energy (4, 6, 9, 12, 15, and 18 MeV). These possibilities accounted for differences between plans, given that step difference between possible parameter values is not constant.

## Results

The results are presented grouped by their anatomic location. In one rectal recurrence case, neither RO2 nor RO3 could define any plan. In the remaining 14 cases, the values for applicator diameter and energy never differed by more than one step, taking into account the available steps defined at the end of the Methods section. Treatment parameters are described in the Table.

### Breast cancer

Segmented regions for breast cancer were always the tumor and the risk area below it. The criteria followed to obtain those regions were completely equivalent for the three ROs, with slight variations in high risk area size. There was very high accordance in treatment parameters, and applicator positioning differences were below 1.2 cm for all cases.

### Rectal cancer

According to the results of these cases, the segmentation limit for the high risk area in rectal cancer was the mesorectal space, although RO1 took into account the tumor location and involved nodes to select a more restricted area. These differences led to applicator position differences up to 3.3 cm in three cases (Rectal 1, 2, and 4). In one case (Rectal 3) the procedure was similar for RO2 and RO3, and RO1 planned a complex approach including two treatment fields. Applicator positions for Rectal 5 and Rectal 6 were not compared because the surgical access was anterior in the RO1 plan, whereas RO2 and RO3 simulated a transperineal procedure.

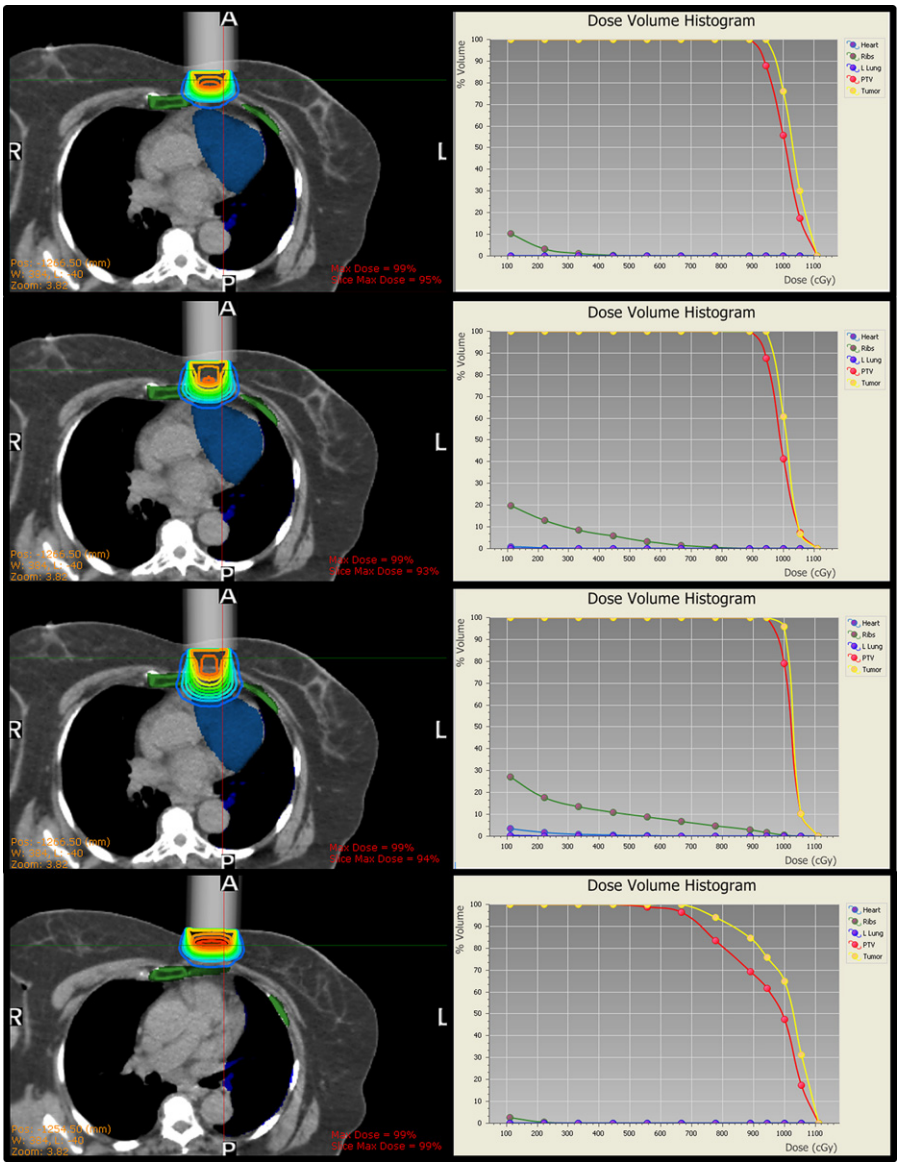


**Fig. 5.** Breast cancer patient with alternative idealized simulations and their corresponding dose−volume histograms for heart, ribs, lung, planning target volume, and tumor regions. Planning target volume corresponds to the post tumorectomy surgical bed. The first three rows correspond to the same applicator and position but with increasing energies (6, 9, and 12 MeV) that modify dose contribution in tissues at risk. The last row shows the effect of an incorrect positioning of the applicator.

## Retroperitoneal sarcoma

Retroperitoneal sarcomas are complex anatomic targets for the postsurgical IOERT technique. However, the results in this case show consistency in the definition of the tumor, risk area, and treatment parameters. Applicator placement difference was less than 1 cm.

## Pancreatic cancer

Segmentation in this case was comparable for RO1 and RO2, whereas RO3 contoured only the celiac trunk but not the tumor. Because of this, the applicator position for RO3 was quite different from that of RO1. RO1 was also less conservative in terms of diameter and energy.

## Rectal cancer monotopic recurrence

Plans were equivalent for the first case, although RO2 and RO3 segmented the tumor only, whereas RO1 included also a high risk area, with complete accordance in the final position and treatment parameters.

The second case could not be preplanned by either RO2 or RO3 based on the clinical information provided. The case was quite atypical, and they could not identify the risk area without knowledge obtained during the actual surgical procedure.

## Ovarian cancer monotopic recurrence

Segmentation, treatment parameters, and positions were all similar in this case.

**Table** Results for the cohort of cases studied

| Case description | Radiation oncologist | Energy (MeV) | Diameter (cm) | Bevel angle (degrees) | Applicator position difference (cm) |
|---|---|---|---|---|---|
| Breast 1 | 1 | 6 | 7 | 0 | — |
| | 2 | 6 | 7 | 0 | 0.379 |
| | 3 | 6 | 7 | 0 | 1.193 |
| Breast 2 | 1 | 6 | 7 | 0 | — |
| | 2 | 6 | 5 | 0 | 0.532 |
| | 3 | 4 | 6 | 0 | 0.324 |
| Breast 3 | 1 | 6 | 6 | 0 | — |
| | 2 | 6 | 6 | 0 | 0.704 |
| | 3 | 6 | 6 | 0 | 0.625 |
| Rectal 1 | 1 | 12 | 7 | 45 | — |
| | 2 | 12 | 8 | 45 | 3.22 |
| | 3 | — | — | — | — |
| Rectal 2 | 1 | 12 | 7 | 45 | — |
| | 2 | 9 | 7 | 45 | 0.73 |
| | 3 | 9 | 8 | 45 | 3.3 |
| Rectal 3 | 1 | — | — | — | — |
| | 2 | 9 | 8 | 30 | — |
| | 3 | 9 | 7 | 30 | — |
| Rectal 4 | 1 | 12 | 7 | 30 | — |
| | 2 | 9 | 8 | 45 | 2.64 |
| | 3 | 9 | 8 | 45 | 1.06 |
| Rectal 5 | 1 | 9 | 7 | 30 | — |
| | 2 | 9 | 8 | 45 | — |
| | 3 | 9 | 8 | 45 | — |
| Rectal 6 | 1 | 12 | 8 | 45 | — |
| | 2 | 12 | 7 | 45 | — |
| | 3 | 12 | 7 | 45 | — |
| Sarcoma | 1 | 12 | 10 | 0 | — |
| | 2 | 9 | 12 | 0 | 0.77 |
| | 3 | 9 | 10 | 0 | 0.84 |
| Pancreas | 1 | 9 | 9 | 0 | — |
| | 2 | 6 | 6 | 0 | 1.83 |
| | 3 | 6 | 6 | 0 | 6.49 |
| Rectal relapse 1 | 1 | 12 | 7 | 45 | — |
| | 2 | 9 | 7 | 30 | 1.72 |
| | 3 | 9 | 8 | 30 | 1.2 |
| Ovarian relapse | 1 | 9 | 7 | 30 | — |
| | 2 | 9 | 7 | 45 | 0.58 |
| | 3 | 9 | 7 | 30 | 0.68 |
| Ewing sarcoma | 1 | 12 | 9 | 0 | — |
| | 2 | 9 | 10 | 30 | 4.13 |
| | 3 | 9 | 10 | 30 | 3.46 |

RO1, RO2, and RO3 indicate single radiation oncologist results. The columns for every case show the treatment parameters selected by the user (treatment energy, applicator diameter, and bevel angle). The last column depicts the applicator positioning error in millimeters using the RO1 position as a reference when treatment plans were comparable.

### Ewing sarcoma

This was an extremely complex case because the access to the posterior risk area location implied the need to approach the patient with a certain body angulation during surgery. The tumor segmentation was correct for the three users, but RO2 and RO3 were not able to identify the surgical requirements on patient lateral positioning, and they performed the simulation with the patient in a supine position and using anterior access. This was why the treatment parameters and position were so different.

## Discussion

Treatment planning is now a standard and necessary step in external radiotherapy workflow. The use of image studies to determine planning volume and organs at risk, together with dose estimation algorithms, has improved the quality and accu racy of these procedures. However, these contributions have not yet been incorporated into IOERT because of the restrictions that surgical conditions enforce. The treatment planning system reported here overcomes part of these limitations, offering the

RO new capabilities: to evaluate different treatment approaches, coordinate the decision process with the surgeons, prepare the intervention, and consequently be more confident during the final procedure. The evaluation has also demonstrated these contributions in a representative set of clinical cases that have been preplanned by expert and less experienced users. The results obtained for every location will be very helpful in defining new protocols on the use of this type of tool for IOERT planning.

Breast cancer is a main indication for IOERT, inasmuch as random studies (8, 9) are being carried out to demonstrate the equivalence with external fractionated radiotherapy in breast conserving surgery. Consequently, our results showing complete equivalence between the planning parameters for all the users are promising. Slight deviations in the size of the applicator in one of the cases are fully consistent with differences in clinical practice between institutions, and are always 1 cm up or down (8).

The results for the six cases of rectal cancer are more heterogeneous, but they provide important details about the possible role of the Radiance system in treating these cancer types and locations. The decisions involved in the segmentation are crucial for the rest of the planning procedure. The specific surgical protocol followed in every institution is also responsible for planning differences. The long experience in rectal cancer at HGUGM (10, 11) allows for more sphincter preserving resections and uses an anterior surgical approach, whereas the standard procedure for RO2 and RO3 is perineal. Both protocols can be carried out with the treatment planning system, although it seems reasonable to look for consensus solutions when determining planning volumes for irradiation. Regarding the treatment parameters, all users selected energies of 9 or 12 MeV, diameters of 7 or 8 cm, and a beveled applicator.

The remaining cases included various neoplastic entities and anatomic locations (retroperitoneal sarcoma, pancreas, ovarian and rectal relapse, and Ewing sarcoma). Despite the complexity of these interventions (12−15), the results on most simulations were similar. Considering the successful cases (three breast cancer, three rectal cancer, retroperitoneal sarcoma, and rectal and ovarian monotopic recurrences), the average applicator position difference was $1.2 \pm 0.95$ cm, with 82.3% of the cases below 2 cm. The differences in energy and diameter were always within one step of the possible values, and the choices for bevel angle diverged only in some cases between 30° and 45°. These plans can be considered clinically equivalent.

In those cases where the approaches are dissimilar, the cause has always been lack of information on how the surgical process was actually performed. This finding encourages the need for close collaboration between ROs and surgeons to obtain the preplan that will be most adequate for guiding the real treatment. The evaluation of these results suggests two main aspects to be addressed to obtain comparable plans: correct identification of high risk areas and knowledge of the modifications that related structures will experience during surgery. The alternative solutions are always related to one of these factors.

Even though treatment planning systems are an essential part of the external radiotherapy workflow, this possibility has not been available in IOERT until now. The lack of such tools has limited the spread and acceptance of this technique (16, 17). Our work contributes to the solution of simulation and preplanning needs, demonstrating the system in several real clinical cases with encouraging results. The ongoing clinical testing will continue collecting users' experience, which will allow adapting and improving the system capabilities. The introduction of the preplanning phase in IOERT guarantees documentation of the procedure and facilitates quality assurance (18). It may also support the main factors limiting the adoption of this technique by reducing the learning curve of the RO and improving communication with the surgical team.

The main limitation of the study is the use of preoperative images that do not represent the modification of patient's anatomy during surgery. The clinical user must apply expert knowledge to evaluate the differences between preplanning and the real procedure. This limitation will be solved with the inclusion of two features that are currently research projects under development: intraoperative imaging and advanced dose modeling. Besides the advantages offered by these contributions, the current system already fulfills several of the IOERT needs that had been identified in previous literature reports and institutional expert practice (1).

The Radiance treatment planning system offers a multidisciplinary and user friendly environment to define and test the IOERT parameters. It allows comparing several approximations with the clinical case, facilitating the selection of the best treatment parameters. This feature is a new contribution that has not been available before. The cases presented here, simulated by different ROs, have shown the ability of the system to solve users' requirements in different clinical scenarios. The stability of the current development has allowed the installation and evaluation of Radiance systems in four hospitals in Spain (HGUGM, Clínica La Luz, HPC, Hospital Ramón y Cajal). These centers are now collaborating in the establishment of new protocols for IOERT that involve simulation and planning with the presented tool.

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