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Imaging opportunities for treatment planning in intraoperative electron beam radiotherapy (IOERT): Developments in the context of RADIANCE system

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ABSTRACT

Aim: The purpose of this report is to store the information of the pre-planning and compare this data with the actual data of the procedure.
Background: Currently, intraoperative electron beam radiotherapy clinical practice lacks a treatment planning system.
Materials and methods: The RADIANCE concept approaches treatment planning by providing the user with a navigation platform based on a three-dimensional imaging system in which the radiation oncologist can target the tumor and risk areas in different sections (axial, coronal, sagittal), while a volume rendering engine displays a 3D image that is automatically updated as we make any changes of the space. Finally, the user may select the parameters of the applicator, energy and dose of treatment to optimize the procedure. Six cases are clinically described and illustrated.
Results: RADIANCE is a useful tool in planning IOERT. Tumor segmentation and risk areas with minimal guide in the selection of parameters for the applicator. Complex locations are challenging, where the experience and skill of the radiation oncologist is necessary to optimize the process. New developments include imaging innovated uses. Intraoperative imaging will approach reality and allow real time, dosimetry estimations, stereotactic recognition of patient and tumor bed position, will guide automatization of radiation beam recognition and pre-robotic arrangements with linear accelerator movements.
Conclusions: RADIANCE offers a new imaging expansion for IOERT, in the context of a multidisciplinary approach to optimize and define the treatment parameters to approximate the actual treatment radiotherapy procedure.

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1. Background

Radiation therapy (RT) involves the use of ionizing radiation for the treatment of malignant conditions. The main aim of intraoperative electron radiotherapy is the irradiation of the tumor bed avoiding critical organs involvement during the surgical procedure. This procedure involves a complex technique that combines surgery with radiation therapy applied to patients with surgically accessible tumors. Therefore, it involves a modified strategy of conventional radiation therapy and surgery.[1] Although treatment planning is essential in radiotherapy,[2,3] the lack of planning tools influences the development of IOERT. Oncologists and surgeons must identify, during surgery, the risk areas and displace noninvolved organs. Both specialists must choose cone diameter, bevel angle and energy of electrons according to their knowledge, experience and the information obtained during the procedure in real time, which is a limitation for objective monitoring of variables such as toxicity and coverage of target volume.[1] The need to adjust the irradiation not only to the tumor volume but also to the anatomy of each patient makes the use of CT (computed tomography), MRI (magnetic resonance imaging) and positron emission tomography–computed tomography (PET/CT) indispensable for RT. Intraoperative radiotherapy minimizes the toxicity and increases the therapeutic index by mechanical displacement of mobile normal tissues.[4] RADIANCE is the only radiotherapy treatment planning system designed for IORT. The RADIANCE project is an initiative developed by GMV (privately owned technological business group) with the participation of Hospital General Universitario Gregorio Marañón (HGUGM) and Consorcio Hospitalario Provincial de Castellón (HPC). The main objective of the project is to simulate the virtual position of the applicator superimposed on a CT scan or MRI. New imaging developments do extend the benefit of pre-, intra- and post-planning in IOERT.[5]

2. Aim

The purpose of this report is to store the information of the pre-planning and even compare planning with the actual data of the procedure.

3. Materials and methods

RADIANCE facilitates the user to plan and simulate IOERT, allowing the radiation oncologist to interact and decide with the surgeon on different aspects during the procedure. The workstation has the ability to work with a CT before surgery, including tumor location, allowing the user to move through the different sections (axial, coronal, sagittal), while a volume rendering engine displays a 3D image that is automatically updated as we make any changes. The system allows a pre-planning before surgery in order to improve the surgical procedure, a real time planning during surgery in order to

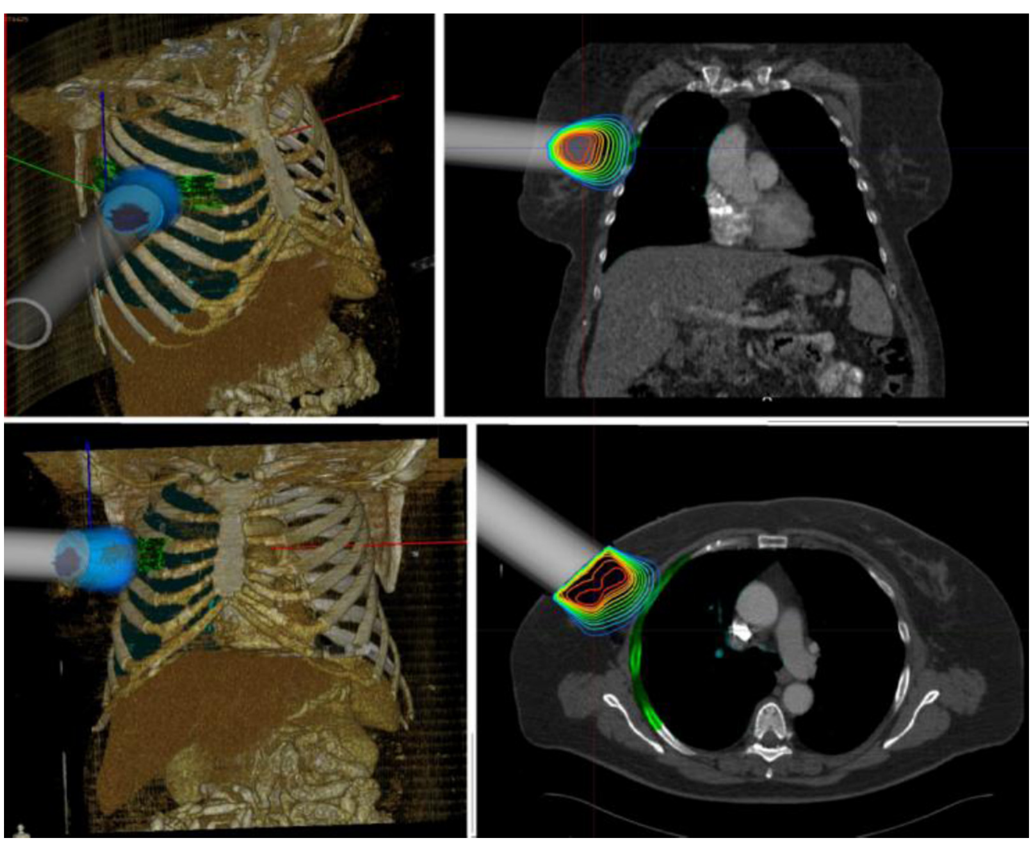

Fig. 1 – Intraoperative electron-beam radiation therapy planning in breast cancer requires segmentations in the tumor region and adjacent areas of risk, reconstruction of the tumorectomy cavity and interposition of protection of the chest wall.

modify and update and a post-planning to track tissue toxicity and tumor characteristics.

Here are the steps for planning the IOERT:

- *Navigation, segmentation and multi-planar reconstruction*: The graphics engine of the station is provided with a developed system of three-dimensional reconstruction and volume rendering in real time, provided to the oncologist that represents different segmentations on the axial, coronal, and sagittal axes. The program allows the rotation and the possibility to change the volume rendering. Unlike external beam radiation therapy, the tumor is not the main objective of planning, as this will be removed during the surgical procedure. Still, it should be segmented as it facilitates correct definition of the tumor bed region and/or area at risk for residual tumor that will guide positioning of the applicator to encompass the target. The risk organs that will be displaced or manipulated during surgery should also be taken into account. Finally, planning the treatment volume includes the tumor bed, considered a high-risk area of tumor recurrence and residual tumor, together with the anatomical structures left in the surgical post-resection space.
- *Determination of surgical frame and applicator parameters*: With the tool that defines the surgical frame, we can approximate the expected anatomical access during the surgical procedure. This will optimize the position of the applicator in the space, improving the representation process in three dimensions and the geometrical and physical limitations of the procedure. After defining the parameters, the user can select the best-suited applicator and orient the surgical frame in relation to the patient's anatomical position. The workstation has the ability to modify parameters such as diameter, bevel angle and orientation in space depending on tumor size and position and structures that must be protected.
- *Simulation and optimization of treatment parameters*: The IORT optimization parameters allow the user to modify the geometry of the applicator position and orientation depending on the patient's anatomy. After that, the user can select the energy of the electrons, which will be represented by a dose–volume histogram of the region of interest. The parameters can be enhanced to provide the best coverage of high-risk areas with an acceptable dose. Dose calculation can be carried out by superimposing measured data on water phantoms or by using dose calculation algorithms, which take into account the densities of the surrounding tissue. The final result has the ability to store information in a database for comparisons between different users.
- *Reporting*: RADIANCE provides a document which includes applicator parameters (energy, diameter, bevel angle, position, and orientation), dose–volume and isodose curves and linear accelerator configuration and to capture 3D images that the user generated during the pre-planning.

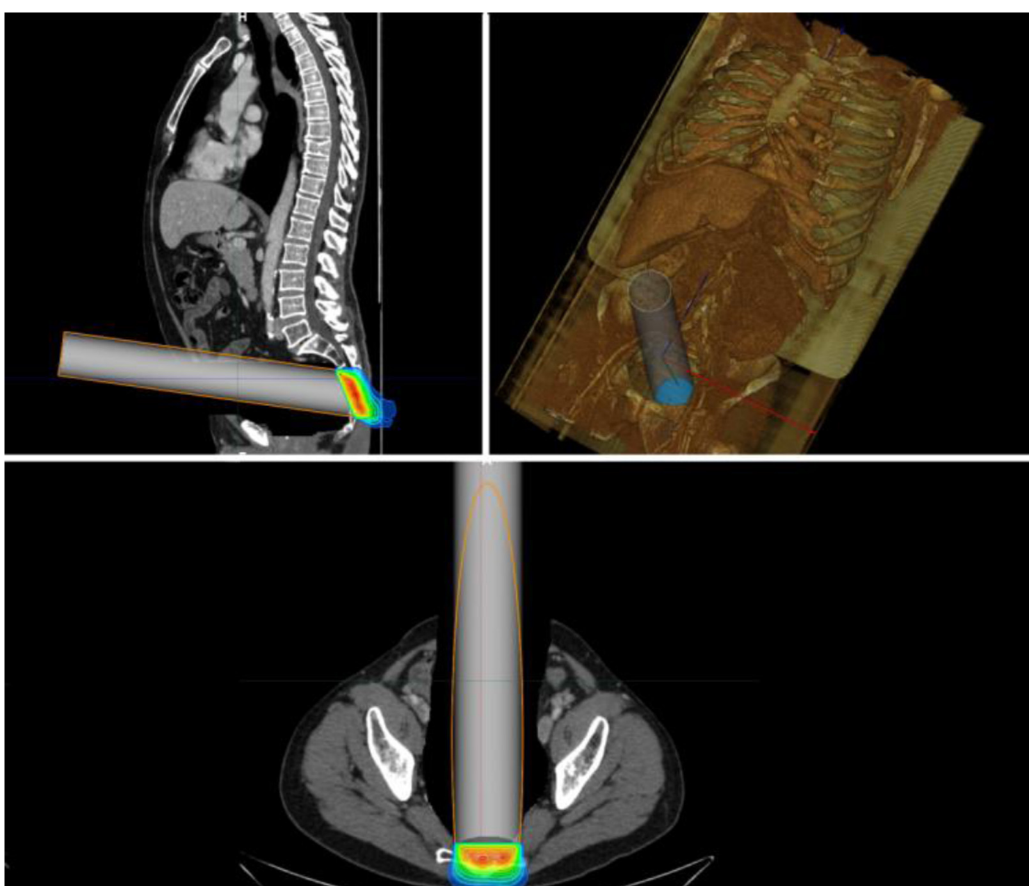

Fig. 2 – Rectal cancer patient, boosted to the presacral space.

4. Results

The validity and usefulness of RADIANCE planning tools for IORT was assessed in a comparative study conducted with the participation of three radiation oncologists, one of them with over twenty years of experience in IORT and two with four years of experience. Fifteen cases based on the most representative locations of IORT treatments were evaluated including: 3 breast cancers, 6 primary rectal cancers, 1 retroperitoneal sarcoma, 1 resectable pancreatic cancer, 2 rectal monotopic recurrences, 1 ovary monotopic recurrence and 1 Ewing sarcoma.[5] Examples of practice-based RADIANCE operation require each user to perform a simulation based on imaging tests before surgery, taking into account clinical history data. Next, some typical IOERT candidates are illustrated and discussed.

- *Breast cancer*: IOERT planning in breast cancer requires segmentations in the tumor region and adjacent areas of risk, reconstruction of the tumorectomy cavity and interposition of protection of the chest wall (Fig. 1).
  - Case 1 Early stage breast cancer: 65 years old, cT1N0M0, luminal A adenocarcinoma, left breast upper-outer quadrant. Sentinel node biopsy negative. Plus tumorectomy plus IOERT (5 cm diameter applicator, 10 MeV electrons, chest wall protection, 21 Gy). Definitive pathology: Well differentiated adenocarcinoma, estrogen receptors 90%, progesterone receptors 80%, cerb-2 negative, Ki67 70%. Follow up at 32 months with no evidence of disease (Fig. 1).
- *Rectal cancer*: In the planning of rectal cancer it is important[6] that the tumor risk area segmentation includes the mesorectum. The experience and knowledge of radiation oncologist is decisive to delineate the target precisely and simulate the surgical resection tentatively.
  - Case 2 Primary rectal cancer: Female, 65 years old, diagnosis of locally advanced primary rectal cancer cT4N0M0. Imaging characteristics 8.5 cm diameter with extension to muscle piriformis and gluteus. Neoadjuvant chemoradiation, posterior exenteration (R2 resection). IOERT (5 cm diameter applicator, 15 MeV electrons, 15 Gy). Restaging ypT3N0M0. Follow up at 15 months with local control (Fig. 2).
- *Retroperitoneal sarcoma*: Although segmentation of the target in the treatment of sarcomas is challenging in IOERT planning, a high consistency in defining parameters such as tumor volume, risk areas, treatment parameters and normal tissues to be displaced is consistent for trained oncologist.
- *Pancreatic cancer*: The segmentation performed by different radiation oncologists or surgeons might be variable in terms of defining the tumor volume and the risk area.[7,8]
  - Case 3 Resected adenocarcinoma of the pancreas: 57 years old. cT2N0M0 (head of the pancreas 3 cm maximal dimension, no vascular invasion, endoprosthesis). Treated with preoperative chemoradiation, restaging with stable disease. Duodenopancreatectomy plus IOERT (cone 8 cm diameter applicator, 12.5 Gy, 10 MeV electrons, single field). Pathologic restaging ypT2N0M0. Follow up no evidence of disease at 28 months (Fig. 3).

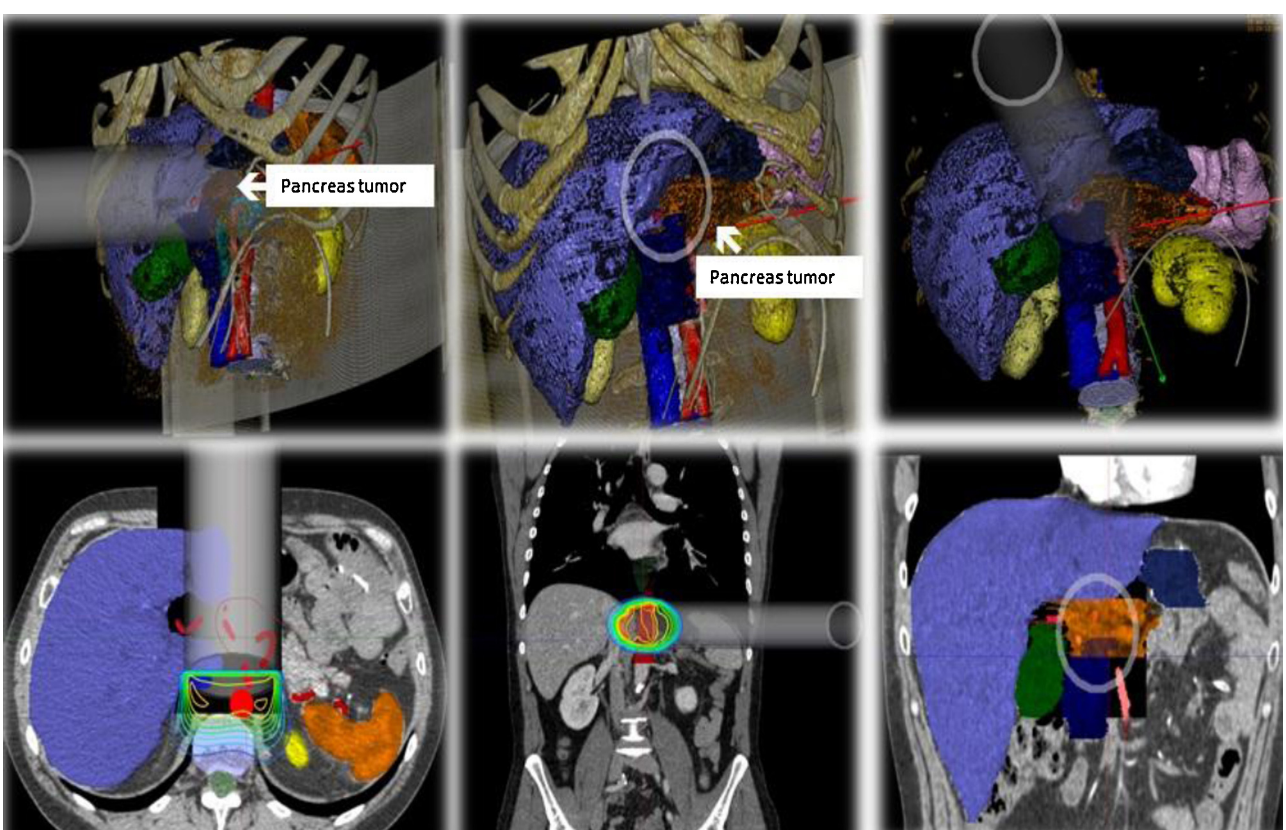

Fig. 3 – Patient with a resected pancreatic tumor receiving a boost to the retroperitoneal–retropancreatic space.

- *Rectal cancer monotopic recurrence*: In localized relapse a definition of risk area needs to be consistent with the treatment parameters. Difficulty can be seen in estimating extended surgical resection margin and its relationship with the tumor bed region.[9]
  - Case 4 Recurrent rectal cancer: Post-anterior rectal resection. 82 years old, male. Diagnosis of cT3N+ rectal cancer 3 years ago. Pain, pre-sacral 5 cm diameter mass with extension to the coccyx. Neoadjuvant chemoradiation, posterior exenteration plus inferior sacrectomy and IOERT (10 cm diameter applicator, 10 MeV electrons, 12.5 Gy, protection of centro-pelvic stitches by led). Status at 28 months with local control and liver metastasis (Fig. 4).
- *Gastroesophageal tumor*[10]:
  - Case 5 Locally advanced adenocarcinoma of the gastroesophageal junction: 59 years old, male. Dysphagia, cT3N1Mo. Neoadjuvant treatment with chemoradiation (Cisplatin plus 5FU plus 45 Gy), programmed radical surgery plus IOERT (inferior mediastinum, 8 cm applicator, 6 MeV electrons, 10 Gy, 2 fields inferior mediastinum and celiac trunk). Restaging pathology ypT1N0M0. Follow up with no evidence of disease at 37 months (Fig. 5).
- *Ewing sarcoma*: Bone resection is uncertain to be pre-planned, because it requires an intuition of the surgical body position determined to identify the surgical requirements for optimal approach. RADIANCE allows to position the patient prone and supine.
  - Case 6 Extremity soft tissue sarcoma: 35 years old female. Soft tissue mass in the upper left extremity. Imaging characteristics: 9 cm diameter, intracompartimental, liposarcoma. Limb preserving radical surgery. R0 resection. IOERT (12 cm diameter applicator, 10 MeV electrons, 12.5 Gy, single field). No neuron-vascular protection. External beam radiotherapy 50 Gy/5 weeks. At 45 months of follow up alive with no evidence of recurrence. Moderate fibrosis in the radiotherapy region (Fig. 6).

5. Discussion

The development of effective tools for planning IOERT has been limited due to the complexity to reproduce the surgical procedure and the lack of standardization of these processes.[1] In external radiation treatments, planning is a critical step that uses standardized imaging studies to determine the

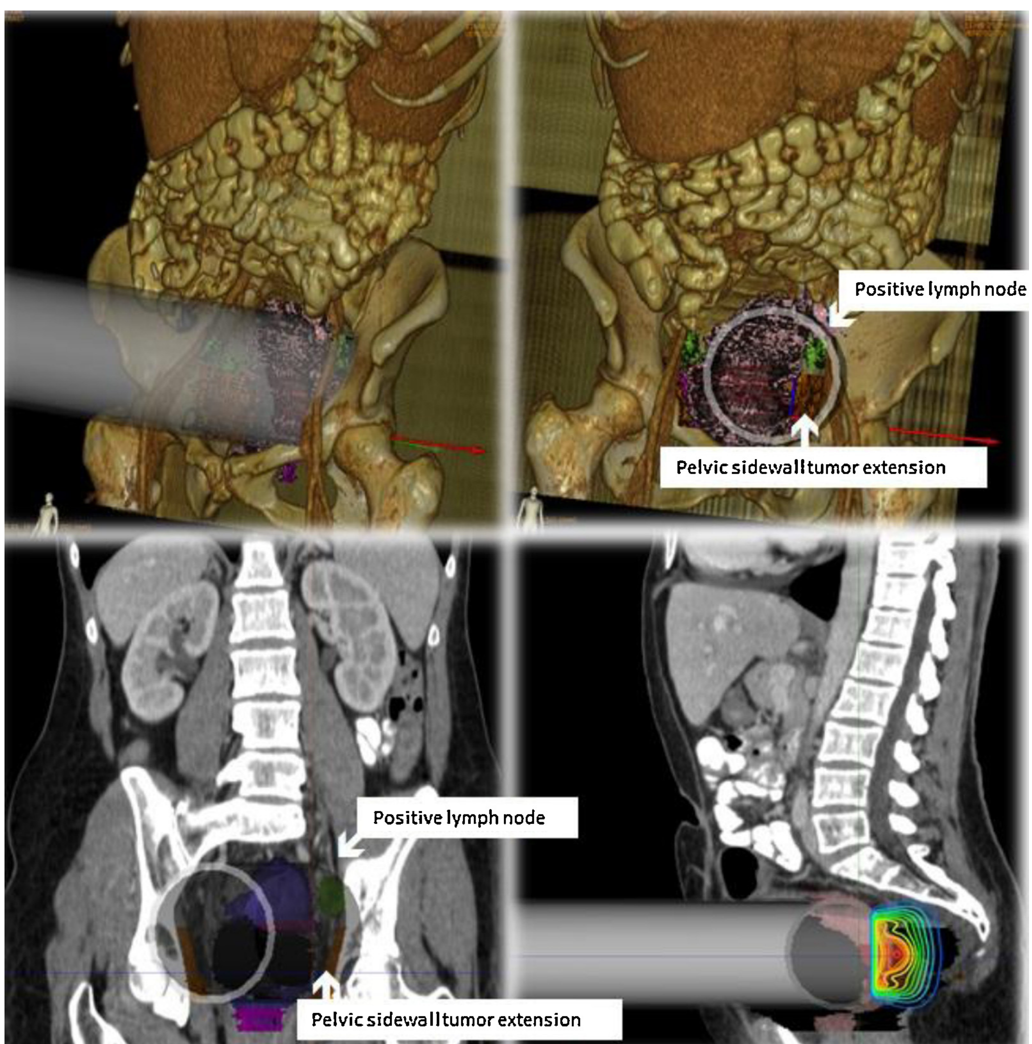

Fig. 4 – Patient with a locally recurrent rectal cancer, receiving a boost to the posterolateral pelvic sidewall.

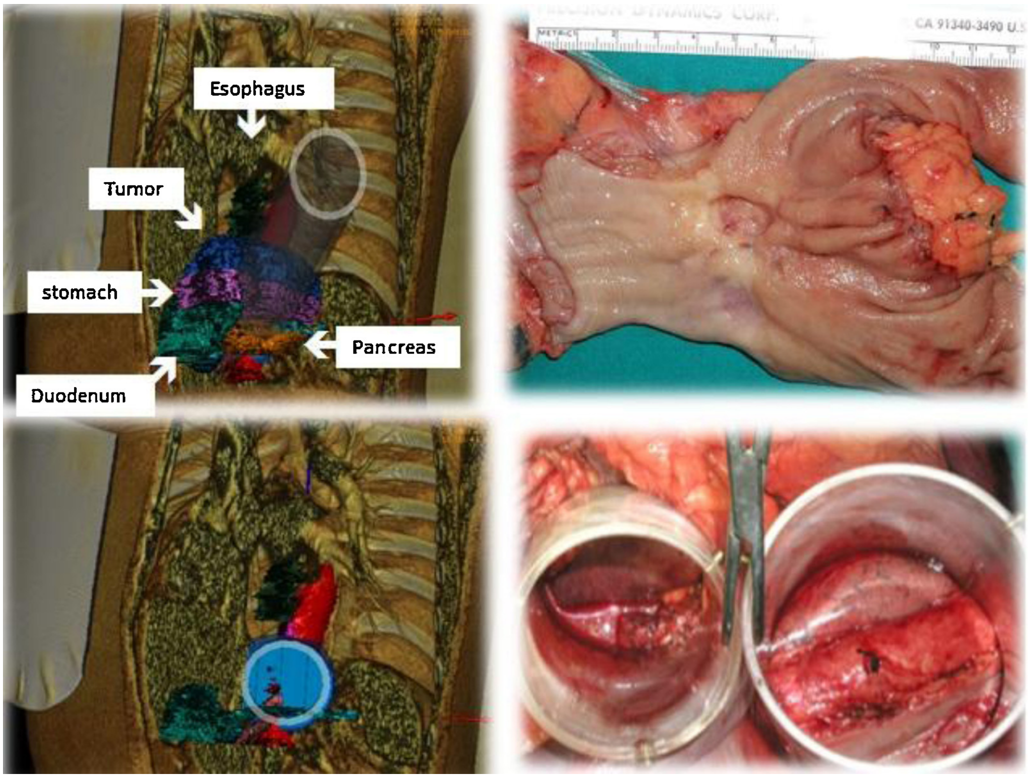

Fig. 5 – Patient with a gastroesophageal junction cancer receiving a two-field boost.

volume and organs at risk. Planning in external radiotherapy is far from perfect, but their limitations are well accepted in practice. Establishing and consolidating an IOERT program involves many aspects from the institutional point of view as it requires structural organization and human resources, such as modified accelerators, multidisciplinary team, coordinated action of surgeons, anesthetists, medical physicists, radiation oncologists, nurses.[5]

The RADIANCE system offers users a supported learning curve, acquiring new skills and the ability to evaluate combined cancer treatments, decision processes coordinated with surgeons and to optimize the final treatment. RADIANCE can help address the needs of pre-planning and simulation systems illustrated with real cases with positive results. Images before surgery, showing variations in patient anatomy during surgery requires to explore intraoperative imaging and advanced models of dose for further technological improvement. Developmental and innovative research projects in imaging opportunities for IOERT have generated pilot information in breast cancer, retroperitoneal and extremity sarcoma. Patients required transportation to the CT scan used for external radiotherapy simulation and the images

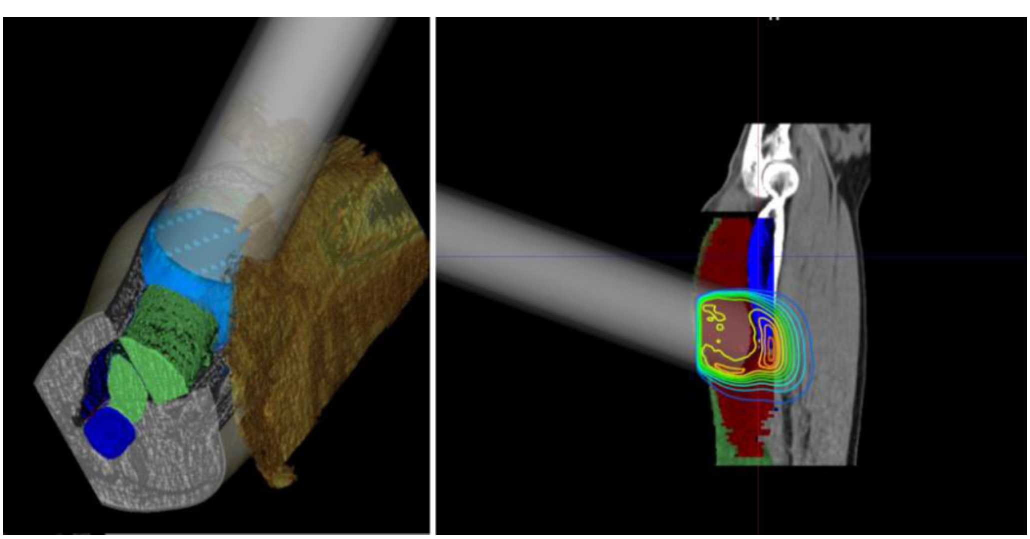

Fig. 6 – Patient with an upper extremity soft tissue sarcoma, receiving a boost to the tumor cavity.

we are obtained with the IOERT applicator in place.[5] The breast cancer and the extremity sarcoma model proved to be feasible and the images obtained allowed generating dose distribution within a close to real-time situation. In the retroperitoneal sarcoma case, the metallic surgical retractors used for deep-intra-abdominal exposure and displacement of movable normal tissues generated imaging interferences that limited the ability to estimate the status of the tumor bed region (presence or not of fluid) and the cavity of dose-distribution in the manipulated anatomy. Nevertheless, the scene for improved IOERT treatment planning is to move to 3D reconstruction of the altered anatomy after resection, normal tissue displacement, tumor bed definition and applicator positioning. An additional development is the recognition of patient positioning and tumor bed identification using markers. RADIANCE planning will automatize a significant part of the IOERT decision-making process.[5]

Breast cancer represents a major indication for IOERT. Minor differences in the implementation of the process subject to user-related variations and intervention protocols of different hospitals might be addressed by pre- and intra-planning imaging evaluation.[5]

The requirements of rectal cancer are more heterogeneous, reflecting the difficulty of planning. Schedules change according to the protocol followed in each institution, with parameters such as anal margin resection or surgical approach being more conservative. Despite these differences a proper simulation can be made with the planning system, seeking a consensus to determine the irradiation volume, segmentation of risk areas and to establish the framework surgery. Applicator parameters from the comparison results between IOERT practitioners in expert institutions are similar, with minor variations in energy, cone diameter and bevel angle, which is a high consistency in the process of standardization.

Regarding the rest of the illustrated cases, a lot of them entail individualized difficulty, nevertheless the results are clinically solid adapted variations regarding the position of the applicator, the energy, the diameter of the cone or the bevel angle.[5]

The lack of information about the surgical procedure and the need to improve the relationship and communication between the RO and the surgical team is particularly evident with the incorporation of a treatment system into IOERT practice. Two aspects to consider strongly are the correct identification of risk areas and knowledge of the structures that are modified during the surgical procedure.[5]

The future of this tool is to check and collect different experiences allowing users to adapt and improve the tools available. RADIANCE offers a multidisciplinary approach and an easy way to define and optimize treatment parameters giving a real approximation of these treatment parameters. Intraoperative imaging will maximize the potential of this tool.

Conflict of interest

Nothing declared.

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