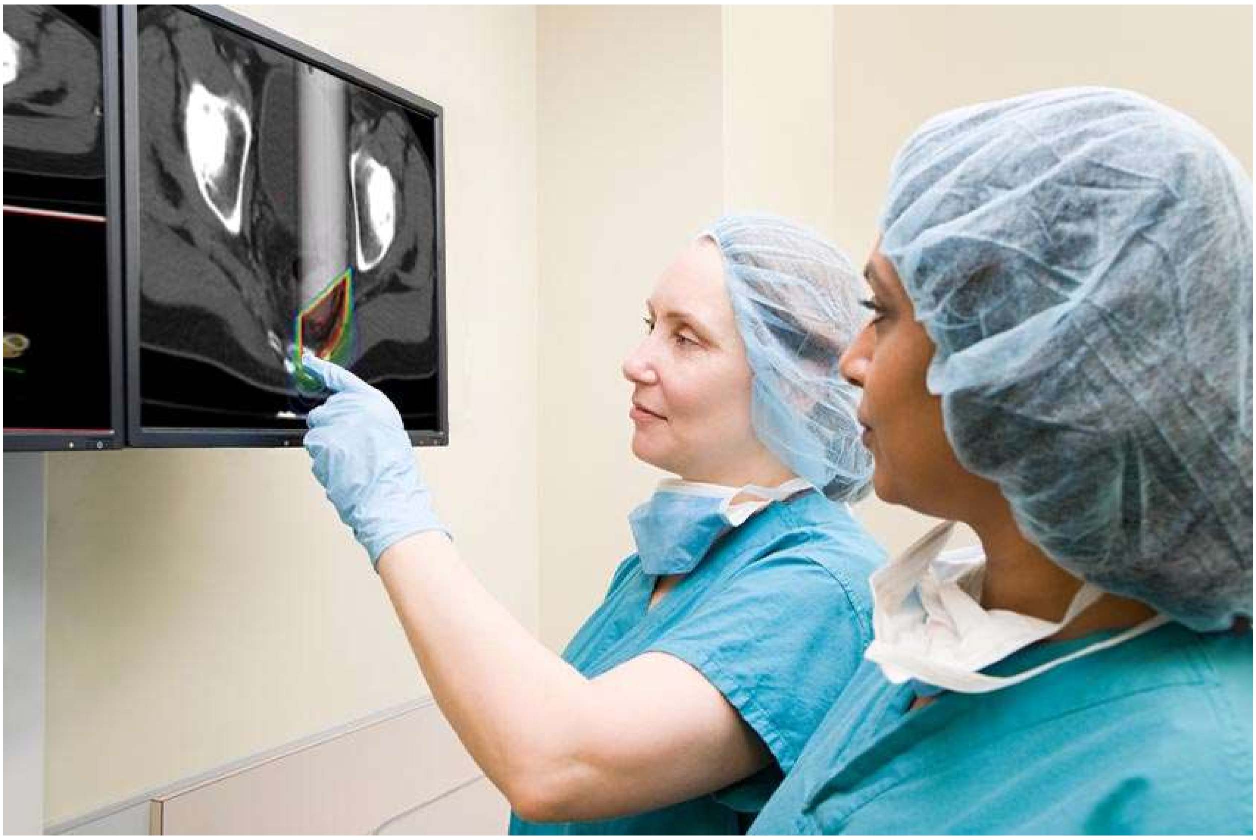

RADIATION TREATMENT SIMULATION PLATFORM FOR IORT SUITABLE DEVICES

TECHNOLOGICAL INNOVATION FOR IORT SUITABLE DEVICES TREATMENT SIMULATION

Radiance, the treatment simulation software for IORT suitable devices, improves the safety of the procedures by means of a pre-, intra- and post simulation of the treatment, following the requirements from AAPM TF-48 and TG-72 reports, and ICRU. In this simulation, it is possible to alter the different parameters of the procedure to evaluate the outcome without stress in the treatment decision-making process.

Radiance works with either IORT devices like the INTRABEAM® System as well as with MOBETRON.

Radiance can be used in all indications for IORT suitable devices. That includes not only IORT itself, but also intracavity and surface techniques as well.

Radiance has medical device certification class IIb from CE and class II from FDA.

Sep 2020 http://www.gmv.com/radiance

CE
1639

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INTRODUCTION

Radiation therapy (RT) involves the use of ionizing radiation for the treatment of malignant diseases. Radiation Oncology (RO) is the clinical specialty devoted to the diagnostic aspects, clinical care and therapy oriented to the use of radiation treatments as well as the assessment of alternative or related treatments [Palacios 2002].

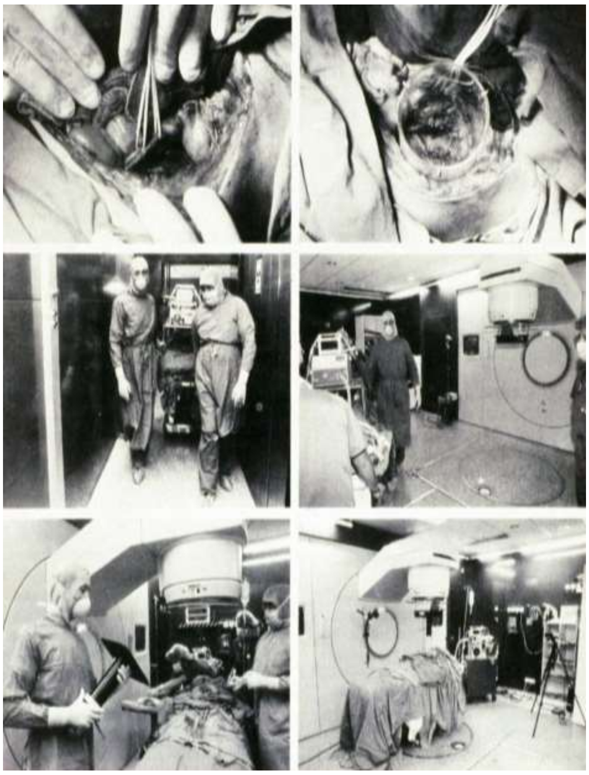
Its main characteristic is the technical complexity of its procedures, the costly investment in equipment as well as its specific legal regulations that cover not only the products quality control, but also the radioprotection to the patients and staff in the welfare units. Oncology, Radiobiology and Radiophysics are the knowledge areas that lay the scientific foundations of RT [Palacios 2002, González 2005].

The goal of RT is the irradiation of tumoral areas or anatomical areas of interest (risk of relapse areas) avoiding, as possible, affecting critical organs. The choice of the volume of irradiation, the total dose for the tumor, as well as the division or the use of other concomitant treatments is the basis for planning the RT. The need to adapt the irradiation, not only to the tumoral volume, but also to the anatomy of each patient, makes the use of CT, NMR and/or PET/CT images indispensable for RT, as they allow to take anatomical references and delimit the area for irradiation [Calvo 1998, Nieto 1999].

Together with the raise of state-of-the-art linear accelerators and the possibility of adding instruments - such as multi-sheet collimators, special applicators for intraoperative and stereotactic RT, tomographies in Tomotherapy or Intensity-Modulated Radiation Therapy (IMRT) – the possibilities of giving a more accurate and less toxic radiation have increased, that is, therapeutic benefits have been achieved.

The development of computer systems, the advance in Radiobiology, a better knowledge on the mechanisms involved in cell survival and the response of normal tissues, as well as the implementation of new quality control programs, are also new achievements to be considered in the progress of RT [Pérez 2007, Murillo 2000, González 2001].

In this specific case, we focus on **Intraoperative Radiotherapy** (IORT), which is a technique that combines surgery with radiation therapy applied to patients with tumors surgically assessable, resectionable and with a high relapsing level. It entails the direct application of a unique dose of radiation. For this purpose, the area to irradiate is defined trying to protect healthy tissues through the withdrawal of mobile or displaceable structures or through the protection of fixed ones. In general, it is used as reinforcement (boost) in combination with external radiotherapy, although it can be also applied, in specific cases, as a single radiation treatment technique [Calvo 2006, Gunderson 1999, Gerard 1997].



IORT suitable devices, electron based ones and low energy photons ones, have been developed in the last decades in order give the dose directly in the operating theater. These devices are not only capable to be used for IORT, but also irradiate targeted lesions using interstitial, intracavity or surface irradiation techniques.

In order to give external radiation therapy, a dosimetry calculation is required, from CT images alone or merged with other modalities (such as NMR or PET/CT images), to obtain complementary information. These images introduced in a planning equipment, allow the calculation of the dose distribution by evaluating the interaction of the radiation beams with the affected tissues.

Thus, one of the current main limitations in IORT lies in the difficulties that the planning process entails. The retraction of the patient's structures and the removal of affected tissues contribute to the modification of the patient's geometry. Therefore, it is difficult to carry out a feasible dosimetry calculation from pre-operative images. This fact brings up two problems to the planning:

- **Before surgery:** it is complex to estimate the dose to be applied.
- **After surgery**: since such images are difficult to be obtained, the results cannot be assessed.

In addition, as IORT is an invasive technique that introduces an applicator to reach the tissues to be irradiated, the operatory area has to be adapted in order to reach an ideal position of the remaining parts of the tumor or tumor bed.

Currently, it is very difficult to plan the radiation therapy process beforehand; that is why the radiation oncologists and surgeons must choose during surgery the applicator dimension, its positioning, the bevel angle and the linear accelerator parameters according to their medical and surgical experience and the information gathered during the procedure.

This means that the previous dosimetry estimation of the radiation to be applied is not good enough to properly assess, with certain precision, the results obtained (complete scope of the tumor bed, dose on healthy tissues and critical organs, etc.). Therefore the possible beneficial and deleterious effects of irradiation cannot be explained.

The professional willing to simulate or plan an IORT procedure needs a tool that allows them to estimate the applicator position and the dose distribution that will be applied to the anatomical volume determined by them. In order to assess the results of a radiosurgery therapy, it would be desirable to know the exact dose received and therefore being able to gather accurate treatment results, as indicated in the reports from AAPM TF-48 and TG-72.

Radiance is a revolutionary technology which address all previously mentioned difficulties in the dose planning and documentation processes.

SECTION 2
MAIN FEATURES

Radiance is the only available Radiotherapy Treatment Simulation Platform that has been specifically designed for Intraoperative Radiotherapy (IORT) suitable devices and the only one that works in such field of radiotherapy.

Radiance introduces a new step in the IORT procedure, the preplanning phase. In this simulation, it is possible to alter the different parameters of the procedure to evaluate the outcome without stress in the real treatment decision-making process. This pre-simulation can be improved during and after the treatment, especially with the availability of intra-operative imaging, having then a very accurate plan, and post operative imaging.

Radiance is a state-of-the-art development unrivalled today worldwide. It uses advanced visualization, simulation and dosimetry algorithms. DICOM images are loaded and their volumetric representation built on the fly. The computation of both graphics and dosimetry computation algorithms is carried out in almost real time. The reporting capabilities of radiance; compatible with what it is requested in AAPM TF-48, AAPM TG-72 and ICRU reports; exceed significantly the current documentation procedure, improving the quality of posterior analysis of clinical cases.

We describe below the most noteworthy features of ***Radiance***.

1. COMPATIBILITY

Radiance has been design to work with either IORT devices like the INTRABEAM® System as well as MOBETRON.

Radiance supports a complete set of applicators both for IOERT and IORT devices like the INTRABEAM® System.

Radiance can be used in all indications for IORT suitable devices. That includes not only IORT itself, but also intracavity and surface techniques as well.

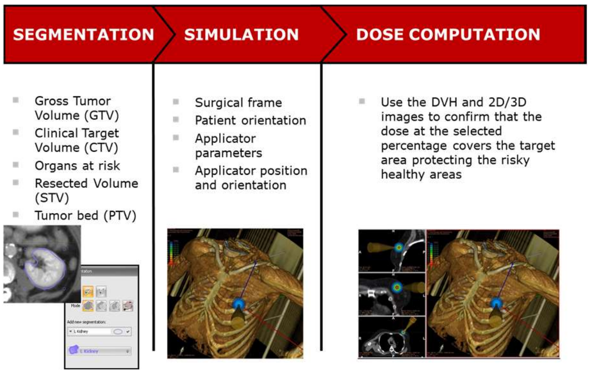
2. WORKFLOW

Radiance allows the user to simulate the IORT treatment by loading and visualizing CT images of a patient and finding the best parameters involved (applicator´s geometry, accelerator´s parameters, etc) so that the dose deposit is maximized on the tumor or tumor bed while being minimized on the regions to protect.

Each of the steps involved during planning with radiance is summarized in the following way:

- Loading of 3D Images (typically CT scans although other modalities are also accepted).
- Navigation on the patient to determine course of action.
- Identification of regions of interest, including GTV (Gross Tumor Volume), CTV (Clinical Target Volume), organs at risk.

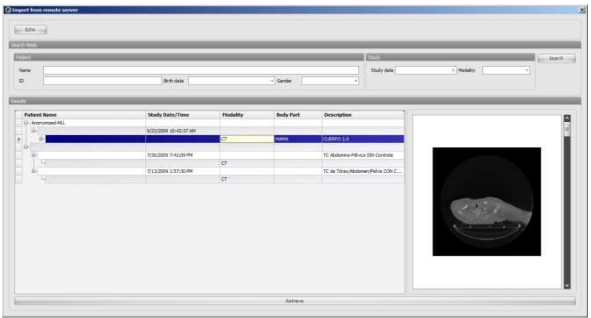
- Determination of Surgical Frame.
- Definition of the resection (Surgical Target Volume – STV).
- Definition of the PTV (Planning Target Volume) removing the STV from the CTV.
- Simulation bolus, protections, air, etc.
- Optimization of IORT parameters with help of the DVH (Dose Volume Histogram).
- Reporting.



3. LOAD IMAGES

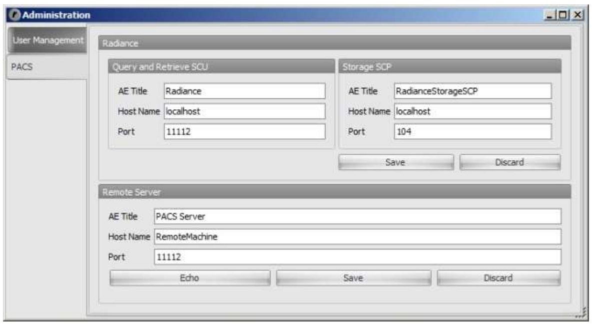
Radiance is compatible DICOM V3 standard (http://dicom.nema.org/).

User can load DICOM 3D images (CT, NRM) that reside on a local drive (hard disk, DVD, USB memory) as well as retrieve them from a PACS/RIS system through its query & retrieve console.



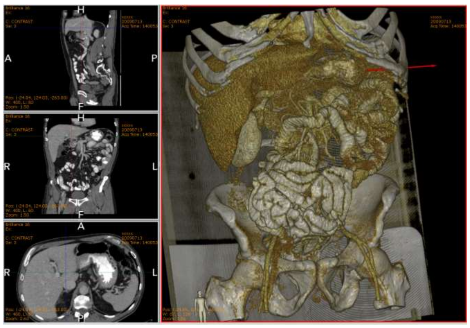
A storage SCP service is available so that images can be sent from another DICOM node such as other planning systems.

The PACS interface configuration is fast and simple.

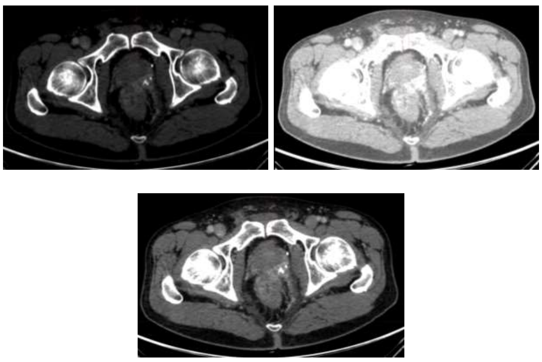


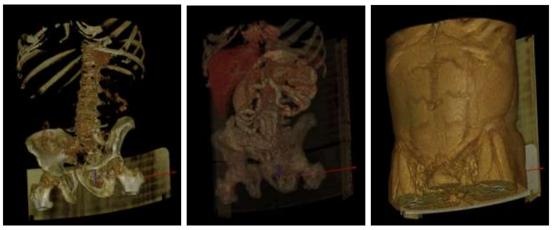
4. MPR AND VOLUME RENDERING

A state of the art 3D GPU based graphic engine provides high quality Multi-Planar Reconstruction (MPR) and volumetric rendering (VR) of the patient's image in real time. Both MPR and VR views can be rotated, panned and zoomed in/out with no delay. ***Radiance*** allows fast visualization of very large 3D studies with no required preprocessing.



Different contrast windows and opacity tables can be used to enhance the visualized images allowing the user to highlight anatomic elements and regions of interest.





Interactive geometrical meshes can be added to the views, for instance to exemplify the movement of the applicator or the 3D dose deposit. Also, graphics can be overlayed on 2D views to depict the isodose curves on a certain cross-section.

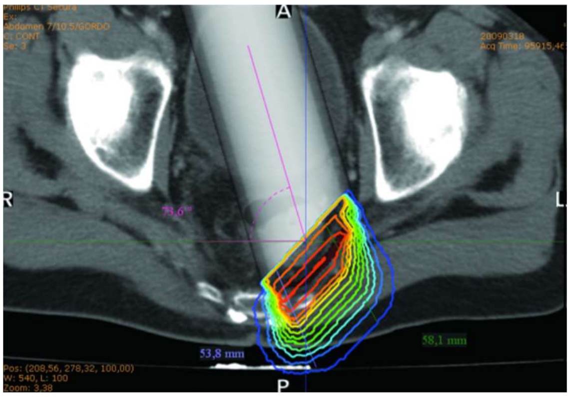
By allowing manipulation of the views it is possible to place the patient in both supine and prone positions.

5. MEASUREMENT TOOLS

Radiance has a complete set of tools to measure distances and angles accurately within the scene.

A rule tool allows the user to measure distances in any of the MPR views through the selection of an initial and end points. This tool is useful to calculate, for instance, the depth of the effective dose on a particular slice.

In addition, an angle measurement tool allows the user to measure sexagesimal angles in any of the MPR views. Users can calculate an angle, by selecting three non-collinear points on the image. This is useful, for instance, to determine the incidence angle of the applied dose.



6. CONTOURING

The contouring tool is used to identify the areas of interest in the procedure, i.e., the regions to be treated, the regions to be protected and the regions that are resected during surgery.

These regions can be shown/hidden, outlined or removed from the image to simulate the resected tumor.

The process is carried out by manual contouring using polygonal, free hand or pearl tools. Refinement of contours can be achieved by allowing union/difference/intersection operations of that contour as well as scaling and moving tools. A copy/paste tool is also provided so that a base contour can be copied across slices.

In order to minimize user interaction an interpolation of contours is also provided: This allows the reconstruction of a whole 3D region based on a few contours located in non-consecutive slices, which speeds up the process and reduces errors.

Automargin functionality allows growing contours to quickly create volumes larger than a reference one.

DICOM.RT Structures coming from other planning or contouring software can also be loaded into the system.

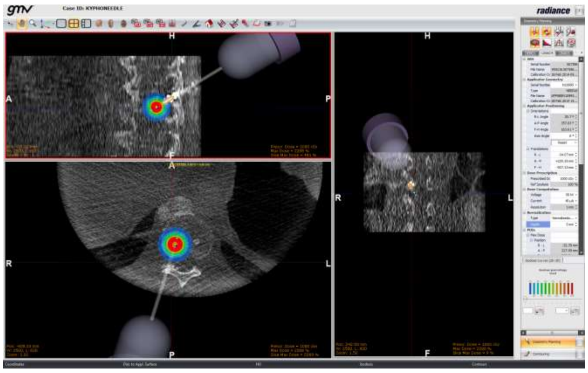
7. SIMULATION

Next step in the IORT procedure definition, once we have determined the target and the organs to protect, is to define the surgery approach and the applicator parameters, which we call navigation.

It is possible to navigate along the complete set of 2D MPR views in any orientation to determine the incision to be made during surgery, the location of organs at risk, organs to protect and to be aware of possible complications.

The surgery simulation is initiated by the surgical frame. This surgical frame resembles the incision made by a surgeon.

Then, the different feasible positions and orientations of the applicator are evaluated following its anatomical restrictions (incisions and organs restrictions, especially bones) and the degrees of freedom of the linear accelerator. Surgeon and Radiation Oncologist can evaluate together the best surgical approach to optimize the access to the area to be treated with the applicator.



After definition of the surgical frame, the surgeon can define the resection of the tumor (STV) that is planned, having them the area to be treated (Planning Target Volume – PTV), the tumor bed, as the result of the remaining CTV after removing the STV.

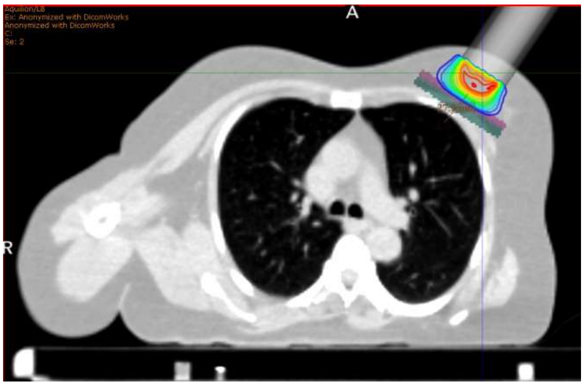
The system allows the selection of applicator and beam characteristics.

Radiance allows simulation (designing and testing) of bolus and protections (radiation shields) before the actual treatment.

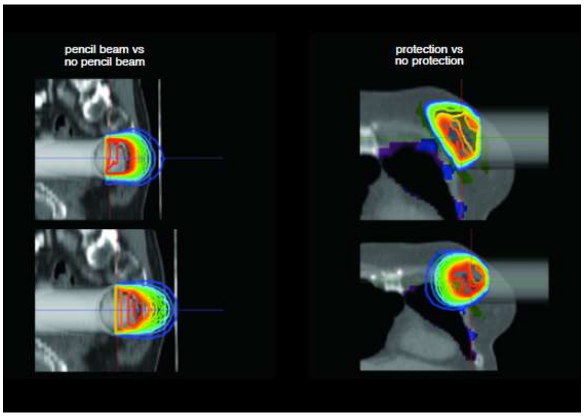
Protections and bolus are special types of contours that can be created by the user.

Sometimes, depending on the location of the area to be treated, the user may wish to protect surrounding regions which need to be spared from irradiation. For this purpose external elements manufactured with specific materials, from which density and effect on the attenuation of radiation have been previously studied, are used.

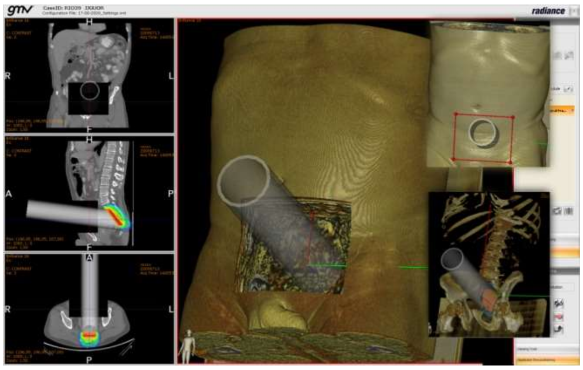
A user can add as many protections as needed. Protections can be positioned, oriented and resized in 3D space at will.



In the following figure, the difference between using and not using an heterogeneous calculation algorithm can be seen in a rectal cancer (left column), the effect of using and not using protections in a breast cancer case can also be seen (right column).



Optimization of IORT parameters is achieved by allowing the user to change the geometry of the applicator, the position and orientation of the applicator and by selecting the treatment unit parameters.



8. STATE OF THE ART DOSE COMPUTATION ALGORITHMS

The calculation of dose deposition, according to the current characteristics of the applicator, is carried out depending on the type of linear accelerator.

For electron devices, (either mobile or conventional linear accelerators) two dose computation algorithms are available in ***radiance***.

- An adapted and validated fast implementation of the Pencil Beam algorithm used in external radiotherapy.
- Monte Carlo algorithm.

For INTRABEAM® there are also two dose computation algorithms:

- Dose painting algorithm.
- Hybrid Monte Carlo algorithm.

By using CT images, radiance takes into account the necessary information on radiation attenuation of the tissues for dosimetry calculation. For any other type of images, the computation algorithm will not handle the different densities of the tissues, assuming the tissue is water for computation purposes.

MOBETRON

Pencil Beam

The "Pencil Beam" algorithm for electrons is mainly based on the work of Fermi-Eyges. In this, the authors take into account the multiple Coulomb scattering of primary electrons as the primary phenomenon that produces the probability distribution within a material reached by a conveniently collimated narrow electron beam. This multiple scattering has an essentially Gaussian treatment, or at least it can be treated with sufficient accuracy by Gaussian functions. Besides, there are some additional effects which are considered in this implementation, such as:

- Stopping radiation production.
- Dispersion of individual electrons on large angles.
- Redistribution of the energy of the beam by means of secondary electrons.
- Widening of the electrons range.

Pencil Beam implementation included in ***Radiance*** takes into account all these effects while having a very fast execution (it takes only a few seconds to compute). According to our tests results, it performs far better than other implementations found in the literature (see references at the end of the document). The limitation of the semi-infinitive layer approach and the poor backscattering modeling is covered by the available Monte Carlo dose computation algorithm.

Monte Carlo

Monte Carlo algorithm is a fully parallel implementation which can run in the different cores of the workstation reducing the total computation time to obtain the dose deposition (experiments give us a computation time of around 1-10 minutes, depending on applicator diameter and energy).

A complete set of phase spaces have been obtained using Monte Carlo to compute the dose on water of 60.000 annular mono-energetic sources (with a bin of x MeV) with different radius. During the commissioning of the system, an iterative algorithm is able to get, in less than two hours, the linear combination of these sources which best adjust to the experimental measurements (PDD and profiles) for the specific applicator, energy and bevel.

From the particle-material simulation kernel, ***Radiance*** implements DPM in a full recodification with a parallelization architecture and several implementations optimization, which means a fast and reliable (as the optimizations does not impact on the physics) execution.

Building a minimal LINAC model for both PB and MC algorithms needs just a subset of the measurements needed for the commissioning of the system.

INTRABEAM®

Dose Painting

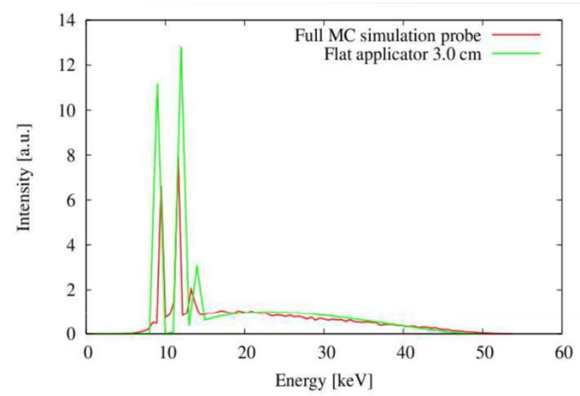
The dose painting algorithm for INTRABEAM® is based on an interpolation of the specific (i.e. applicator/XRS dependent) depth dose along the clinical axis, and either assume perfect isotropy (spherical, needle), or 'generic' lateral off-axis ratio for flat/surface.

To model this algorithm, the calibration files for the applicator (either spherical, needle, flat or surface) are needed.

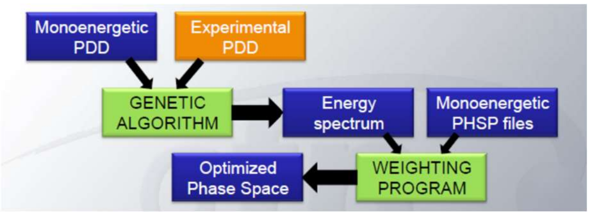
This interpolated dose volume is displayed over the patient image according to the applicator position/orientation. No heterogeneity correction is computed.

Hybrid Monte Carlo

In this method, a simulation of the radiation device and filter/applicators is performed in the most realistic and detailed way possible. This simulation will then predict the initial energy spectrum of the particles generated before the main collimators and filters or flattening foils of the devices, and the flux of particles generated at the exit of the device.



In a second step, a genetic algorithm may be employed to fit the actual PDD measured in water for a particular radiation device. The genetic algorithm fits a sensible spectrum for the primary particles (see for instance the green curve in the figure above), including the adequate combination of characteristic X-rays and tail, weighting with this spectrum the monoenergetic PDD until a good fit with the measured PDD for the actual device is well reproduced. The procedure is sketched in the figure below (M. Vidal et al., 2014).



As a final step, the monoenergetic PHSP files are combined weighting them with the same energy spectrum fit by the genetic algorithm. This final summed PHSP will be employed to compute the dose by the MC algorithms.

From the particle-material simulation kernel, ***Radiance*** takes into account the photoelectric and the Compton effects. The Rayleigh effect is a minor contribution for the small distances involved in this case. The algorithm uses condensation of histories to speed up execution.

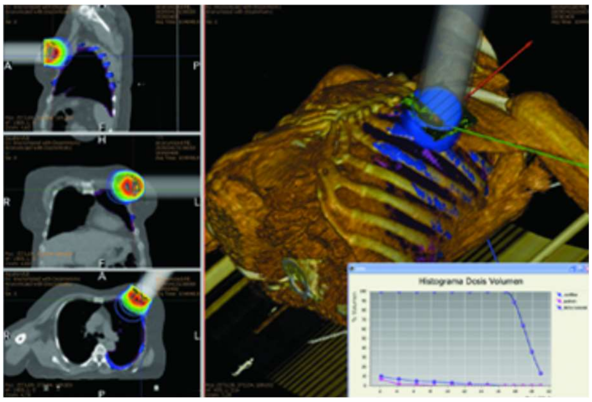
9. DOSE PRESCRIPTION

Dose is prescribed at the desired reference isodose percentage (100% for INTRABEAM®) and at desired depth in the clinical axis.

Dose will be normalized considering the above prescription information.

10. DVH COMPUTATION

A Dose Volume Histogram (DVH) is computed over all regions (risk areas or those to protect) and allows the user to optimize the treatment parameters prior to the treatment. The modification of any parameter during planning (location, orientation, or geometry of the applicator and LINAC´s parameters) implies an automatic recalculation of the DVH.



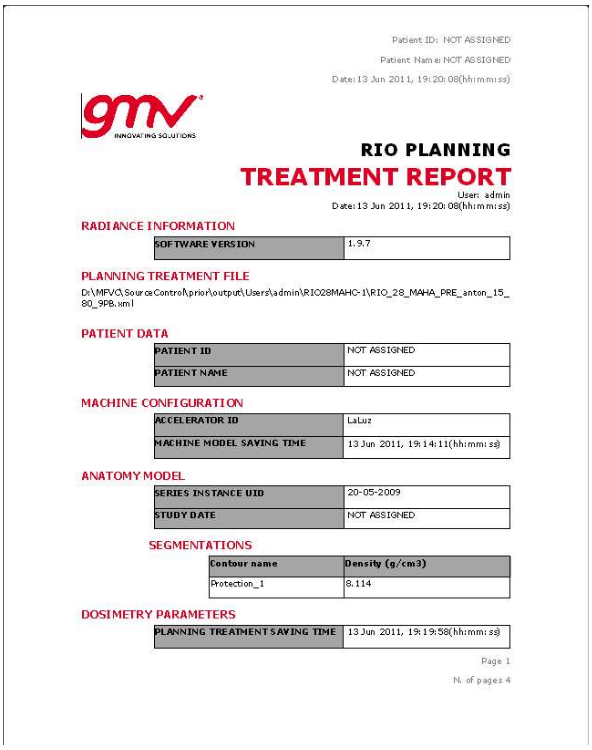
Maximum and minimum dose is indicated as required by ICRU 71.

11. REPORT

The current absence of a complete and homogeneous method for documenting IORT procedures is one of the main limitations when comparing the results and complications of this technique. When the results from an IORT clinical program are presented, the parameters that are generally documented are the energy/voltage and the applicator parameters (diameter and bevel angle).

Radiance stores all treatment information generated by system, including not only the device and applicator parameters, but also position and orientation (with respect to the patient and the LINAC), regions information, dose volume and isodose curves, device configuration as well as all snapshots that the user might have generated. This way, the case can be reproduced quite easily and be compared against another. Radiance allows the use of templates so that the information is structured in the format required by the user.

This documentation can be stored before the treatment (during pre-planning), during the treatment (especially if there is a capability to generate intraoperative imaging) and also after the actual procedure, recording all the final amendments of the original plan. Reports can be exported to Microsoft Word format (among others) so that they can be printed and easily exchanged with other people.


Patient ID: NOT ASSIGNED
Patient Name: NOT ASSIGNED
Date: 13 Jun 2011, 19:20:08(hh:mm:ss)

RIO PLANNING
TREATMENT REPORT
User: admin
Date: 13 Jun 2011, 19:20:08(hh:mm:ss)

RADIANCE INFORMATION

SOFTWARE VERSION	1.9.7

PLANNING TREATMENT FILE
D:\MFVC\SourceControl\prior\output\Users\admin\RIO28MAHC-1\RIO_28_MAHA_PRE_anton_15_80_9PB.xml

PATIENT DATA

PATIENT ID	NOT ASSIGNED
PATIENT NAME	NOT ASSIGNED

MACHINE CONFIGURATION

ACCELERATOR ID	LaLuz
MACHINE MODEL SAVING TIME	13 Jun 2011, 19:14:11(hh:mm:ss)

ANATOMY MODEL

SERIES INSTANCE UID	20-05-2009
STUDY DATE	NOT ASSIGNED

SEGMENTATIONS

Contour name	Density (g/cm3)
Protection_1	8.114

DOSIMETRY PARAMETERS

PLANNING TREATMENT SAVING TIME	13 Jun 2011, 19:19:58(hh:mm:ss)

Page 1
N. of pages 4

12. DICOM.RT COMPATIBILITY

Radiance can import/export ROIs from files in DICOM.RT Structures format.

The dose can be exported in DICOM.RT Dose format so that it can be shared with external software, for instance, to sum the dose up with external radiotherapy in boost treatments.

The dose is exported as physical dose and can be either saved as absolute or relative dose.

SECTION 3
CLINICAL VALIDATION STUDIES

Several studies have been performed to evaluate the feasibility and clinical utility of ***Radiance*** in the planning of intraoperative radiotherapy treatments. Results have been presented in the most important congresses of the specialty.

In the first study, 36 cases have been gathered in the Hospital Universitario Gregorio Marañón and a representative subgroup of 14 has been simulated by three radiotherapy oncologists. The localizations were: breast (6), rectal (6), rectal relapse (1), ovary relapse (1), pancreas (1), retrop. sarcoma (1) and ewing sarcoma (1).

As an example, the result of the simulations of the three breast cases per each radiation oncologist is shown in the next table:

		Energy MeV	Diameter cm	Bevel angle	Position difference (cm)
RO1	BREAST1	6	7	0	
RO2		6	7	0	0.379
RO3		6	7	0	1.193
RO1	BREAST2	6	7	0	
RO2		6	5	0	0.532
RO3		4	6	0	0.324
RO1	BREAST3	6	6	0	
RO2		6	6	0	0.704
RO3		6	6	0	0.625

The conclusions of that study are the following:

- ***Radiance*** is an intuitive planning system that properly simulates the parameters that must be decided in IORT procedures.
- The possibility of studying several plans improves the preparation of the specialist for the real situations to be afforded during the procedure.
- ***Radiance*** allows discussing the best approach for a concrete case and eases the specialist to analyze a simulation prepared by another one. This exchange of specific information about an IORT treatment is an essential contribution to the system.
- The cases and the simulations gathered are type cases that will allow specialists to quickly learn to use ***Radiance***. This learning will also allow studying IORT procedures from an approach that would not be possible without ***Radiance***, as it allows checking what happens when modifying the treatment parameters. Moreover, these training cases ensure the correct use and knowledge of possibilities and properly simulate an IORT procedure with ***Radiance***.

Further studies on the usage of PB (Pencil Beam) and Monte Carlo for specific locations showed that these algorithms identify several aspects of IOERT treatment that cannot be evaluated with conventional water phantom measures. ***radiance*** IOERT simulation and planning system moves one step forward to more precise dose estimation by the inclusion of this algorithm. The use of PB and MC allows quantifying and predicting the influence of several parameters in this IOERT breast model.

Comparisons between different Oncologist Radiotherapists (ORs) showed that the ORs provided completely equivalent plans for 65% of the cases evaluated, and this percentage increases up to 85% if the RO has information about the surgical procedure. This suggests that simulation has to be carried out with specialized surgical input, which will set the criteria to select the surgical access and help in the definition of the high risk areas. When there is agreement in the contouring protocol and information from the surgical procedure, all ORs provide equivalent simulations.

SECTION 4
RADIANCE, THE ESSENTIAL TOOL

SUMMARY

Intraoperative Radiotherapy, IORT, is a kind of therapy that allows the incorporation of a dose absorbed in a single session through high-energy electron beams to cancer treatment. This is done during surgery in a non-resected tumor or at the surgical site, while normal (no tumoral) tissues are displaced from the beam of radiation. The advantage provided by IORT is the possibility of carrying out a visual and palpable demarcation of the tumor, and also of excluding the risk structures from the radiated field, whether by displacing or protecting them.

So far, there was no commercial planning tool available on the market for treatments with this technique; a manual dosimetry was carried out based on the distribution of water-measured doses.

No commercial tool is either available for IORT suitable devices being used in other localizations such as interstitial, intracavity or superficial applications.

The use of a planning tool adds numerous advantages to this type of treatment, along the lines of the recommendations of the AAPM working groups (Task Force 48 and Task group 72) that are considered an international reference in this matter and are widely cited in all the IORT bibliography.

The main improvements achieved with the use of the planning tool are the following:

- It makes possible to know the **exact depth and lateral extent of the tumor** by different means other than the direct manipulation during surgery or ultrasound. Thus, it is possible to choose the optimal position, orientation, size and shape of the applicator as well as LINAC parameters in order **to achieve the recommended coverage of 90%** (TG 48).
- It enables **real dose distribution in the patient and the volumes of interest**, unlike the standard calculation, that only permits to determine the dose in a certain point (approx.) and MU (Monitor Units) calculation (approx.).
- In case the areas to be treated are larger than the size of the measured applicators, it enables the estimation of **the overdose and the underdose in the intersection area between two applicators**. This point is important, as doses given in one-session treatments are very high. TG48.
- The **monitor units must be checked twice**. The planning tool is the only independent means, apart from manual calculation, to that purpose as opposite of using the same equation in a spreadsheet. TG48.
- As it is **a single fraction technique, it is essential to verify that the dose has been administered in the correct anatomic location and at the desired depth** (TG48). Current methods, such as photography, online monitoring and ultrasound are not as accurate as a CT image, which is also the only type of image that permits the use of the information on the tissues real composition in the calculation of the dose.

- The difference in the deposition of the **dose for soft tissues and bones** depends on the energy. In a manual calculation this is not taken into account, whereas the planning tool can simulate it. Validation tests have been carried out to prove this point.
- It makes possible to **calculate the dose for tissues and critical organs**, unlike in usual calculations (TG48), which must be reported for all radiotherapy treatments, according to Spanish Royal Decree 1566/1998 on Quality Assurance criteria for radiotherapy.
- The use of a planning tool is the most effective way of "carrying out an **individualized clinical dosimetry** under the supervision and responsibility of an expert in hospital radiophysics, according to the prescription of the specialist doctor", as stated in the RD 1566/1998, sections 2 and 3.
- It permits to obtain the **maximum and minimum doses** to PTV (Planning Target Volume. Such doses must be included in the final report according to the ICRU 71 (they are not estimated in manual calculation).

The final recommendations document of the TG-72 for mobile accelerators specifies that all aspects related to possible modifications of radiation beams must be examined: gaps, bolus, tissue heterogeneity, and that it is necessary to develop IORT treatment planning tools able to reproduce real treatment situations.

Taking into account everything previously considered, we estimate that the validity of a specific planning tool for Intraoperative Radiotherapy is perfectly justified.

__Radiance__ is not approved or offered in every market and approved labeling and instructions may vary from one country to another. For country-specific product information, see the appropriate country website. Product specifications are subject to change in design and scope of delivery as a result of ongoing technical development.

13. TESTIMONIALS

"IORT parameters can be defined the day before to the treatment 90% of the times, [...] the system enhances the capabilities of documenting the process for posterior analysis", **Prof. Felipe Calvo**, Oncology Department Director, Gregorio Marañon University Hospital, Madrid.

"It is an important advance in the history of IORT [...] The preplanning phase is an important improvement in the IORT treatment of breast cancer [...] Brest surgery can be previously predicted and the different parameters of the treatment can be defined beforehand", **Prof. Roberto Orecchia**, Radiotherapy Division Director, Istituto Europeo di Oncologia, Milan.

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E4. Pascau J et al. "Sistema de simulación quirúrgica y planificación para radioterapia intraoperatoria". CASEIB 2009.

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E15. Calama J et al. Pencil Beam for electron intraoperative radiotherapy. Results of dose calculations in heterogeneous media. GEC-

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E17. Santos JA et al. Initial clinical experience of Pencil Beam dose modelling for Intraoperative Electron Radiation Therapy (IOERT). GEC-ESTRO ISIORT Europe Conference. 7-10 Mayo 2011. Londres. Reino Unido.

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E19. Pascau J et al. "Intraoperative Imaging In IOERT Sarcoma Treatment: Initial Experience In Two Clinical Cases". ASTRO 2011.

E20. Pascau J. "Desarrollos técnicos y tecnológicos. Proyecto *radiance*". Seminario sobre radioterapia intraoperatoria Grupo IMO. 2011

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E22. Felipe A. Calvo, Manuel González-Domingo, Sergey Usychkin. "Encyclopedia of Raditaion Oncology", Chapter "Intraoperative Irradiation". ISBN 978-3-540-85516-3. 2011

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