Practical aspects of inverse-planned intensity-modulated radiation therapy for prostate cancer: a radiation treatment planner's perspective

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Introduction: *From a radiation treatment planner perspective, in the treatment of prostate cancer, inverse-planned intensity-modulated radiation therapy (IMRT) differs considerably from conventional, conformal, and forward-planned IMRT. In this work we aim to discuss the rationale behind the use of inverse-planned IMRT for the treatment of prostate cancer, as well as some of the practical aspects, including the differences in planning strategies, dose fractionation and issues in plan evaluation.*
Discussion: *The primary motivation behind the use of inverse-planned IMRT for prostate cancer radiotherapy is to attempt further dose escalation while maintaining critical structure and healthy tissue sparing at an acceptable level. The sparing of normal tissues is largely dependent on the size of the planning target volume (PTV) defined, and if the PTV overlaps critical structures. Depending on how the PTV is defined it may be impossible to achieve the desired healthy tissue sparing even with IMRT. A second role for the use of IMRT in the treatment of prostate cancer may be to conform the isodose distribution to a complex PTV, such as one that includes the seminal vesicles or the pelvic lymph nodes in the treatment volume. Finally, inverse planned IMRT may be useful in the planning and delivery of simultaneous integrated boosts where different parts of the target structures receive different daily doses. This again has applications for the simultaneous treatment of pelvic lymph nodes with the prostate treatment volume, and presents interesting opportunities for hypo-fractionation. All of these options of course require careful plan evaluation with respect to isodose distributions and dose-volume constraints as well as the radiobiological consequences of using unconventional fractionation.*
Conclusion: *IMRT seems to be the most effective modality for treating complex target geometries and for delivering simultaneous integrated boosts. In particular for prostate cancer, the simultaneous treatment of the prostate and pelvic lymph nodes lends itself perfectly to IMRT, allowing the prostate to receive a higher daily dose per fraction, as well as minimizing the amount of small bowel in the field, while at the same time sparing the rectum and bladder adequately. Inverse-planned IMRT is, however, a complex procedure, and to safely implement it, an extensive patient- and machine-specific quality assurance program is required.*

Key Words: IMRT, prostate, inverse treatment planning

Introduction

Traditionally, patients receiving radiotherapy for prostate cancer were treated with large radiation fields, to allow for planning uncertainties related to the definition of the treatment volume and the mobility of the prostate. Conventional fluoroscopic simulation provided only anatomical landmarks from which one could estimate the target position, and it was not uncommon to see radiation field sizes in the order of 15 cm x 15 cm. Due to these large radiation fields, the morbidity associated with the treatment was not negligible, and therefore the prescribed radiation dose was limited to 45 Gy-55 Gy. An additional trend at the time was the irradiation of the

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pelvic lymph nodes with a dose of at least 45 Gy. The use of conventional simulators allowed for the development of a 4-field "box" technique that attempted to spare some of the healthy tissues surrounding the treatment volume.

Since the introduction of computed tomography-(CT)-based treatment planning, it has become possible to better define a treatment volume in terms of both shape and localization. The International Commission on Radiation Units and Measurements (ICRU) promulgates recommendations in Reports 50 (1993) and 62 (1999) that define target volumes for radiotherapy treatment planning. Gross tumor volume (GTV) is defined as the radiologically or clinically visible extent of malignancy or disease, which for prostate radiotherapy is comprised of the entire prostate that is visible on axial slices. In some cases, portions of the seminal vesicles are included in the GTV. A clinical target volume (CTV) includes the GTV and a margin to allow for microscopic disease, as well as any tissues considered at risk of cancer, such as draining lymph nodes. The planning target volume (PTV) is a larger volume designed to always encompass the CTV so that it takes into account patient setup uncertainties, organ localization, and organ motion during the treatment. This additional margin is typically set at 5 mm-20 mm, which drastically reduces the target volume from that seen with conventional techniques. This volume reduction, along with the use of complex beam configurations (typically 4-7 fields), has resulted in greater healthy-tissue sparing and has allowed an increase in the dose delivered to the prostate to 65 Gy-75 Gy.

The dose-limiting structures in modern-day external-beam radiotherapy of prostate cancer are the bladder and the rectum. Several published papers[1-4] have shown an increasing rate of rectal and bladder complications occurring with increasing radiation dose and increasing volume being irradiated. The challenge is to minimize the radiation dose to these non-target structures, while maximizing the dose to the target. The published literature supports the concept that an increased radiation dose to the prostate correlates with an increase in disease-free survival,[5-6] particularly for intermediate-risk patients. In fact, the Radiation Therapy Oncology Group (RTOG) is conducting a trial (RTOG P0126) comparing 70.2 Gy versus 79.2 Gy, using either CT-based conformal radiation therapy or a newer type of treatment called intensity modulated radiation therapy (IMRT).

In conformal radiotherapy treatment planning, the relevant organs and radiation targets are delineated from a patient's CT scan images. The radiation treatment planner (planner) defines a radiation beam configuration, and the radiation dose distribution is calculated using a computer algorithm. The planner then evaluates the dose distribution. If the treatment plan is judged to be unacceptable, changes are made to either the beam geometry or some other planning parameter, and the dose distribution is recalculated and reevaluated. This process continues in an iterative fashion until the planner determines that the plan is satisfactory.

In intensity-modulated radiation therapy (IMRT) treatment planning, a desired dose distribution using a fixed number of radiation fields is obtained by modulating the intensity throughout each field. This modulation is usually achieved with the use of a multi-leaf collimator (MLC) that is allowed to move through various apertures for each beam orientation. In forward-planned IMRT, a small number of such MLC apertures per field are defined by the planner, and are modified through an iterative process to come up with an acceptable dose distribution. The combination of MLC apertures per beam orientation is then converted into a single sequence that can be automatically and efficiently delivered at treatment time. The process, although intuitive, is limited to simple dosimetric situations. Several authors have demonstrated the use of forward-planned IMRT for prostate cancer.[7-9]

In inverse-planned IMRT, each radiation field is broken up into small elements referred to as beamlets. A computer algorithm, in a process called optimization, is used to calculate the required intensity of each beamlet as follows. First, the planner defines an initial set of beam gantry angles, and a series of dose-volume constraints for each relevant target structure and organ at risk. The computer is used to formulate a mathematical objective function based on the dose-volume constraints and the importance of achieving each of the treatment goals. Each field is divided into hundreds of beamlets, and the algorithm chooses a beamlet intensity pattern for each treatment port and calculates the dose distribution for a given configuration. The radiation doses at each point in the relevant organs and target structures are compared to the user-defined dose-volume constraints, using the objective function. The process is repeated until the function is minimized and a solution is found. The user then analyzes the results, and decides whether or not the plan is adequate. If changes are required, the planner may change the dose-volume criteria or some of the physical parameters defining the treatment-beam geometry. Once a suitable plan is found, the required beamlet intensities are converted into a deliverable

MLC-leaf sequence for the treatment of the patient. There are numerous publications discussing the treatment of prostate cancer with inverse IMRT.[10-12]

Our aim in this article is to discuss, from a radiation treatment planner's perspective, issues and strategies with respect to inverse-planned IMRT treatment planning. This approach differs considerably from conventional, conformal, and forward-planned IMRT treatment planning.

Discussion

Planning concerns

For treatment planning purposes, we can consider three categories of prostate patients: patients requiring irradiation of the prostate alone, those requiring irradiation of the prostate and seminal vesicles, and, those requiring irradiation of the prostate (or post-surgical bed), seminal vesicles, and draining pelvic lymph nodes. We also consider that all prostates have a rectum posterior and adjacent, and a bladder anterior and adjacent, and recognize that these structures are dose-limiting organs. In this study, the RTOG guidelines for rectal and bladder sparing have been used as endpoints when assessing treatment plans. Only cases where the target dose exceeds 79.2 Gy are examined, since we know that using 3-D conformal CT-based planning techniques or IMRT, lower doses can be safely delivered with acceptable toxicity to the dose-limiting structures.

PTV margin

A principal planning concern for all three categories of patients is the size of margin used to define the PTV. By definition, the PTV is an overlapping organ, and since the bladder and rectum are anatomically adjacent to the GTV (prostate or prostate and seminal vesicles), portions of these organs may be included in the PTV and will also receive the doses prescribed to the PTV. This of course means that the larger the PTV, the larger the volume of overlapping critical structures receiving such doses. Several studies have correlated the incidence of rectal complications to the volume of rectum irradiated and the radiation dose delivered.[1-4] In fact, at least in one early study of patients treated with IMRT of the prostate, the dose to the portion of the PTV overlapping rectum was compromised, so as to deliver a tolerable dose of radiation to the critical structure.[11] The current RTOG P0126 protocol for high-dose prostate radiotherapy suggests using a PTV margin of 5 mm to 10 mm. Meeting these requirements may necessitate the use of daily prostate localization.

Target geometry

A second concern from the planner's perspective is target geometry. For the case of a CTV consisting of the prostate alone, the target has a simple convex shape. It can adequately be treated to 79.2 Gy with either CT-based conformal radiotherapy using judicious use of shielding, or with inverse-planned IMRT, both respecting the RTOG P0126 standards for critical-structure sparing. Figure 1 shows an example of a 3-D conformal plan for treating the prostate alone. Illustrated in Figure 2 is an axial distribution planned with IMRT for a CTV consisting of the prostate only.

For a patient being treated to the prostate and seminal vesicles, the superior portion of CTV in the region of the seminal vesicles partially wraps around the rectum, creating a concave target. This is a

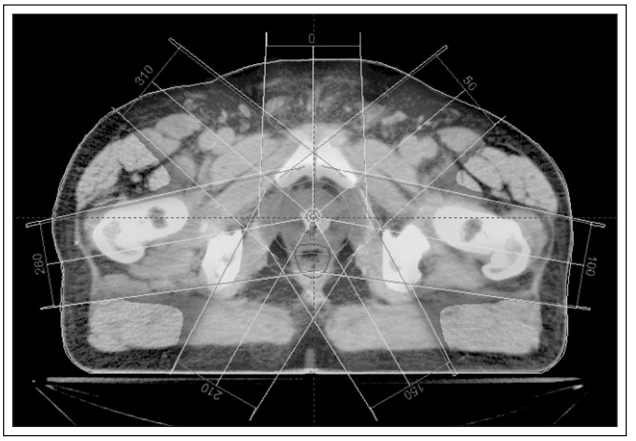

Figure 1. Example of typical CT based conformal radiotherapy plan for a prostate patient. The patient is treated with 7 beams, and the target contains the prostate and a 7 mm PTV margin.

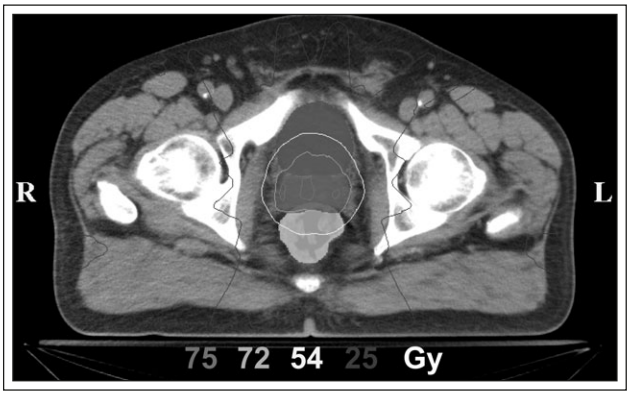

Figure 2. Example of typical inverse plan IMRT radiotherapy plan for a prostate patient. The patient is treated with 7 beams, and the target contains the prostate and a 7 mm PTV margin.

situation better suited to IMRT, which handles concave targets well, as can be seen in Figure 3.

The last category of patient is one for whom the CTV is comprised of the prostate, seminal vesicles, and pelvic lymph nodes. Conventionally, the treatment is given in two phases. The first phase delivers 50 Gy–54 Gy using large fields in a 4-field box configuration including the prostate, lymph nodes and some appropriate margin. The second phase boosts the prostate and seminal vesicle dose to 65 Gy-75 Gy. One difficulty with this course of treatment is the high dose received by a large volume of small bowel during the first phase. A clear advantage of IMRT over conformal planning is the ability to conform isodose distributions to multiple convex- or concave-shaped structures, such as the PTV in this case, see Figure 2. But perhaps even more interesting is the ability of IMRT to deliver simultaneous integrated boosts (SIB), where different targets receive different doses simultaneously. It is possible in this case to simultaneously deliver 54 Gy to the lymph node PTV and 70 Gy to the prostate and seminal vesicles PTV, while still adhering to the RTOG P0126 criteria for critical-structure sparing and keeping most of the small bowel under 25 Gy, see Figure 4. The issue of concern here, however, is fractionation. Clearly, the 70-Gy prostate target and the 54-Gy nodal target are not receiving the same daily dose when using the SIB technique. In fact, if we want to deliver the traditional nodal irradiation dose of 50 Gy in 35 fractions — so that the prostate and seminal vesicles GTV receives the 70 Gy in 2-Gy fractions — the nodal PTV will receive 1.43 Gy/day. One solution may be to increase the daily nodal dose. We can prescribe 54 Gy to the nodal PTV and 70 Gy to the prostate and seminal vesicles PTV, in 33 fractions Figure 4. This results in a fractionation of 2.12 Gy/day for the prostate PTV and 1.67 Gy/day to the nodal PTV.

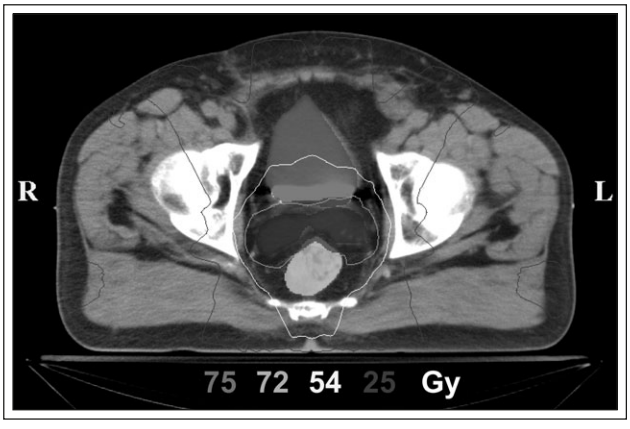

Figure 3. Example of typical inverse plan IMRT radiotherapy plan for a prostate patient. The patient is treated with 7 beams, and the target contains the prostate and the seminal vesicles and a 7 mm PTV margin.

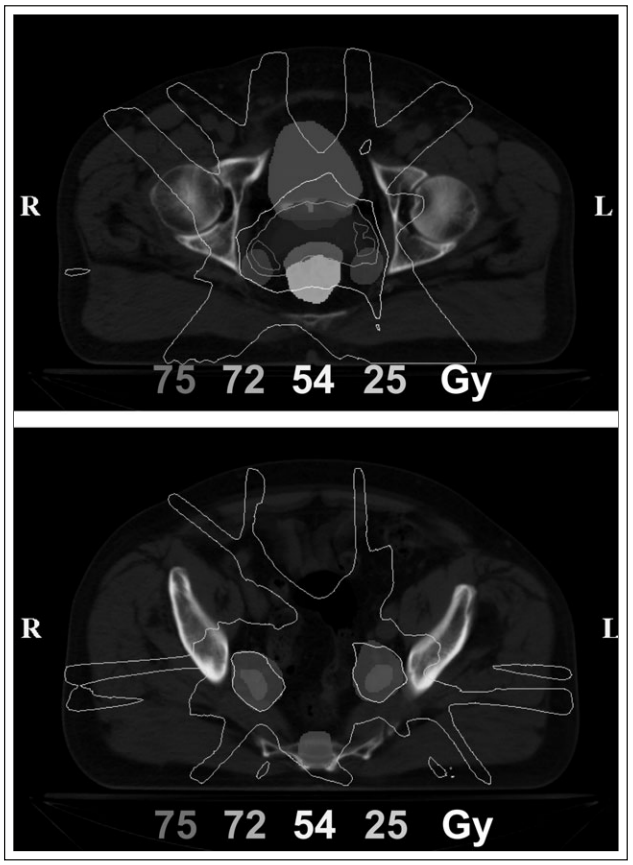

Figure 4. Example of inverse plan IMRT radiotherapy plan for a prostate patient requiring pelvic node irradiation. The patient is treated with 7 beams, and the high dose target (70 Gy) contains the prostate and the seminal vesicles and a 7 mm PTV margin. The nodes are included in a CTV target which simultaneously receives 54 Gy.

High daily doses

Another situation where inverse IMRT may be useful is the delivery of very high daily fractionations (> 3 Gy) to the prostate PTV. At conventional dose levels and fractionations, the use of conformal radiotherapy yields acceptable rectal and bladder complication rates.[13] It is not clear, however, what the tolerance doses are for high fractionations. Using the biological effective dose (BED)–extrapolated response dose (ERD) model,[14-15] we can estimate the tolerance doses for different fractionations and apply them as planning constraints. For example, using the RTOG parameters for rectum and bladder dose constraints for 79.2 Gy in 1.8 Gy fractions, we can calculate the equivalent constraints

TABLE 1. **Rectal and bladder dose limits for an increased fractionation of 3 Gy/day based on RTOG P0126 guidelines and the biological effective dose (BED) - extrapolated response dose (ERD) formalism**

RTOG parameters (1.8 Gy/day)			GTV 3 Gy/day (α/β=3)		
Volume (%)	**Rectum dose (Gy)**	**Bladder dose (Gy)**	**Volume (%)**	**Rectum dose (Gy)**	**Bladder dose (Gy)**
15	75	80	15	60	64
25	70	75	25	56	60
35	65	70	35	52	56
50	60	65	50	48	52

GTV = gross tumor volume; Gy = gray (radiation dose); RTOG = Radiation Therapy Oncology Group

for an accelerated regime of 60 Gy in 20 fractions, see Table 1. At these high daily doses, even the modest improvement in rectal or bladder sparing provided by IMRT may reduce the risk of complications.

Conclusion

In summary, we have reviewed several situations in which inverse-planned IMRT can be useful for the radiotherapy treatment planning of prostate cancer. IMRT seems to be the most effective modality for treating complex target geometries such as concave volumes, and for delivering simultaneous integrated boosts. This suggests that the simultaneous treatment of the prostate and pelvic nodes is the configuration that benefits the most from IMRT radiation treatment planning.

Thus far, we had only considered the radiation treatment planning issues and indications for inverse-planned IMRT of the prostate. This technique is, however, complex to perform and requires considerable experience to be implemented safely. The delivery of complex dynamic radiation treatment fields is not well understood, and there should be an extensive patient- and machine-specific quality assurance program when performing IMRT. Institutions should not concede to financial and political pressures to implement this treatment modality for prostate patients, unless the limitations are clearly understood and a program to ensure quality has been implemented. □

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