Prostate IMRT: Promises and Problems

Chandra Burman, Ph.D.
Memorial Sloan-Kettering Cancer Center, New York, NY 10021

Introduction

Prostate is one of the treatment sites that is well suited for IMRT. For localized prostate cancer radiation therapy it is one of the effective modalities. However, radiation induced complications such as, urinary incontinence, rectal bleeding are some of the side effects. With traditional treatment techniques such as 4-field box or bi-lateral arc, doses in the range of 60-70Gy can be delivered. To deliver higher doses, up to 75.6Gy, 3-dimensional conformal radiation therapy has been used successfully [1]. However, there are indications that the use of higher doses can lead to better outcomes [2-4]. To test the hypothesis, our institution (MSKCC) has been involved in a dose escalation trial [5]. Within this study doses at 81Gy and 86.4Gy have been successfully delivered, without exceeding concomitant normal tissue complication. It has been possible with the use of IMRT. In this presentation we will discuss our experience in the use of IMRT for the treatment of localized prostate cancer and some of the clinical outcome; rationale for using IMRT; problem in defining the target and normal tissues; dose-volume criteria for evaluating treatment plans.

Patient Immobilization and CT Scan

The patient's pelvis is immobilized in the treatment position using a thermoplastic mold. Prone treatment position is preferred [6]. However, if patient is unable to lie comfortably in this position, a supine position is used. In order to enhance the bowel located near the PTV, an oral bowel contrast is administered prior to the procedure. A rectal catheter is used to localize the lumen on the CT images.

To obtain volumetric data set for treatment planning, the patient is scanned in an approximately 20 cm region above and below the isocenter. A slice spacing and thickness of 3-5 mm is used.

PTV

For localized disease, the CTV includes the prostate and the seminal vesicles. The PTV is defined by adding 1cm margin around the CTV, except posteriorly at the rectum interface where a 6mm margin is used. We have found these margins to be adequate in terms of clinical response of these patients [5].

Normal Tissues

The physician also outlines the rectal wall, bladder wall, small and large bowel in the vicinity of the seminal vesicles. For rectal wall, outer rectum circumference and inner lumen are contoured on the CT images. Similarly, the outer and inner surfaces of the bladder wall are outlined. Portions of the small and large bowel are contoured if they are located within a centimeter of the PTV. The planner outlines the femoral heads and the skin.

IMRT treatment planning

A 5-field beam arrangement is used for the IMRT. The beams are placed at the specified angles as shown in figure 1. An inverse treatment planning [6] approach is used. For optimization purpose, the following artificial structures are created by the planner – PTVE, defined by expanding the PTV by ~3mm, except at the rectum interface; RECTOE, created by extending the outer rectal wall superiorly and inferiorly by 12mm; BLADO, outer rectal wall. For our treatment planning system, we have found that the use of PTVE in the optimization provides better coverage of the PTV near the periphery. The use of RECTOE reduces the probability of hot spots occurring within the portions of the rectum that have not been contoured. Boolean operations are used to divide the PTV in two parts: (1) PTVE_R, which is PTVE not overlapping with the rectum, and (2) OVERLAP_R, portion of the PTVE overlapping with the rectum. This division of the PTVE helps planner to steer hot spots away for the rectum. As a starting point the dose volume constraints, as shown in table I are used. However, after reviewing the dose distribution, the constraints are modified to obtain clinically satisfactory dose distribution. The optimization produces an intensity profile for each beam. An example of the profile is shown in figure 2. In our treatment planning system for each intensity-modulated beam a "fluence" aperture is also determined. This aperture can be displayed in the beam's-eye view or can be projected on the DRR.

Table I: Dose and dose volume constraints used as the starting point for 81 Gy prostate plans.

PTV excluding rectum overlap (PTVE_R)	Prescription dose = 100% Minimum dose =98%, penalty =50 Maximum dose = 102%, penalty =50
PTV and rectum overlap (OVERLAP_R)	Prescription dose = 95% Minimum dose = 93%, penalty = 10 Maximum dose =96%, penalty = 20
Rectum (RECTOE)	Maximum dose = 95%, penalty = 20 70% of the volume receives < 40% of prescription dose, penalty =20
Bladder (BLADO)	Maximum dose =98%, penalty = 35 70% of the volume receives <40% of prescription dose, penalty = 20

The dose calculation is based on the beam intensity profiles. To create the treatment plan, planner combines the contribution from each beam. The isodose distributions and the dose volume histograms are evaluated according to the clinical criteria, as discussed below. If the plan does not meet the clinical requirements the optimization constraints are adjusted until the desired dose distribution is achieved.

Plan Evaluation

Isodose distributions on three mutually perpendicular planes through the isocenter – axial, sagittal and coronal, and DVHs are generated. The plans are normalized 100% (81Gy) isodose covers the PTV, except in the overlap region of PTV and rectum. The maximum dose limit within PTV is 110-percent. The DVHs for the PTV, rectal wall, bladder wall, femurs and bowel are calculated. Figure 3 shows the dose distribution for the 81 Gy plan and figure 4 shows the dose-volume histogram in absolute dose. The plan evaluation criteria for the PTV are: (1) the maximum dose within PTV < 90 Gy and ≥ 90% PTV must receive 77Gy. For the rectal wall there are constraints: (1) in the high dose region no more than 30% of the rectal wall should receive ≥75.6 Gy. In the intermediate dose region no more than 53% of the rectal wall should receive ≥ 47Gy. For the bladder wall there is only dose constraint in the intermediate dose region – no more than 53% of the rectal wall to receive 47 Gy or higher. The maximum dose to the femurs should be less than 68Gy. The maximum dose limits for the large and small bowels are 60 and 50Gy, respectively.

If it is not possible to treat the initial PTV to full prescription dose without violating the constraints, a cone down treatment is planned, using the superior jaw to shield the bowel. If this method blocks the portions of the prostate, the physician outlines a new cone down PTV and new plan is generated. A composite plan is designed to ensure that the maximum bowel dose constraints are not violated.

MU calculation and DVA files

There are two methods to deliver the dose using MLC – step and shoot, and dynamically (DMLC). In the first approach multiple static MLC apertures deliver the dose. Whereas, in the DMLC approach [7] the leaves move while the dose is being delivered, thus modulating the beam intensity. At our institution IMRT is delivered by DMLC. The radiation oncologist reviews the plan and the prescription isodose level to deliver the dose is selected. Based on the intensity profiles, selected treatment isodose level, dose per fraction (1.8Gy) and dose rate, a computer algorithm determines the leaf motion as a function of MU for each beam. The leaf-motion information is stored in a file known as leaf sequence file or the "DVA file." The monitor units are corrected for the collimator scatter factor (Sc) and phantom scatter factor (Sp). For the dose delivery the DVA files are transferred to the treatment machines.

Treatment Delivery

The DVA file controls the leaf motion during the treatment delivery. The motion of each leaf pair determines the dose under the leaf pair, as shown in figure 5. A computer continuously monitors the leaf motion. If, for some reason, a leaf is lagging, it holds the beam pulses until the leaf is in the correct position. If the dose delivery is interrupted during the treatment, the leaf motion can be resumed and remaining dose can be delivered by entering the total and remaining monitor units.

Clinical Outcomes
In the dose escalation study at our institution, the prescription dose was systematically increased from 64.8 to 86.4Gy by increments of 5.4Gy in consecutive group of patients. The purpose of the study was to determine the toxicity of the high-dose 3DCRT; identify the highest feasible tumor dose; evaluate the impact of PTV dose on the rates of local control.

Toxicity of 3DCRT and IMRT
On of the major complication of prostate radiation therapy is rectal bleeding. With 3DCRT and IMRT the rate of grade 3 rectal complication is small. However, a significant number of patients develop grade 2 rectal bleeding. Zelefky et al have followed these patients and some of the results are given in table II.

Table II: Percent grade 2 rectal toxicity at ~36 month

Dose	Toxicity
3DCRT	
64.8-70.2 Gy	6%
75.6 Gy	18%
81.0 Gy	16%
IMRT	
81 Gy	3%

Local Control
The patients treated with 3DCRT and IMRT have been followed for local control. PSA relapse-free survival provides a good indication of the efficacy of the radiation therapy. Depending on the extent of the disease these patients can be classified as favorable, intermediate, or unfavorable risk. The table III shows the relapse free survival rate for unfavorable risk patients.

Table III: PSA relapse free survival in unfavorable risk patients by dose

Dose	Survival @ 84 months
64.8 Gy	21%
75.6 Gy	43%
81 Gy	66%

Conclusions
The interim results at our institution indicate that high-dose 3DCRT is feasible and effective. IMRT represents a true advancement in the use of radiation for the cure of prostate carcinoma. Treatment to higher dose levels improves the disease-free survival of the favorable, intermediate and unfavorable risk patients. Currently these patients are being followed by post-irradiation biopsy, and there are indications that a dose of at least 81Gy may be required for maximal local tumor control. Patients at MSKCC are with intermediate and unfavorable risk characteristics are now being treated to 86.4 Gy. Such

high dose levels can only be delivered with advanced IMRT techniques that minimize the volume of normal tissues treated to high dose levels.

References:

[1] Leibel SA, Heimann R, Kutcher GJ, et al. Three-dimensional conformal radiation therapy in locally advanced carcinoma of the prostate: preliminary results of phase I dose-escalation study. Int J Radiat Oncol Biol Phys 1994;28:55-63.

[2] Leibel SA, Kutcher G, Zelefsky M, et al. 3-D Conformal Radiotherapy for Carcinoma of the prostate. In Meyer J, Purdy J, eds. 3D Conformal Radiotherapy. Frontiers in radiation therapy and oncology. Basel: A Karger, 1996;29:229-237.

[3] Hanks G, Martz K, Diamond J. The effect of dose on local control of prostate cancer. Int J Radiat Oncol Biol Phys 1988;13:1299-1305.

[4] Vicini FA, Abner A, Baglan KL, et al. Defining a dose-response relationship with radiotherapy for prostate cancer: Is more really better? Int J Radiat Oncol Biol Phys 2001;51:1200-1208.

[5] Zelefsky MJ, Leibel SA, Kutcher GJ, et al. The feasibility of dose escalation with three-dimensional conformal radiotherapy with patients with prostatic carcinoma. Cancer J 1995;1:142-150.

[6] Spirou SV, Chui CS. A gradient inverse planning algorithm with dose volume constraints. Medical Physics 1998;25:321-333.

[6] Zelefsky MJ, Happersett L, Leibel SA, et al. Effect of treatment positioning on normal tissue dose in patients with prostatic treatment with three-dimensional conformal radiotherapy. Int J Radiat Oncol Biol Phys 1997;37:13-19.

[7] Spirou SV, Chui CS. Generation of arbitrary fluence profile by dynamic jaws or multileaf collimators. Med Phys 1994;21:1031-1041

Figures:

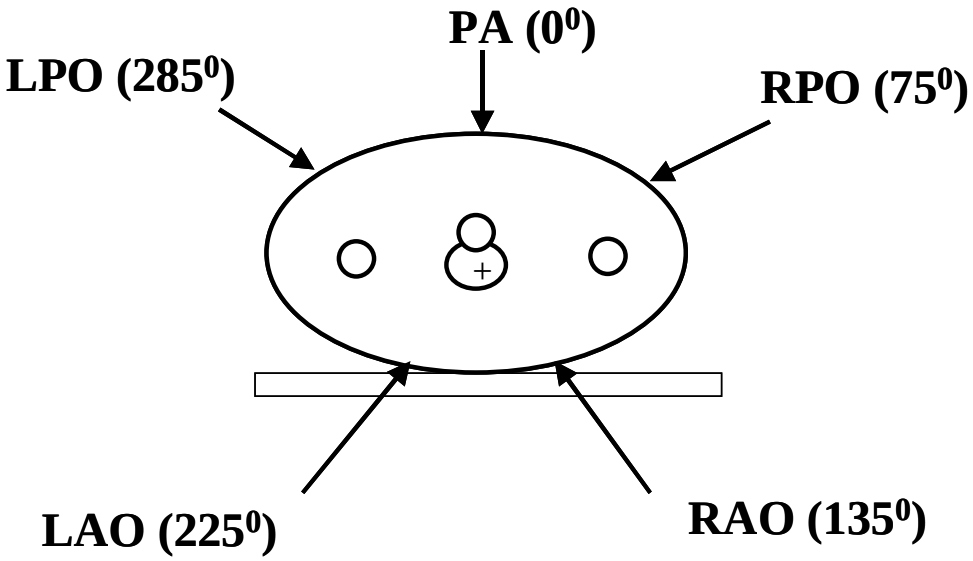

Figure1: Schematic showing the beam directions for 5-field IMRT plan

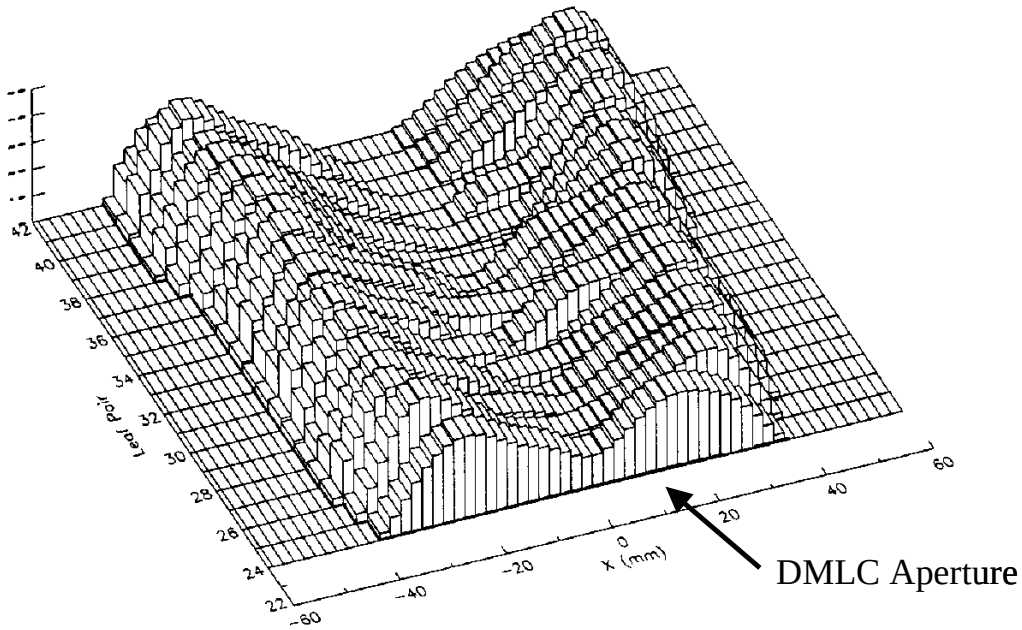

Figure 2: The intensity profile for the PA field. The outline of the fluence aperture is also shown.

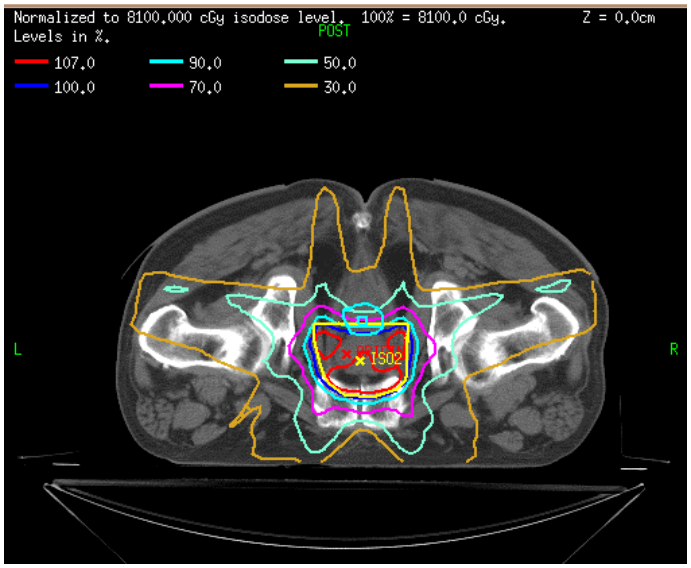

Figure 3: Percent isodose distribution for the 5-field IMRT plan on an axial plane. 81Gy is prescribed to 100%

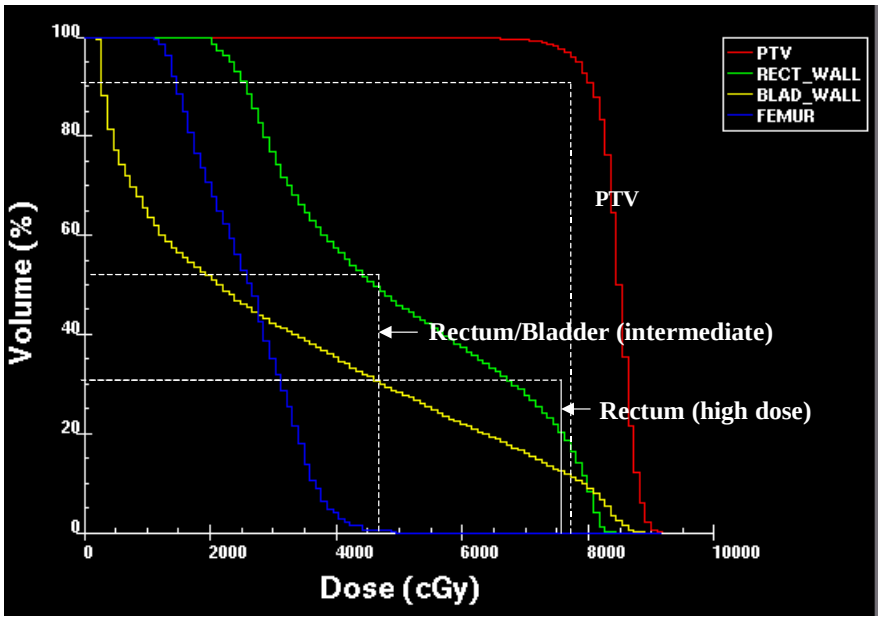

Figure 4: Dose-volume histogram for the 81Gy plan in absolute dose.

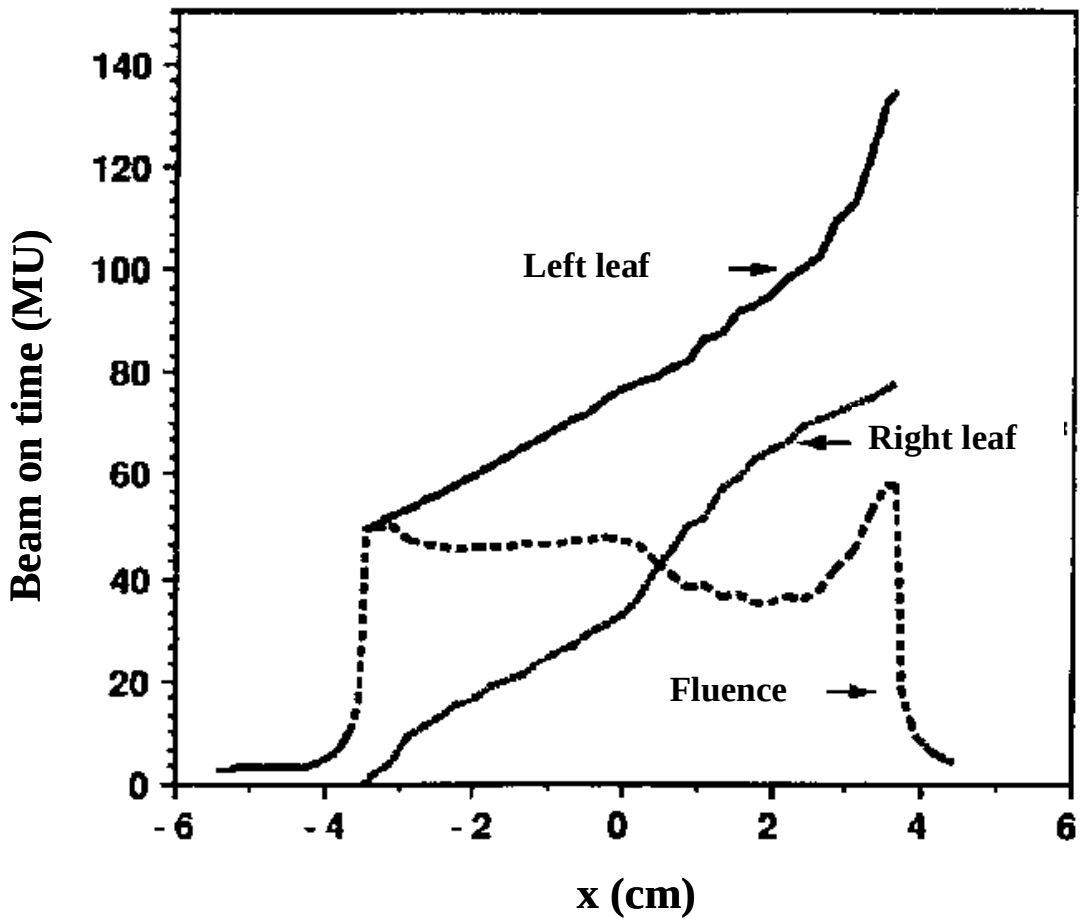

Figure 5: A leaf-pair motion as a function of dose (MU) and the resulting fluence under the leaves.