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PHYSICS CONTRIBUTION

INTRAOPERATIVE DYNAMIC DOSE OPTIMIZATION IN PERMANENT PROSTATE IMPLANTS

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Purpose: With the advent of intraoperative optimized planning, the treatment of prostate cancer with permanent implants has reached an unprecedented level of dose conformity. However, because of well-documented (and unavoidable) inaccuracies in seed placement into the gland, carrying out a plan results in a large degree of variability relative to the intended dose distribution. This brings forth the need to periodically readjust the plan to allow for the real positions of seeds already implanted. In this paper, an algorithm for performing this task, hereby described as intraoperative dynamic dose optimization (IDDO), is presented and assessed.

Methods and Materials: The general scheme for performing IDDO consists of three steps: (*1*) at some point during the implant, coordinates of implanted seeds are identified; (*2*) seed images are projected onto the reference frame of the ultrasound images for planning; and (*3*) the plan is reoptimized. Work on the first two steps is reported elsewhere. Here, we focus on the strategy for implementing the reoptimization step. An optimal treatment plan is first obtained based on initial operating room–acquired ultrasound images. We analyze the sensitivity and effect of the IDDO procedure with respect to the total number of reoptimizations performed. Specifically, we consider reoptimizing 2, 3, and 4 times. When two reoptimizations are used, half of the seeds from the initial optimal plan are implanted. The first reoptimization is performed on the remaining possible seed positions, and all the seeds designated in this reoptimized plan are implanted. The second (final) reoptimization is done on the remaining unused seed positions to ensure 100% coverage of the gland and to eliminate possible cold spots in the gland. Similarly, when three reoptimization steps are used, one-third of the seeds from the initial optimized plan, one-half of the seeds from the first reoptimization, and all seeds from the second reoptimization are implanted. The third (final) reoptimization is performed to assist in eliminating possible cold spots. Reoptimizing four times proceeds in a like manner. Fifteen patient cases are used for comparison. Strict dose bounds of 100% and 120% of the prescription dose are imposed on the urethra, and 100% coverage is imposed on the prostate volume. To assist in achieving good conformity, prostate contour points are assigned a target upper dose bound of 150% of the prescription dose.

Results: A two-way comparison is performed: (a) initial optimized plan, (b) IDDO plan. Postimplant dose analysis, coverage and conformity measures, as well as actual dose received by urethra and rectum are used to gauge the results. The initial optimized plan consistently provides 93% prescription dose coverage to the gland with average conformity index of 1.32. The urethra dose ranges within 100% to 150%, and the maximum dose delivered to the rectum reaches 91% of the prescription dose. On average, about 50% of the urethra receives more than 120% of the prescription dose, and 19% of the rectum volume receives more than the 78% upper dose limit. For the IDDO plan, 100% postimplant coverage with 1.16 conformity is achieved. Urethra and rectum dose is maintained within the prescribed 100% to 120% range and 78% upper bound, respectively.

Conclusions: With real-time treatment planning, it is possible to dynamically reoptimize treatment plans to account for actual seed positions (as opposed to planned positions) and needle-induced swelling to the gland during implantation. Postimplant analysis shows that the final seed configuration resulting from the IDDO method yields improved dosimetry. The algorithmic design ensures that one can achieve complete coverage while maintaining good conformity, thus sparing excess radiation to external tissue. The study also provides evidence of the possibility of morbidity reduction to urethra and rectum (because of reduced dose delivered to these structures) via the use of IDDO planning. Clinical studies are needed to validate the importance of our approach.

Prostate implants, Intraoperative planning, Dynamic dose optimization, Urethra complications, Automated treatment planning, Postimplant analysis.

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INTRODUCTION

There has been a resurgence of interest over the last five to ten years in the use of permanent implantation of radioactive sources to treat patients with clinically localized prostate cancer. With the development of improved techniques using computed tomography (CT)-based or ultrasound-based transperineal implantation technology, the published results of prostate-specific antigen control for patients with early-stage prostate cancer treated with this modality have shown significant improvement compared with the open retropubic technique (1) and are in the range of 80% to 90% at 5 years or longer (1–3).

Despite the improvement in implant techniques, approaches for planning and for assessing the quality of implantation vary from one center to another. At Memorial Sloan-Kettering Cancer Center (MSKCC) we have developed and have successfully implemented intraoperative conformal optimization and planning for ultrasound-based prostate implants, which obviates the need for preplanning (4–7, 9–11). At the time of implant, patients are placed in the extended lithotomy position and a urinary catheter is inserted. An ultrasound probe is positioned in the rectum, and the prostate and normal anatomy are identified. Needles are inserted through the perineal template at the periphery of the prostate. The prostate is subsequently scanned from apex to base, and these 0.5 cm spaced images are transferred to the treatment planning system using a PC-based video capture system. On the computer monitor, the prostate contours as well as the urethra are digitized on each axial image; the digitization requires approximately 1 min. Needle positions are identified on each image, and their coordinates are incorporated into a computerized optimization program. This sophisticated optimization program incorporates acceptable dose ranges allowed within the target as well as dose constraints for the rectal wall and urethra. This approach has led to the achievement of an unprecedented level of dose conformity in treatment plans.

Nevertheless, because of well-documented and unavoidable inaccuracies in seed placement into the gland, carrying out a plan results in a large degree of variability relative to the intended dose distribution. Figure 1 illustrates the magnitude of the problem by comparing, for a random group of 17 patients treated at MSKCC, the percentage urethral volume covered by 150% of the prescription dose (blue: planned; red: assessed at postimplant evaluation) and also 200% of the prescription dose (yellow: postimplant evaluation; the planned percentage volume was always zero because the upper dose bound for urethra is set to be 150%). Postimplant evaluation was done within 2 h after implantation to assess how closely the actual dose delivered matched

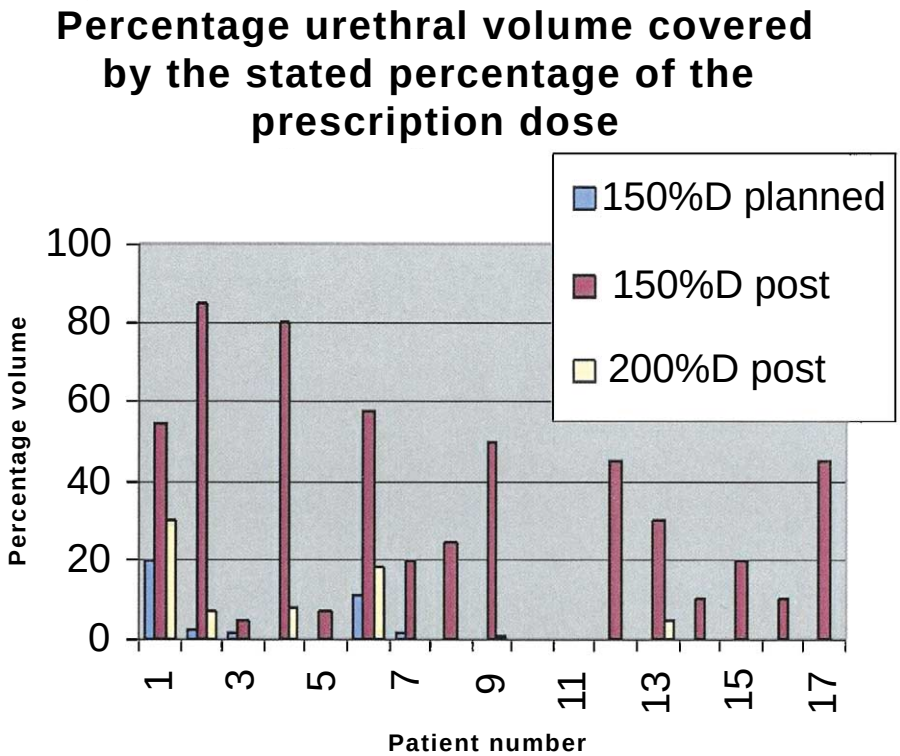

Fig. 1. The magnitude of dose discrepancy observed in postimplant analysis when intraoperative optimized plan with no IDDO is performed. For a random group of 17 patients treated at Memorial Sloan, the figure compares the percentage urethral volume covered by 150% of the prescription dose (blue: planned; red: assessed at postimplant evaluation) and also 200% of the prescription dose (yellow: postimplant evaluation; the planned percentage volume was always zero because the upper dose bound for urethra is set to be 150%).

Table 1. The incidence of acute Grade 2 urinary toxicity

Planning technique	Ave. urethra dose $D_{urethra}/D_{Prescription\ dose}$	% Incidence of toxicity	
		<6 months	6–12 months
Preplanning	182%	85%	58%
I-3D	143%	46%	23%
p value		0.01	0.01

Table 1 compares the average urethral dose and the incidence of acute Grade 2 urethral toxicity for two alternative treatment approaches: (*1*) preplanned CT-based implantation (involving data for 247 patients), and (*2*) an intraoperative computer-optimized conformal planning technique (I-3D) involving 182 patients). The table shows the incidence of acute Grade 2 urethral toxicity during the first 6 months and from 6 to 12 months after the procedure, as well as the average urethral dose (expressed as percentage of the prescription dose) for the two types of treatments.

the planned dose. (For Patients 10 and 11, both the planned and the assessed dose received by the urethral volume was below 150% of prescription dose.) This brings forth the need to periodically readjust the plan to allow for the real positions of seeds already implanted. Such readjustment should lead to improved postimplant dosimetric measurement upon completion of seed implantation. An algorithm for performing this readjustment, hereafter referred to as intraoperative dynamic dose optimization (IDDO), is reported in this paper.

Because of the increasing number of centers performing prostate implants in the United States, the potential significance of IDDO may be far-reaching. The resultant outcome of the seed placement is often suboptimal in terms of areas of tumor underdosage and unnecessarily high doses delivered to normal tissues. Such outcomes result in higher likelihood of tumor recurrence or increased treatment-related toxicity. Note that urethra-related complication rates—a reduction of which could be a major result of the IDDO approach—are considerably higher for brachytherapy than for teletherapy. Larger than planned doses to the urethra can have significant consequences in terms of late urinary toxicity. In a recent analysis (11), dosimetric parameters and acute urinary toxicity for a cohort of 182 patients treated using an intraoperative computer-optimized conformal planning technique (I-3D) were compared in their outcome with that of 247 patients previously treated at MSKCC with a preplanned CT-based implantation approach. Table 1 shows the incidence of acute Grade 2 urethral toxicity during the first 6 months and from 6 to 12 months after the procedure, as well as the average urethral dose (expressed as percentage of the prescription dose) for the two types of treatments.

Besides correcting for inaccuracies in seed placement, the viability of being able to reoptimize in real time also allows modification of plans due to unforeseen difficulties during an operation. These modifications can potentially correct any areas of tumor underdosage before completion of the procedure. In addition, the operator will become more cognizant of the real-time dose to the urethra and rectum, and dynamic adjustment of the intraoperative plan can be made to ensure that the final dose delivered to these structures remains as low as possible. Finally, the availability of IDDO will eliminate the need for immediate postimplant evaluation of the treatment.

METHODS AND MATERIALS

Reconstruction of seed coordinates and image transformation

The implementation of IDDO requires real-time dosimetric information which is based on the actual positions of seeds already implanted. The seed reconstruction procedure developed at MSKCC makes use of three fluoroscopic images taken at different angles. Briefly, the software developed identifies seeds in each image, matches them, and calculates their coordinates in the patient's coordinate system (PCS). Contours of the prostate and other structures (urethra, rectum, etc.) are outlined by the physician in the ultrasound coordinate system (UCS) referenced with respect to the ultrasound probe. To fuse the two spaces (PCS and UCS), the ultrasound probe is momentarily replaced with a geometrically identical unit that has several reference points that can be identified both in the PCS and in the UCS. This fixes the transformation between the two coordinate systems. Our preliminary study indicates that this momentary replacement has a negligible effect on prostate geometry and location (12). Doses to structures (e.g., prostate, urethra) outlined in the ultrasound images are evaluated from the seeds actually implanted, and the plan is modified using the reoptimization tool described below. For further details on seed reconstruction, see references 13–22.

The automated 3D treatment planning system used for IDDO

Our treatment planning models employ integer programming techniques and use 0/1 variables to record placement or nonplacement of seeds in a prespecified three-dimensional grid of potential locations. The template used is the standard needle template which has standard seed spacer locations. Dosimetric constraints to assist in producing good coverage and conformal plans are incorporated into the model, along with strict dose restrictions on the urethra and rectum. The basic treatment planning model (and varia-

Table 2. Lower and upper dosimetric bound specifications as multiples of target prescription dose

	Rectum	Urethra	Contour	Uniformity
Lower bound	0	1.0	1.0	1.0
Upper bound	0.78	1.2	1.5	1.6

Table 2 shows the target dose bounds, expressed as multiples of the prescription dose to the prostate, which was patient-dependent. Note that the lower bound for rectum points was set to zero, because there is no therapeutic reason to deliver any radiation to the rectum. In contrast, because the urethra is surrounded by the prostate, too little dosage to the urethra may be indicative that diseased tissue proximal to the urethra is not receiving adequate dosage. Tighter upper bound is used for the prostate contour points to assist in obtaining good conformal plans.

tions), and the optimization engine developed for real-time plan generation are reported in (5, 6, 8). At the start of the implantation process, contours of the prostate and other structures are outlined by the physician in the UCS. Four separate categories of points, corresponding to distinct anatomic structures, are specified for monitoring and controlling dosimetry. *Contour points* define the boundary of the diseased organ in each of the slices; the regions enclosed by each boundary are populated with uniformly spaced points, termed *uniformity points;* and points representing the urethra and rectum in each slice are also specified. The models include dosimetric lower and upper bounds—specified as multiples of the prescription dose—for each point type, as shown in Table 2.

For this study, our goal is to design treatment plans such that the entire prostate receives 100% prescription dose coverage while achieving conformity to the greatest extent possible. (Conformity is a measure of how well the prescription isodose surface conforms to the target volume; it is computed as the ratio of the total volume enclosed by the prescription isodose surface to the target volume enclosed by this same surface.) The treatment planning model places strict lower and upper dose bounds on the urethra as well as a strict upper dose bound on the rectum. The objective strives to provide sufficient dose to the prostate volume while minimizing excess dose exterior to the gland.

The treatment planning system, which consists of the modeling component and a computational engine for solving the resulting optimization problems, provides a very flexible environment for simultaneously incorporating multiple physical constraints within the planning process. An implementation of this treatment planning system has been used successfully in our computerized treatment planning study (5), a recent magnetic resonance spectroscopy–guided dose-escalation study (23), and a continuous dose-control investigation for multi-period treatment planning (24).

Intraoperative dynamic dose optimization (IDDO)

For the IDDO study described herein, additional software modules have been developed and interfaced with the computerized treatment planning optimization system described above. These modules facilitate the calculation of radiation dose received intermittently during the implantation process. Broadly speaking, four basic modules are involved in the IDDO system: seed reconstruction, coordinate transformation, dose calculation, and reoptimization.

During implantation, an initial optimal treatment plan is obtained based on initial operating room–acquired ultrasound images using the real-time treatment planning system (5). The input for each reoptimization step consists of (*1*) the positions of seeds already deposited in the prostate, needed for the computation of the current dose distribution; (*2*) possible remaining positions for further seed placement; (*3*) dose bounds for various anatomic structures; (*4*) coverage and conformity requirements; and (*5*) dose limits for urethra and rectum.

Let *d(r)* denote the dose contribution of a seed to a point *r* units away, let x_j be the 0/1 indicator variable for recording placement or nonplacement of a seed in grid position *j*, and let X_j be a vector corresponding to the coordinates of grid position *j*. Once a seed is implanted in grid position *j*, let $Y_j(t)$ denote the coordinates of the seed at the beginning of iteration *t*. Note that the coordinates of an implanted seed may change due to possible organ motion and swelling over time; the coordinates are determined using the three-fluoroscopic-image reconstruction technique mentioned earlier. Associated with each point *Q* at iteration *t* are target lower and upper bounds, $L_Q(t)$ and $U_Q(t)$, on dose remaining to be delivered. These bounds are computed according to the formulas

$$L_Q(t) = L_Q - \sum_{j \in N_t} d(\|Q - Y_j(t)\|)$$

$$U_Q(t) = U_Q - \sum_{j \in N_t} d(\|Q - Y_j(t)\|) \qquad (1)$$

where L_Q and U_Q are desired lower and upper bounds on *total* dose received by point *Q*, and N_t is the set of grid positions already occupied with a seed at the beginning of iteration *t*. If *N* denotes the set of all grid positions, then the dosimetric constraints for point *Q* at iteration *t* are given by

$$\sum_{j \in N \setminus N_t} d(\|Q - X_j\|)\, x_j \geq L_Q(t)$$

$$\sum_{j \in N \setminus N_t} d(\|Q - X_j\|)\, x_j \leq U_Q(t). \qquad (2)$$

Here, $N \setminus N_t$ denotes the set of grid points in *N* that are not in N_t; i.e., the set of grid points not yet occupied with a seed. Unfortunately, it is generally not possible to satisfy all such constraints simultaneously. Therefore, we modify the upper bound constraint to allow violations. We do so by introducing an indicator variable to denote the satisfaction of the upper bound constraint for each point *Q* of the prostate. In

Table 3. Comparing postimplant coverage and conformity of 15 patients with implant planning and IDDO planning

	Implant planning		2 reoptimizations		3 reoptimizations		4 reoptimizations	
Patient ID	Coverage	Conformity	Coverage	Conformity	Coverage	Conformity	Coverage	Conformity
Minimum	0.90	1.29	1.0	1.11	1.0	1.09	1.0	1.09
Maximum	0.99	1.35	1.0	1.19	1.0	1.17	1.0	1.16
Mean	0.93	1.32	1.0	1.16	1.0	1.15	1.0	1.14
Standard Dev.	0.02	0.03	0.0	0.03	0.0	0.02	0.0	0.02

Table 3 illustrates coverage and conformity scores when using implant planning (non-IDDO), and IDDO with 2 reoptimizations, 3 reoptimizations, and 4 reoptimizations. Observe that, in general, dynamic dose correction is useful for ensuring full postimplant coverage as well as improvement in conformity. On average, conformity improves from 1.32 for the non-IDDO plan to 1.16, 1.15, and 1.14, respectively, for the IDDO 2-, 3-, and 4-reoptimization schemes.

IDDO = intraoperative dynamic dose optimization.

particular, if $u_Q(t)$ denotes this 0/1 indicator variable, then the modified upper bound constraint is:

$$\sum_{j \in N \setminus N_t} d(\|Q - X_j\|)\, x_j - M_Q(1 - u_Q(t)) \leq U_Q(t), \quad (3)$$

where M_Q is a large positive constant. Note that if $u_Q(t) = 1$, then the upper bound at iteration t for point Q is satisfied. In order to drive as many of these 0/1 variables to 1 as possible, we use the optimization objective: maximize $\Sigma_Q(u_Q(t))$. This objective maximizes the volume of the prostate achieving the upper bound constraints at iteration t; which in turn helps to achieve the tightest conformity possible in the optimal treatment plan. It should also be emphasized that as we proceed with correcting dose for each intraoperative dose reoptimization iteration, we ensure 100% coverage of the gland based on the current dose distribution, and impose strict cumulative dose restrictions on the urethra and rectum.

Experimental design, data, and criteria for comparing plans

There are various ways to carry out the IDDO procedure. In this study, we analyze the sensitivity and effect of the IDDO procedure with respect to the total number of reoptimizations performed. Specifically, we consider reoptimizing 2, 3, and 4 times. In all cases, an initial optimization is performed after loading needles have been inserted. When two reoptimizations are used, half of the seeds from the initial optimal plan are implanted. The first reoptimization is performed on the remaining possible seed positions, and all the seeds designated in this reoptimized plan are implanted. The second (final) reoptimization is done on the remaining unused seed positions to ensure 100% coverage of the gland and to eliminate possible cold spots in the gland. Similarly, when three reoptimization steps are used, one-third of the seeds from the initial optimized plan, one-half of the seeds from the first reoptimization, and all seeds from the second reoptimization are implanted. The third (final) reoptimization is performed to assist in eliminating possible cold spots. Reoptimizing four times proceeds in a like manner. Note that once a reoptimized treatment plan is obtained, the radiation oncologist performs the loading of seeds as they are accustomed. No specific order of needles is imposed on the oncologist.

As indicated in Eq. 2, at each reoptimization step, reoptimization is performed on the remaining possible seed positions; this includes all positions that are currently not occupied by a seed. In particular, a reoptimized plan may ask for additional placement of needles. Note also that there is an important distinction between the final reoptimization step and immediate postimplant evaluation of treatment. Unlike postimplant dosimetric evaluation, the last optimization step offers a chance to adjust dosimetry by placing additional seeds, should this be necessary. We remark that all reoptimization steps can be accomplished quickly (less than 5 min).

Fifteen patient cases are used in our study. In each case, iodine-125 with initial air kerma strength of 0.57 U is used as the radioactive source, and a prescription dose of 144 Gy, using the TG43 dosimetry formalism (25), is prescribed. Lower and upper dose limits on the urethra are set to 100% and 120% of the prescription dose, respectively; and an upper dose limit on the rectum is set to 78% of the prescription dose. Although we have not established a dose–response curve for rectum toxicity (for low-dose-rate treatments), the 78% bound appears to be a safe limit. After loading needles are inserted into the gland, ultrasound images are taken every 5 mm using a transrectal ultrasound device. The clinicians then outline the prostate surface for each slice based on these images. The resulting information provides the initial prostate volume with initial potential seed positions superimposed.

For each patient case a two-way comparison is performed: (a) plan based on real-time intraoperative planning with no dynamic dose correction (we call this the *implant plan*); and (b) plan based on intraoperative dynamic dose optimization (referred to herein as the *IDDO plan*). Note that the implant plan refers to the optimal treatment plan obtained when the initial optimization is performed after loading needles have been inserted.

IDDO planning is performed "theoretically" on the patients to assess the feasibility of improved dosimetry while maintaining low dose to urethra and rectum. In particular, a

Table 4a. Postimplant average minimum and maximum doses in urethra (Gy); prescription dose: I-125 144 Gy

Urethra dose analysis	Implant planning	IDDO planning		
		2-reopt	3-reopt	4-reopt
$Min\ D_{urethra} / D_{Prescription\ dose}$	107.9%	101.6%	101.0%	101.6%
$Max\ D_{urethra} / D_{Prescription\ dose}$	143.5%	119.8%	119.9%	119.7%
$Ave\ D_{urethra} / D_{Prescription\ dose}$	131.2%	114.8%	113.6%	113.2%

Table 4b. Postimplant dose–volume distributions for urethra (in each dose interval from 100% to 150% of prescription dose at 10% dose increment)

Dose interval (% of prescription dose)	Implant planning	IDDO planning		
		2-reopt	3-reopt	4-reopt
100–110%	15%	23.5%	25.0%	22.5%
110–120%	35%	76.5%	75.0%	77.5%
120–130%	27%	—	—	—
130–140%	15%	—	—	—
140–150%	8%	—	—	—

Abbreviations: IDDO = intraoperative dynamic dose optimization; reopt = reoptimizations.

Table 4a reports the postimplant average minimum and average maximum doses to the urethra; Table 4b reports the dose–volume distribution in the urethra. IDDO planning ensures that 100% of the urethra volume is below the 120% dose level. In contrast, although strict urethra dose bounds were designated in the implant plan, due to unavoidable needle distortion and seed displacement during implantation, there is a considerable difference in the dose actually delivered to the structure. On average, about 50% of the urethra receives more than 120% of the prescription dose.

simulation model to simulate the displacement of seeds during implantation was developed so as to provide an empirical formulation for use within the IDDO framework. An initial optimal treatment plan is obtained based on initial operating room–acquired ultrasound images using the real-time treatment planning system. The input for each reoptimization step consists of (*1*) the simulated, shifted positions of seeds already deposited in the prostate, needed for the computation of the current dose distribution; (*2*) possible remaining positions for further implants; (*3*) dose bounds for various anatomic structures; (*4*) coverage and conformity requirements; and (*5*) dose limits for urethra and rectum.

Postimplant dose analysis, coverage and conformity measures, as well as dose received by urethra and rectum are used to gauge the results. In all cases, the implant plan was actually performed on the patient, and the postimplant results reported for the implant plan is that observed. The postimplant dosimetry results reported for the IDDO plans are based on the simulation model. Recall that *conformity* is computed as the ratio of the total volume enclosed by the isodose surface determined by the prescription dose to the target volume enclosed by this same surface. *Coverage* is computed as the ratio of the target volume enclosed by the prescription isodose surface to the total target volume. Hence, a conformity index is always greater than or equal to 1, and a coverage index is always less than or equal to 1. In either case, an index value of 1 indicates perfect conformity / coverage.

RESULTS

Table 3 illustrates coverage and conformity scores when using implant planning (non-IDDO), and IDDO with 2 reoptimizations, 3 reoptimizations, and 4 reoptimizations. Observe that, in general, dynamic dose correction is useful for ensuring full postimplant coverage as well as improvement in conformity. On average, conformity improves from 1.32 for the non-IDDO plan to 1.16, 1.15, and 1.14, respectively, for the IDDO 2-, 3-, and 4-reoptimization schemes. Although each reoptimization iteration requires only a few minutes, clearly it is not necessary to reoptimize often; even the 2-reoptimization scheme shows much improvement over the non-IDDO plan, and improvement appears to plateau at 3 reoptimizations.

Table 4a reports the postimplant average minimum and average maximum doses to the urethra, and Table 4b reports the dose–volume distribution in the urethra. Dynamic dose correction in IDDO planning ensures that 100% of the urethra volume is below the 120% dose level. In contrast, although strict urethra dose bounds were designated in the implant plan, due to unavoidable needle distortion and seed displacement during implantation, there is a considerable difference in the dose actually delivered to the structure. On average, about 50% of the urethra receives more than 120% of the prescription dose. Tables 5a and 5b show analogous postimplant dose analysis for the rectum. For the implant plan, on average the maximum dose to the rectum is 91% of

Table 5a. Postimplant average minimum and maximum doses in rectum (Gy); prescription dose: I-125 144 Gy

		IDDO planning		
	Implant planning	2-reopt	3-reopt	4-reopt
$Min\ D_{rectum} / D_{Prescription\ dose}$	45.1%	41.0%	40.7%	40.9%
$Max\ D_{rectum} / D_{Prescription\ dose}$	91.0%	77.1%	76.6%	76.7%

Table 5b. Postimplant dose–volume distributions for rectum percentage of volume (in each dose interval from 40% to 100% of prescription dose at 20% dose increment)

Dose interval (% of prescription dose)		IDDO planning		
	Implant planning	2-reopt	3-reopt	4-reopt
40–60%	40%	60.0%	60.5%	62.5%
60–80%	45%	40.0%	39.5%	37.5%
80–100%	15%	—	—	—

Abbreviations as in Table 4.

Tables 5a and 5b show analogous postimplant dose analysis for the rectum. For the implant plan, on average the maximum dose to the rectum is 91% of prescription dose, whereas rectum dose is kept below 78% of prescription dose for the IDDO plans.

prescription dose, whereas rectum dose is kept below 78% of prescription dose for the IDDO plans.

A sufficient body of literature exists to support the statement that postimplant dose analysis obtained via implant planning is far superior to that obtained from preimplant planning (i.e., planning based on simulation before the time of implantation) (5, 6, 9, 11, 26–29). To help illustrate the extent of improvement, we analyzed a sample of 15 patient cases for which preplans were designed and used for implantation. We found postimplant coverage ranged from 75% to 85% (average 80%). This contrasts to coverage scores ranging from 90% to 99% (average 93%) when implant planning is used, as indicated in Table 3. In terms of conformity, preplans achieved scores ranging from 1.34 to 1.57 (average 1.44), whereas implant planning resulted in scores ranging from 1.29 to 1.35 (average 1.32). The poor postimplant results for preplans can be explained by the fact that there is a discrepancy between the prostate volume and organ position during simulation and during implantation. In general, a preimplant plan only provides a crude estimate of the final seed configuration used for actual treatment.

DISCUSSION

Planning treatment at the time of implant (implant planning) leads to much better postimplant dosimetry than preplanning. However, even when implant planning is used, planned coverage and conformity scores may still not be realized postimplant. In particular, insufficient dose to the prostate volume and excess dose to external proximal tissue, urethra, and rectum are often observed for implant plans. Our study shows that periodic intraoperative readjustment of a plan to account for the real positions of seeds already implanted (IDDO planning) can provide improved postimplant dosimetric results. The IDDO planning system we implemented guarantees 100% postimplant coverage to the gland, while improving conformity on average from 1.32 to 1.16 compared with implant planning.

The conformity improvement suggests the possibility of a reduction in normal tissue toxicity. In particular, our study illustrates the importance of intraoperative readjustment in terms of potential reduction of urethral and rectal morbidity. Even if one imposes dose bounds on the urethra and rectum for the implant plan, one risks exposing them to excess dose due to inaccuracies in seed placement and needle distortion. Our study illustrates that dose to the urethra and rectum can be well-controlled—and that postimplant dose levels to these structures can be achieved as prescribed by the physician—via our IDDO planning system.

The IDDO treatment planning system used in this study is based on the technology of integer programming. It offers a flexible environment for imposing various clinical criteria simultaneously during plan generation. On average, approximately 8 central processing unit (CPU) minutes are needed to produce the initial plan, while it takes about 2–5 CPU minutes to generate the reoptimized plan for each iteration in IDDO. In general, the computational effort decreases as fewer potential seed positions are left to be optimized. Of the IDDO schemes considered here, the best results are achieved using three reoptimizations.

In summary, our results suggest that the IDDO treatment planning technique for prostate brachytherapy offers a practical way of achieving postimplant dosimetry goals, including improved postimplant dose coverage and conformity and reduced irradiation to urethra and rectum. With real-time treatment planning, it is possible to dynamically reoptimize treatment plans to account for actual seed positions (as opposed to planned positions) and

needle-induced swelling to the gland during implantation. Lower urethral doses achieved may positively impact the quality of life of treated patients by lowering acute toxicity profiles after treatment. Empirical tests indicate that the proposed IDDO procedure is practically feasible to carry out in the clinic. It requires less than 5 min to reoptimize, and reoptimization need be performed only 2 or 3 times; furthermore, seed reconstruction can be accomplished in 10 min. Hence, the entire process can be completed within 30 min. Clinical studies are needed to validate the importance of our approach. The range of expected improvement in conformity and coverage is not large. However, the study provides evidence of the possibility of morbidity reduction to urethra and rectum via the use of intraoperative dynamic dose optimization planning.

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