IPIP: A new approach to inverse planning for HDR brachytherapy by directly optimizing dosimetric indices

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Purpose: Many planning methods for high dose rate (HDR) brachytherapy require an iterative approach. A set of computational parameters are hypothesized that will give a dose plan that meets dosimetric criteria. A dose plan is computed using these parameters, and if any dosimetric criteria are not met, the process is iterated until a suitable dose plan is found. In this way, the dose distribution is controlled by abstract parameters. The purpose of this study is to develop a new approach for HDR brachytherapy by directly optimizing the dose distribution based on dosimetric criteria.
Methods: The authors developed inverse planning by integer program (IPIP), an optimization model for computing HDR brachytherapy dose plans and a fast heuristic for it. They used their heuristic to compute dose plans for 20 anonymized prostate cancer image data sets from patients previously treated at their clinic database. Dosimetry was evaluated and compared to dosimetric criteria.
Results: Dose plans computed from IPIP satisfied all given dosimetric criteria for the target and healthy tissue after a single iteration. The average target coverage was 95%. The average computation time for IPIP was 30.1 s on an Intel(R) Core^{TM}2 Duo CPU 1.67 GHz processor with 3 Gib RAM.
Conclusions: IPIP is an HDR brachytherapy planning system that directly incorporates dosimetric criteria. The authors have demonstrated that IPIP has clinically acceptable performance for the prostate cases and dosimetric criteria used in this study, in both dosimetry and runtime. Further study is required to determine if IPIP performs well for a more general group of patients and dosimetric criteria, including other cancer sites such as GYN. © *2011 American Association of Physicists in Medicine*. [DOI: 10.1118/1.3598437]

Key words: HDR, optimization, conformal radiotherapy, prostate therapy, integer program, IPIP

I. INTRODUCTION

High dose rate (HDR) brachytherapy is a radiation therapy for cancer. In HDR brachytherapy, radiation is delivered directly to the tumor site via a moving radioactive source in temporarily inserted catheters. Dose is controlled by altering the dwell times, the time spent at points along the catheters. Studies have shown that brachytherapy is a highly effective treatment.[1–8]

Inverse planning explicitly uses anatomical information and dwell positions when computing HDR brachytherapy dose plans. Clinical experience with HDR brachytherapy has led to organ doses that are correlated with biologically acceptable results,[9] more specifically, the eradication of the tumor with reasonable side effects to healthy tissue. Recently, these organ doses have become the dosimetric criteria that form the objective of many dose planning systems.

Many planning systems provide tools to quickly evaluate dose distributions and guide the user toward a final dose plan. However, finding a suitable dose plan may take several attempts. During dose planning, a set of computational parameters are hypothesized that will give a suitable dose plan (i.e., one that meets all dosimetric criteria). A dose plan is computed using these parameters, and if any dosimetric criteria are not met, the process is repeated until a suitable plan is found. In this way, the dose distribution is controlled by abstract parameters. The purpose of this study is to develop an inverse planning method for HDR brachytherapy that directly controls the dose distribution through dosimetric indices.

We formulated HDR dose planning as an optimization model known as a mixed integer program. A mixed integer program is an optimization model where some or all of the variables are restricted to taking on integer values. Dosimetric criteria can be directly incorporated into our model using integer programming constraints. Since the constraints in mixed integer programs are hard constraints, our model is guaranteed to meet the given dosimetric criteria if physically possible; otherwise it will be declared infeasible. However, many integer programs are difficult to solve in a reasonable amount of time.[10] This is the case for our model, and in our initial tests, reasonably sized instances of our model did not provide an optimal solution, even given several hours. As a consequence, we also develop a heuristic for our model that can provide clinically viable dose plans in under 1 min.

Although the mathematical formulation of our model generalizes to any brachytherapy cancer site where planning can be restricted by dosimetric indices, this study focuses on HDR brachytherapy planning for prostate cancer because dosimetric criteria are readily available.[9] In the following section, we give some background on inverse planning and integer programs.

II. BACKGROUND

In HDR brachytherapy, the tumor site is referred to as the clinical target volume (CTV), and surrounding healthy organs are referred to as organs at risk (OAR). A physician prescribes a dose, Rx [Gy] that should be delivered to as much of the CTV as possible, subject to constraints on the dose to OAR. The dose delivered to an entire organ is quantified by dosimetric indices. For example, the $V_{100}^{\text{Prostate}}$ is the prostate volume receiving at least 100% of the prescription dose.

In inverse planning, organ volume is discretized into dose points that are usually evenly spaced. The dose received at a dose point is considered representative of the dose received in the near vicinity of the dose point. Given a dose threshold for an organ, a dosimetric index is the number of dose points receiving more than the dose threshold times the volume a single dose point represents.

Clinical experience has determined ranges for dosimetric index values that are correlated with acceptable biological outcomes such as nonrecurrence and minimal side effects to OAR. These dosimetric indices and their acceptable ranges constitute dosimetric criteria. For example when treating prostate cancer, the RTOG-0321 dosimetric protocol[9] states that the $V_{100}^{\text{Prostate}}$ (i.e., CTV coverage) should be greater than 90% of the prostate volume and the V_{75}^{Rectum} should be less than 1 cm^3. The objective of HDR brachytherapy planning is to determine a set of source dwell times that achieve the given dosimetric criteria.

In iterative approaches to HDR brachytherapy planning such as in Ref. 11, suitable dose plans are computed by assigning penalties to dose points and finding a dose plan that minimizes the total penalty. For any given dose plan, dose points are penalized for receiving dose in an undesirable range. For example, a dose point in the CTV could be penalized for receiving less than Rx, and a dose point in the rectum could be penalized for receiving more than 75% Rx.

The importance of individual dosimetric criterion is represented by the relative magnitude of the penalty weights. For instance, if the penalty for the CTV is more than that of the rectum, then achieving CTV coverage is more important to the physician than controlling the dose to the rectum. Penalties are useful when a standard set of dosimetric criteria is not known because it allows physicians to balance CTV coverage with OAR exposure in a single objective.

However, using penalties to achieve a prespecified set of dosimetric criteria can be difficult because penalties do not provide direct control over dosimetric indices. As a consequence, achieving dosimetric criteria with penalties requires several attempts. A set of penalties are hypothesized that will achieve dosimetric criteria; then a dose plan and dosimetric indices are computed. The process is repeated until a dose plan meeting all dosimetric criteria is achieved. Although a suitable dose plan can usually be found, it can be a time consuming process. Figure 1 (left) shows the clinical workflow using this approach.

The model and heuristic presented in this study utilize optimization models from mathematical programming. In the following paragraphs we give a brief overview of these models and describe their relationship to brachytherapy dose planning.

A mixed integer program (MIP) is an optimization model of the form:

$$\begin{aligned}(\text{MIP})\quad &\text{Maximize } c^T x\\ &\text{Subject to :}\\ &Ax \le b,\\ &x_i \in \mathbb{R}, i \in \{1,\ldots,k\},\\ &x_i \in \mathbb{Z}, i \in \{k+1,\ldots,n\},\end{aligned}$$

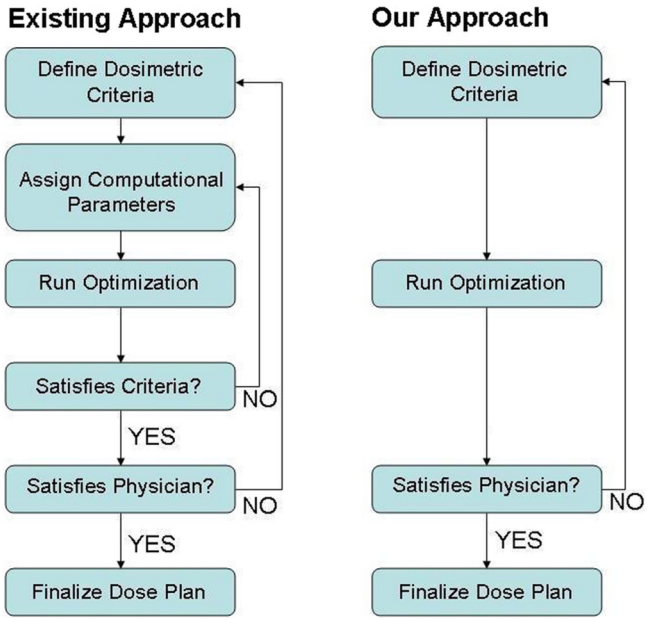

FIG. 1. Clinical workflow for current approach (left) and our approach (right). With current approaches, physicians iterate through dosimetric criteria and parameters during dose planning. In our approach, iterations are only done using dosimetric criteria.

where the known parameters c, A, and b are $n \times 1$, $m \times n$, and $m \times 1$ matrices of real numbers, respectively, x is an $n \times 1$ vector of unknown variables, and $\mathbb{R}$ and $\mathbb{Z}$ are the set of real numbers and integers, respectively. A feasible solution is an x that satisfies every constraint. The term $c^T x$ is called the objective function. The last two constraints say that some of the variables can take on real number values, and some are restricted to be integers. The goal of a mixed integer program solver is to find an optimal solution – a feasible solution with the highest objective function value. If there are no variables in MIP that are restricted to be integers, then MIP reduces to a linear program (LP). LPs are efficiently solvable,[12] even on a personal computer.

Integer programs have been used to model prostate permanent-seed (PPI) brachytherapy and external beam dose planning.[13–18] In particular, Ferris *et al.* used integer programs to constrain dosimetric indices for PPI. Integer programs that have applied these constraints to PPI brachytherapy have been solved within a few minutes using customized approaches that take advantage of the binary nature of placing a seed (i.e., either it is placed or it is not). Although the study here applies similar constraints to HDR brachytherapy, the same mathematical tools cannot be applied to our model because dwell times are continuous rather than binary. In other words, tools that exploit the mathematical structure created by the binary variables associated with seed placement cannot be applied to the same model with continuous dwell times.

III. METHOD AND MATERIALS

III.A. Model formulation

In this section, a mixed integer program for HDR brachytherapy planning is developed. A description of subscripts, parameters, and variables in this model are given for reference in Table I.

Dosimetric indices are estimated by sampling from a uniform grid of dose points that have been generated from evenly spaced anatomy image cross sections. The formulation of our model assumes the same set of dose points. The subscript "s" denotes organs, and "i" and "j" denote dose points and dwell positions, respectively. The set of dose points in an organ is G_s, and P_{si} is the three dimensional coordinate of a dose point in G_s. The number of dose points in an organ is N_s. Dwell positions are denoted by T_j, and the number of dwell positions is N_T.

TABLE I. IPIP term definitions.

Term	Description
S	Subscript for organs
I	Subscript for dose points
J	Subscript for dwell positions
G_s	The set of dose points in organ s
P_{si}	The 3D coordinates of dose point i in G_s
N_s	The number of dose points in G_s
T_j	The 3D coordinates of dwell position j
N_T	The number of dwell positions for this patient
D_{sij}	The dose rate from T_j to P_{si}
t_j	Dwell time at T_j
D_{si}	Dose at P_{si}
R_s	Threshold dose for G_s
M_s	Maximum dose for G_s
X_{si}	Indicator variable for P_{si}
V_s	Dosimetric index for G_s
L_s	Lower bound for v_s
U_s	Upper bound for v_s

The dose-rate parameter, D_{sij} [cGy/s], is the dose received at P_{si} for every second the source remains at T_j. R_s [cGy] is the dose required for P_{si} to be counted in the dosimetric index for G_s. The maximum allowed dose for dose points in G_s is M_s [cGy]. L_s and U_s are the lower and upper bounds for the dosimetric index for G_s, respectively.

The optimization variables are the dwell times, t_j [seconds], the dose at each dose point d_{si} [cGy], the dosimetric indices for each organ, v_s, and the indicator variables, x_{si}. The dwell times are continuous variables that represent the source time spent at T_j. The total dose received at P_{si} is the sum of the contributions from every dwell position, $d_{si} = \sum_{j=1}^{N_T} D_{sij} t_j$. The indicator variables are binary variables that should have the following behavior:

$$x_{si} = \begin{cases} 1 & \text{if } d_{si} \geq R_s \\ 0 & \text{otherwise} \end{cases}$$

Finally, the dosimetric index for G_s is the sum of all the indicator variables, $v_s = \sum_{i=1}^{N_s} x_{si}$.

We called the model Inverse Planning by Integer Program (IPIP). It is presented below.

(IPIP)

Maximize v_0

Subject to :

$$d_{si} = \sum_{j=1}^{N_T} D_{sij} t_j, \qquad \forall s, i \in G_s, \quad (1)$$

$$R_s x_{si} \leq d_{si} \leq R_s + (M_s - R_s) x_{si} - \epsilon, \qquad \forall s, i \in G_s, \quad (2)$$

$$v_s = \sum_{i=1}^{N_s} x_{si}, \qquad \forall i \in G_s, \quad (3)$$

$$L_s \leq v_s \leq U_s \qquad \forall s, \quad (4)$$

$$t_j \geq 0 \qquad \forall j, \quad (5)$$

$$x_{si} \in \{0, 1\} \qquad \forall s, i \in G_s. \quad (6)$$

The objective of IPIP is to maximize v_0, CTV coverage. The first constraint (1) integrates the dose at P_{si} from every dwell position. The purpose of constraints (2) and (6) is to enforce the relationship between d_{si} and x_{si}. For a given dose at P_{si}, if $x_{si} = 1$, constraints (2) reduces to $R_s \leq d_{si} \leq M_s - \epsilon$, and if $x_{si} = 0$, it reduces to $0 \leq d_{si} \leq R_s - \epsilon$. Conversely, if $d_{si} \geq R_s$, then $x_{si} = 1$, and if $d_{si} < R_s$, then $x_{si} = 0$. Therefore, $x_{si} = 1$ if and only if $d_{si} \geq R_s$, and the indicator variables behave as desired.

The parameter ϵ is a small number that is included so that the value of x_{si} has no ambiguity when $d_{si} = R_s$. More specifically, if d_{si} equals R_s, then 1 or 0 is valid for x_{si} even though it should take the value 1 according to our definition. For very small ϵ, constraints (2) becomes an approximation to $R_s x_{si} \leq d_{si} < R_s + (M_s - R_s) x_{si}$, which ensures that $x_{si} = 1$

when $d_{si} = R_s$. If this level of precision is not required, then ϵ can be omitted from the formulation.

Constraint (3) integrates the dosimetric indices over all the indicator variables. Constraint (4) enforces dosimetric criteria. Since dose points lie on a uniform grid, each dose point is representative of an equal organ volume. Therefore, constraining the amount of organ volume receiving R_s dose is equivalent to constraining the number of dose points receiving R_s. For example, if each dose point represents 0.1 cm^3 of organ volume, and no more than 1 cm^3 of organ can receive greater than the threshold dose, then the number of dose points in the organ that can receive greater than the threshold dose is 10 dose points.

Constraint (5) restricts the dwell times to be nonnegative and (6) constrains the indicator variables to be binary.

IPIP is a direct approach to finding dose plans using dosimetric criteria. However, our initial tests showed that standard solvers could not find an optimal (or feasible) solution reliably for reasonably sized instances, even given several hours. Therefore, as described in the following section, we developed a fast heuristic method for computing feasible solutions.

III.B. IPIP heuristic formulation

The computational difficulty in solving IPIP comes from the binary variables, x_{si}, that make IPIP a MIP. In this section, we develop a heuristic to quickly determine values for the indicator variables in IPIP. Using this heuristic, dose plans can be computed from IPIP.

For this heuristic, IPIP is relaxed by using fewer and less restrictive constraints. The resulting optimization model is an LP, which can be solved quickly. The dose plan computed from this relaxation is analyzed, and based on this analysis, the indicator variables from dose points associated with OAR are set to either 1 or 0. With the indicator variables determined, a dose plan can be computed as the solution to another linear program.

The following relaxations are applied to IPIP: (1) The binary restriction for the indicator variables in IPIP is relaxed (i.e., the constraint $x_{si} \in \{0, 1\}$ becomes $0 \leq x_{si} \leq 1$), and (2) constraints on dosimetric indices are removed. After some substitutions, the resulting optimization problem is the following linear program referred to as the heuristic relaxation (HR).

$$\text{(HR)} \quad \text{Maximize} \sum_{i=1}^{N_0} x_{0i}$$

Subject to:

$$\sum_{j=1}^{N_T} D_{sij} t_j \geq R_s x_{0i}, \qquad \forall i \in G_0,$$

$$\sum_{j=1}^{N_T} D_{sij} t_j \leq M_s - \epsilon, \qquad \forall s, i \in G_s,$$

$$t_j \geq 0 \qquad \forall j,$$

$$0 \leq x_{0i} \leq 1, \qquad \forall i \in G_0.$$

Since dosimetric indices are not constrained in HR, the indicator variables that make up the dosimetric indices are removed. As a result, the dose at an OAR dose point is only limited by the maximum dose, M_s. The indicator variables for the CTV (i.e., x_{0i}) are retained and the sum is maximized in the objective.

In general, a dose plan computed from HR will not satisfy the dosimetric criteria for the OAR in IPIP (i.e., $v_s > U_s$). The next step of this heuristic is to take dose plans computed from HR and make them feasible for IPIP. To accomplish this, constraints are added to HR to ensure that $v_s \leq U_s$ for the OAR.

In IPIP, the dose at P_{si} should be less than R_s when $x_{si} = 0$ and less than M_s when $x_{si} = 1$. In other words, the value of the indicator variable x_{si} determines the dose limit at P_{si}. Therefore, setting x_{si} to 0 or 1 is equivalent to setting the dose upper limit for P_{si} to R_s or M_s, respectively. HR is equivalent to setting all the OAR indicator variables to 1, making the dose upper limit to these dose points equal to M_s. However, this will most likely produce an unusable dose plan that delivers excessive dose to the OAR.

To correct this excessive dosing, new constraints are added to HR restricting all but U_s of the OAR indicator variables to 0. That is, all but U_s of the dose points in an OAR will be constrained to receive less than R_s dose. This procedure guarantees that v_s is less than U_s for the OAR.

However, the U_s dose points should be selected in a way that can still produce high CTV coverage. To make this selection, the dose plan computed from HR is analyzed, and the U_s dose points in G_s receiving the most doses retain a dose upper limit of M_s. The remaining dose points are restricted to receive less than R_s. This can be accomplished by adding the constraint $\sum_{j=1}^{N_T} D_{sij} t_j \leq R_s - \epsilon$ to the $N_s - U_s$ dose points in G_s that are receiving the least dose in the HR dose plan.

The reason this method of selection was chosen is as follows. Without the dose restrictions to OAR, an HR dose plan will likely be too hot. Therefore, the dose to some of the dose points must be reduced to make it feasible for IPIP. Our heuristic assumes that adding constraints that reduce the dose to the dose points receiving the least dose will have the least impact on the HR dose plan. In other words, the HR dose plans are cooled as little as possible to make them feasible for IPIP. In this way, high coverage is retained.

A common dosimetric criterion is for CTV coverage to be more than a certain percentage of the CTV. This is represented in IPIP by the constraint $L_0 \leq v_0$. This constraint was removed in HR and is not enforced by the additional constraints added later on. As a consequence, meeting lower bound dosimetric index constraints is not guaranteed by this heuristic. However, usually the only dosimetric index with a lower bound constraint is for CTV coverage, and maximizing this dosimetric index is the objective of HR. Therefore, if the upper bound constraints are not too stringent, this criterion is likely to be met or come close to being met.

Our IPIP heuristic is summarized as follows:

(1) Solve HR and store dwell times.
(2) Using the dwell times from HR, for each organ except the CTV, let P_{si^*} denote the U_s dose points receiving the most doses in that organ.

(3) For every $P_{si} \notin P_{si*}$ add the constraint $\sum_{j=1}^{N_T} D_{sij} t_j \leq R_s - \epsilon$ to HR.
(4) Resolve updated HR to get dose plan.

For the sake of brevity, we will not distinguish between IPIP and this heuristic for the remainder of the paper.

III.C. Patient data sets

We applied IPIP retrospectively to 20 prostate cancer patient cases. These patients were chosen to have a wide range of prostate volumes ranging from 23 to 103 cm^3. After catheter implantation, a treatment planning pelvic CT scan was obtained for each patient. Three-millimeter-thick CT slices were collected using a spiral CT. The CTV and OAR (urethra, rectum, and bladder) were contoured using the Nucletron Plato Version 14.2.6 (Nucletron B.V., Veenendaal, The Netherlands). The CTV included only the prostate and no margin was added. When segmenting the bladder and rectum, the outermost mucosa surface was contoured. The urethra was defined by the outer surface of the Foley catheter, and only the urethral volume within the CTV was contoured. The OAR were contoured on all CT slices containing the CTV and at least two additional slices above and below. Implanted catheters were also digitized.

For the contoured anatomical structures, dose points were generated by sampling from a uniform grid with 2 mm spacing in the x–y direction and 3 mm spacing in the z direction. Dose points were also generated in the body tissue (space between organs) with 4 mm spacing in the x–y direction. For the 20 cases, the total number of dose points for IPIP ranged from 8860 to 25288. To reduce the computation required, every dose point more than 3.5 cm from the xy-centroid of the dwell positions was omitted in the optimization. However, they were included when computing the dosimetric indices. Our tests showed that removing these dose points had no effect on the dosimetric index values. Specifically, the computation of the dosimetric indices with some of the dose points omitted was the same in IPIP as computed independently using all the dose points. The number of dose points after this removal ranged from 6144 to 15568.

III.D. Dose rate calculations and clinical criteria

The dose-rate contribution to a dose point from a source dwell position is a function of the distance between them. The dose-rate parameters were calculated as specified in the AAPM TG-43 dosimetry protocol.[20] The radioactive material used in the source was ^{192}Ir, and the prescription dose was 9.5 Gy.

The dosimetric criteria used in this study can be found in Table II. The specifications for the $V_{100}^{Prostate}$, $V_{125}^{Urethra}$, V_{75}^{Rectum}, and $V_{75}^{Bladder}$ are defined by RTOG-0321.[9] RTOG specifies that the $V_{125}^{Urethra}$ be much less than 1 cm^3. We interpreted this to mean less than 0.1 cm^3.

The $V_{150}^{Prostate}$ is not explicitly constrained by the RTOG-0321 protocol. The $V_{150}^{Prostate}$ is restricted by the homogeneity index (HI), where

TABLE II. Dosimetric criteria.

Index	Requirement
$V_{100}^{Prostate}$	$\geq 90\%$
$V_{150}^{Prostate}$	$\leq 45\%$
$V_{125}^{Urethra}$	≤ 0.1 cm^3
$V_{150}^{Urethra}$	$=0$ cm^3
V_{75}^{Rectum}	≤ 1 cm^3
V_{100}^{Rectum}	0 cm^3
$V_{75}^{Bladder}$	≤ 1 cm^3
$V_{100}^{Bladder}$	$=0$ cm^3
V_{200}^{Body}	$=0$ cm^3

$$\mathrm{HI} = \frac{V_{100}^{Prostate} - V_{100}^{Prostate}}{V_{100}^{Prostate}}.$$

It is generally preferred that HI ≥ 0.6 ; however, lower values of HI are acceptable if they allow for higher CTV coverage. For this study, we constrain HI to be greater than 50% to maintain some control over the $V_{150}^{Prostate}$ while not being overly restrictive. Since we expect target coverage over 90%, this restriction on HI can be enforced with $V_{150}^{Prostate} \leq 45\%$.

The restrictions that the $V_{150}^{Urethra}$, V_{100}^{Rectum}, $V_{100}^{Bladder}$, and V_{200}^{Body} be equal to 0 are not specified by RTOG but are considered preferable when possible at our clinic. The preference of the V_{200}^{Body} comes from the desire to keep hot spots localized within the CTV.

The parameters used for IPIP to reflect these dosimetric criteria can be found in Table III. The values of 8 and 83 for U_s represent the number of dose points in 0.1 and 1.0 cm^3, respectively, based on our grid spacing. The value of U_s for the $V_{150}^{Prostate}$ is 45% of the number of dose points in the prostate. The dose to prostate dose points should be unrestricted so we have used an unrestrictively high number, 20 000 cGy. We did this to avoid using infinity, which creates numerical problems with our optimization solver. The dosimetry in our results shows no dose points receiving this dose level for any patient.

III.E. Method evaluation

We used Matlab v. R2008b (Mathworks Inc.) to compute dose plans from IPIP. The linear programming optimization was done using the Matlab interface for the Mosek Optimization Toolbox v.5,[21] a medium to large scale optimization package. All computations were performed on a personal computer with an Intel(R) Core^{TM}2 Duo CPU 1.67 GHz

TABLE III. IPIP parameters.

Organ	s	R_s	M_s	U_s
Prostate	0	950	20000	N_0
Prostate	1	1425	20000	.45 N_0
Urethra	2	1140	1425	8
Rectum	3	712	950	83
Bladder	4	712	950	83
Body	5	1900	1900	0

processor, 3 Gib RAM, and the Windows 32-bit operating system. We recorded the compliance of IPIP dose plans with our dosimetric criteria and the running time.

For comparison, we will also compute dose plans from Inverse Planning Simulated Annealing (IPSA), a clinically deployed dose planning system used at our clinic. All computational parameters for IPSA were the same as in Alterovitz *et al.*[19] No computational parameters from IPSA were manipulated after the first iteration.

IV. RESULTS

For each patient, IPIP satisfied all our dosimetric requirements on the first iteration. The compliance rate (out of 20 patients) for each individual dose objective is summarized in Table IV. The average CTV coverage from IPIP was 95%. IPSA did not meet all dosimetric criteria for any of the patients and would require manual adjustment. Note that our constraints on dosimetric indices are hard constraints so even the slightest deviation from the requirement is considered a failure, and IPSA dose plans meeting all dosimetric criteria can usually be found with a few adjustments to the optimization parameters.

On average, IPIP computed a dose plan within 30.1 s. The maximum runtime was 86 s. For comparison, IPSA computed a dose plan within 5 s on average, with a maximum runtime of 9 s. However, the time required to make manual adjustments to the IPSA dose plans was not included.

V. DISCUSSION

Although our experiment shows that IPIP can be used to generate dose plans that meet dosimetric criteria, we conducted two side experiments which demonstrated cases where IPIP does not produce good results. In the first side experiment, we insisted that the V_{75}^{Rectum} and V_{75}^{Bladder} be 0 cm^3. The other dosimetric criteria were the same as in the main experiment. The results for a single patient are shown in Table V. CTV coverage, which was lower bound constrained, was only 78%, which did not meet the 90% requirement. However, all other criteria were fulfilled. In this case, the dosimetric criteria was too stringent and additional iterations would be required using more relaxed criteria.

In the second side experiment, we compared two dose plans computed from IPIP for the same patient. The first dose plan used the same criteria as for the main experiment. The second dose plan was computed with the requirement that the V_{75}^{Rectum} and V_{75}^{Bladder} be less than 0.5 cm^3 (instead of 1 cm^3). All other criteria for the second dose plan were the same as for the main experiment. The results are summarized in Table VI.

CTV coverage for the first dosimetric criteria was 96%. To achieve this coverage, almost all of the dose allowance to the rectum and bladder was utilized (i.e., V_{75}^{Rectum} and V_{75}^{Bladder} was close to 1 cm^3). With the second dosimetric criteria, CTV coverage dropped to 91%, but the overdosed volume to the rectum and bladder was cut in half.

Since the objective of IPIP is to maximize coverage within limits to OAR dose, IPIP will tend to utilize the entire OAR dose available to it. More specifically, IPIP will make large increases to OAR dose, within its limits, even to make only small improvements to CTV coverage. In this case, the drop in CTV coverage (5%) between the two dose plans was worth considering, but a physician may still prefer the second dose plan. However, determining the second dose plan cannot be accomplished without iterating through alternative dosimetric criteria.

Although there are circumstances in which dose planning with IPIP requires several attempts, the dose distribution is

TABLE IV. IPSA and IPIP compliance with dosimetric criteria. The data is given as a percentage of patient dose plans (out of 20) that complied with each constraint for each approach. The dosimetric constraints supplied were hard constraints, meaning even the slightest deviation from the limit was considered a failure. Note that no adjustments to the IPSA optimization parameters were made to compensate for unsatisfied criteria. Despite the low compliance rate of IPSA, dose plans meeting all criteria can usually be found using IPSA after a few adjustments to the parameters.

	Approach	
Dosimetric index	IPSA (%)	IPIP (%)
$V_{100}^{\text{Prostate}}$	100	100
$V_{150}^{\text{Prostate}}$	100	100
V_{125}^{Urethra}	85	100
V_{150}^{Urethra}	50	100
V_{75}^{Rectum}	80	100
V_{100}^{Rectum}	55	100
V_{75}^{Bladder}	65	100
V_{100}^{Bladder}	100	100
V_{200}^{Body}	5	100
HI	100	100
All requirements	0	100

TABLE V. Set of dosimetric criteria that cannot be met with IPIP. The V_{75}^{Rectum} and V_{75}^{Bladder} were required to be 0. For this case, CTV coverage was only 78%, which did not meet our 90% requirement. Less stringent dosimetric criteria must be given in the next iteration.

Dosimetric index	Value
$V_{100}^{\text{Prostate}}$	78%
$V_{150}^{\text{Prostate}}$	33%
V_{125}^{Urethra}	0.01 cm^3
V_{75}^{Rectum}	0 cm^3
V_{75}^{Bladder}	0 cm^3

TABLE VI. Comparison of different dosimetric criteria for a single patient. For dosimetric criteria 1, criteria were the same as in the main experiment. For dosimetric criteria 2, the V_{75}^{Rectum} and V_{75}^{Bladder} were restricted to be less than 0.5 cm^3, which was more stringent. By restricting the V_{75}^{Rectum} and V_{75}^{Bladder}, CTV coverage dropped by 5% but with large reduction to OAR exposure.

Dosimetry	Dosimetric criteria 1	Dosimetric criteria 2
$V_{100}^{\text{Prostate}}$	96%	91%
$V_{150}^{\text{Prostate}}$	33%	30%
V_{125}^{Urethra}	0.01 cm^3	0 cm^3
V_{75}^{Rectum}	0.92 cm^3	0.45 cm^3
V_{75}^{Bladder}	0.95 cm^3	0.44 cm^3

controlled by directly specifying dosimetric criteria rather than system-specific optimization parameters.

VI. CONCLUSION

IPIP is a new approach for HDR brachytherapy planning that is intuitive for physicians and less reliant on manual fine tuning than current approaches. IPIP allows physicians to directly specify desired dosimetric indices, rather than system-specific computational parameters when dose planning. Our results demonstrate that IPIP quickly generates dose plans that are consistent with RTOG-0321 standard dosimetric criteria. Further study is required to determine if IPIP can produce similar performance for a more general group of patients and dosimetric criteria, including other cancer sites such as GYN.

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