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Fluence map optimisation for prostate cancer intensity modulated radiotherapy planning using iterative solution method

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Abstract

Here we projected a model-based IMRT treatment plan to produce the optimal radiation dosage by considering that the maximum amount of prescribed dose should be delivered to the target without affecting the surrounding healthy tissues especially the OARs. Fluence mapping is used for inverse planning. This suggested method can generate global minima for IMRT plans with reliable plan quality among diverse treatment planners and to provide better safety for significant parallel OARs in an effective way. The whole methodology is having the capability to handles various objectives and to generate effective treatment procedures as validated with illustrations on the CORT dataset. For the validation of our methodology, we have compared our result with the two other approaches for calculating the objectives based on dose-volume bounds and found that in our methodology dose across the prostate and lymph nodes is maximum and the time required for the convergence is minimum.

Key words: fluence map optimisation; planned target volume; organ at risk; intensity modulated radiation therapy.

Introduction

Fluence mapping is a significant process for inverse planning.¹⁻³ There are two main traits of a good fluence map optimization. Firstly, the maximum amount of prescribed dose should be delivered, and uniformly distributed across the planned target volumes. Secondly, the healthy tissues adjacent to the target region should have the minimum or zero effect due to the radiation dosage, particularly; the distribution of dose across the OARs should not be more than the upper bound of dose recommended by the oncologists. Considering these constraints in mind several works have been done in the literature mainly dedicated to the design of model using dose-volume bounds^{4,5} and corresponding algorithms for the analysis. Considering the complexity of the algorithm and dimension of the problem in mind, most of the models formulated by the authors are either linear or quadratic models.⁶⁻⁸ In these models, two terms are mostly used during analysis for defining the target volume; one is the sum of the absolute value of dosage and another one is the sum of squared value of doses. Constraints on dose-volume are broadly used for the OARs.

In⁴, including linear^{9,10} and quadratic programming models,¹¹⁻¹³ the authors provided a comprehensive survey of several other formulations of the prototypes for treatment planning. Mostly, linear prototypes reduce the weighted summation of dosages or the extreme changes from a recommended dose, while quadratic prototypes reduce the weighted summation of squared variance between definite and recommended dose. These originations integrate linear constraints on the measures to each volume of interest. Different interior point techniques are typically used, to find the quick results, for example, to identify the active set at a solution in a finite number of iterations projected gradient method¹⁴ is used. Similarly, if the problem is combinatorial in nature primal-dual method,¹⁵ or interior point bound generation method¹⁶ is used. Researchers have suggested multiple objective and bounds based clinical goals, to report contradictory models. As the weight is an important factor in each objective, therefore by changing the value of it, we may easily generate an array of solutions.^{17,18}

The models with dose-volume bound is a non-convex optimization problem¹⁹⁻²¹ and the analysis of these problems are complex in nature. Many prototypes and procedures are suggested by the authors in the literature to formulate this problem. In²² author transforms the non-convex model into a linear model by using the concept of conditional value at risk. In¹⁸ authors used an optimization model with multiple dose-volume bounds and in²³ formulated a discrete objective function based least-squares model. For problem solving, various kind of mathematical model centered algorithms, such as gradient algorithms,²⁴ and heuristic algorithms such as simulated annealing and genetic algorithms were suggested by the researchers. Furthermore,^{25,26} used the optimization process based on voxel-dependency to acquire the required dose-volume arc. Furthermore, an idea of dosimetric capacity was projected in²⁷, which was incorporated in IMRT process.

The organization of the paper as follows. In Section-2, we frame the fluence map optimization model centered on multiple dose-volume constraints for radiation treatment planning and developed an optimization algorithm with the basic flowchart of the radiation treatment process. In this section, we have also provided a description of the dataset used for the analysis of the problem. In section-3, we present the simulation-based analysis of the problem and for a different combination of PTVs and OARs formulated the result by satisfying DVCs. Lastly, in Section-4, we recapitulate the outcomes and discuss further directions of study.

Materials and Methods

The aim of radiation treatment optimization planning is to supply the radiation in such a manner that a sufficient amount of radiation should pass through the target with minimum sparing of critical structures. When the optimization problem is converted into a mathematical form, there we may adopt three possible approaches: first is to optimize a function of target dose with bounds on the critical structures (OAR), second is to minimize the dose to the OARs with bounds on the amount of dose to the planned target and the third is to optimize both, a function of planned target dose and the dose to OARs. Here we are addressing the third approach. The general fluence mapping optimization problem formulated as,

$$\underset{x \geq 0}{\text{Minimize}} \quad \chi(D_0x) + \sum_{i=0}^M \psi_i(D_i x) + \theta(dx) \quad \text{Eq. 1}$$

Here $D \rightarrow$ Dose calculation matrices for one or more VOIs; $M \rightarrow$ Number of OARs; $d \rightarrow$ Gradient operator $\chi, \psi, \theta \rightarrow$ Penalty functions.

χ can be the one-sided L1, one-sided L2, or the indicator function. This penalty term penalizes the objective function when there are unsatisfied constraints. The domain of χ is the set of all the points x ($x \in R^n$). It will be null if all the bounds are fulfilled, or we can say that when the existing result is in the feasible set of the problem.

The term $\chi(D_0x)$ represents the least level of radiation delivered to the PTV while the terms $(D_i x)$ are the extreme doses that can be delivered to the OARs. $\theta(dx)$ is the regularization terms for providing a smooth non-negative fluence map. The optimization methods provided here can handle the penalty functions χ, ψ, θ .

χ is the quadratic penalty function:

$$\chi(Dx) = \|Dx - P\|_2^2 \quad \text{Eq. 2}$$

Where $P \rightarrow$ vector that contains the values of prescribed doses that are to be distributed to each voxel in the tumor; $D \rightarrow$ beamlet-to-voxel map matrix; $x \rightarrow$ beamlet intensity vector.

With the suitable choice of χ , the hard constraint that $(D_0x) > P$ may be applied to the fluence map generation method.

Similar choices apply to the penalty function ψ_i , which is selected to impose an upper limit on the dose delivered to the tumor and OARs. ψ_i Includes a one-sided L_2 based penalty function:

$$\psi_i(Q_i) = \frac{\alpha_i}{2} \|Q_i - v_i\|_2^2 \quad \text{Eq. 3}$$

As the fluence mapping is an inverse problem where we need to determine the optimal beamlet intensity for a prescribed dose across the planned target volumes (PTV) and the Organ at risk (OAR). Therefore for fixed values of beam angles first approximate the radiation supplied to the patient using a direct mapping from the voxel dose to the beamlet intensity and at the same time fulfill the criteria of constraints applied across the PTVs indexed by $T \in T$, critical organs indexed by $C \in C$ and, normal tissues indexed by $N \in N$. Let d_T denotes the prescribed amount of dose (often in Gy) delivered to PTV $T \in T$ and for critical organs and normal tissues the maximum, mean and DVH tolerance dose is denoted by d_C^{max} , d_C^{mean} , d_C^{tol} and d_N^{max} , d_N^{mean} , d_N^{tol} respectively. Let D_T , D_C and D_N is the linear beamlet to voxel map dose matrixes for the PTV T , critical organ C , and normal tissues N . Beamlet intensities is encoded by the positive vector x . The value of x cannot be negative in any circumstances. Now the ideal problem of fluence map optimization based on the constraints on OAR and PTV mentioned above can further be reformulated by considering the maximum dose constraints on the PTV as,

$$\underset{x \geq 0}{\text{Minimize}} \quad \sum_{T \in T} \frac{\alpha_T}{2n_T} \|D_T x - d_T\|_2^2 + \frac{\lambda}{2} \|x\|_2^2$$

$$\text{Subjected to } D_C x \leq d_C^{max} \quad C \in C^{max}$$

$$1^T D_C x \leq n_C d_C^{mean} \quad C \in C^{mean}$$

$$\|D_C x - d_C^{tol}\|_0 \leq \frac{n_C \beta_C}{100} \quad C \in C^{tol}$$

Eq.4

New Formulation

$$\begin{aligned}
 & \text{Minimize} \\
 & \quad x \geq 0 \\
 & \quad \sum_{T \in T} \frac{\alpha_T}{2n_T} \|D_T x - d_T\|_2^2 \\
 & \quad + \sum_{C \in \mathbb{C}} \frac{\alpha_C}{2n_C} \|w_C - (D_C x - d_C^{tol})\|_2^2 + \frac{\lambda}{2} \|x\|_2^2 \\
 & \text{Subjected to} \quad \|(w_C)_+\|_0 \leq \frac{n_C \beta_C}{100} \quad ; C \in \mathbb{C}^{tol}
 \end{aligned}$$

Eq. 5

In the new plan, the supplementary variable w_C is enforced to satisfy the DVH constraints, while the residuals $(D_C x - d_C^{tol})$ may not essentially do as such. The weight α_C control w_C to carefully estimate $(D_C x - d_C^{tol})$ and as α_C tends to infinity, the new problem converges to the idealized problem.

The optimization algorithm

The optimization algorithm is comprised of two methods, where the first method is based on the gradient projection, and in the second method, we used the iterative reweighting approach. With the use of method-2, we will be able to demonstrate the effect of the weight factor on the result. Method-2 uses the block coordinate descent approach in the subroutine for the re-weighting of the result. For the convex-cordiality problem suggested in ²⁸ we implemented the variation of the penalty decomposition method.

Figure 1. Flowchart of IMRT Inverse Planning Process

Method-1:

Input $\sigma, x^{(0)}$, Initialize $m=0$, $w_c^{(0)} = \text{proj}_{\varphi_c}(D_C x^{(0)} - d_C^{tol})$.

While $err > \sigma$ do

$$x^{(m+1)} = \text{argmin}_{x \geq 0} f(x, w^{(m)})$$

for $C \in \mathbb{C}$ do

$$w_c^{(m+1)} = \text{proj}_{\varphi_c} \left(w_c^{(m)} - \frac{\alpha_C}{2n_C} (w_c^{(m)} - (D_C x^{(m+1)} - d_C^{tol})) \right)$$

End

$$err = \sum_{C \in \mathbb{C}} \frac{\alpha_C}{2n_C} \|w_c^{(m+1)} - w_c^{(m)}\|_2$$

End

Return $\text{argmin}_{x \geq 0} f(x, w^{(m)})$

Method-2:

Input $\sigma, \tau, x^{(0)}$, Initialize $m=0$, $\alpha_c^0, \varepsilon^0$

While $err > \varphi$ do

Call the subroutine for the values of $x^{(m+1)}$ and $w_c^{(m+1)}$

$$err = \max_{C \in \mathbb{C}} \|w_c^{(m+1)} - (D_C x^{(m+1)} - d_C^{tol})\|$$

for $C \in \mathbb{C}$ do

$$\alpha_c^{(m+1)} = \tau \alpha_c^{(m)}$$

End

$$\varepsilon^{(m+1)} = \rho \varepsilon^{(m)}$$

$$m = m + 1$$

End

Return $x^{(m)}$

Subroutine:

Input $\delta, x^{(0)}$, Initialize $m=0$, $w_c^{(m)} = \text{proj}_{\varphi_c}(D_C x^{(m)} - d_C^{tol})$.

While $err > \delta$ do

$$x^{(m+1)} = \text{argmin}_{x \geq 0} f(x, w^{(m)})$$

$$w^{(m+1)} = \text{argmin}_{w \in \Lambda} f(x^{(m+1)}, w)$$

$$err = \sum_{C \in \mathbb{C}} \frac{\alpha_C}{2n_C} \|w_c^{(m+1)} - w_c^{(m)}\|_2$$

$$m = m + 1$$

End

Return $\text{argmin}_{x \geq 0} f(x, w^{(m)})$

Dataset

CORT database²⁹ of the prostate case is used for the simulation of the examples. The database consists of 180 equi-spaced coplanar beams. For a $1\text{ cm} \times 1\text{ cm}$ of beamlet resolution, the total number of beamlets is 25,404. PTV-68 and PTV-56 are the two main targets around the lymph nodes and prostate, where PTV-68 and PTV-56 are respectively the maximum and minimum dose targets. The OARs include the rectum, bladder, left and right femoral heads, and tissues. The dataset contains a beamlet-to-voxel mapping for 0° to 358° beam angles in increments of 2° . CORT dataset uses monitor units (MU) as the measure to represent beamlet intensities, and indirectly to signify the dose absorbed (SI unit: gray or Gy; $1\text{Gy} = 1\text{ J/kg}$) because 100 MU delivers a dose of 1 Gy. For solving the positive least-squares problems we used the function `minConf_TMP` from the `minConf` package^{30,31} and convex programs were solved with CVX package.³²

Results

For a definite number of beam angles, we define the problem for minimizing the size of the tumor with dose-volume bounds of increasing difficulties on multiple sets of PTVs and OARs. The complete analysis is distributed into several parts. For our different arrays of examples, we use five uniformly spaced

beams where the beam angles are extending in consecutive increments of 72° from 0° to 288° . Voxels in common are allocated as PTVs, in case of overlay between PTVs and OARs. Complete analysis of the work done is simulated in MATLAB R2013a on a computer with a 2.9 GHz dual-core Intel Core i5 processor with 4 GB RAM.

For treatment plans quality measurement, as we may use the differential or cumulative DVH, here we used the cumulative DVH for it. It is also used to check whether an upper dose-volume bound on the critical structure has been satisfied by a specific treatment strategy or not. Let, we consider that a maximum 50% of the bladder volume may overdose 30 Gy. In **Figure 2**, the inner rectangular area denotes the constraints-based region, which encloses all points where a maximum 50% of the bladder volume can receive dosages excess of 30 Gy. Therefore, any dose, which falls exterior to the rectangular region, violates the stated bound, while any dose that contains the area inside the rectangular region will meet the constraint. Therefore, after the analysis, we may conclude, based on the plot shown in the left panel of **Figure 2**, 43.02% of the bladder volume gets the dose greater than 30 Gy, so it violates the dose-volume bound. However, in the right section of **Figure 2**, 24.96% of the bladder volume receives dosages excess of 30 Gy, so it fulfills the dose-volume bound.

Figure 2. Dose-volume histograms with the bounds that maximum 50% of the bladder volume overdose 30 Gy. Left: As 43.02% of the Bladder volume gets 30 Gy, so the treatment plan not satisfied Right: As 24.96% of the Bladder volume gets 30 Gy, hence the treatment plan satisfied.

Figure 3. DVH plot of OAR (Bladder) and PTV-68 for the different fixed dose limits

Table 1. Result of Multiple dose response on one PTV (PTV-68) and one OAR (Bladder)

Parameter	Response - 1			Response - 2			Response - 3		
	PTV-68 D95 (Gy)	OAR %>45 Gy	Time (sec)	PTV-68 D95 (Gy)	OAR %>40 Gy	Time (sec)	PTV-68 D95 (Gy)	OAR %>38 Gy	Time (sec)
Initialization	83.24	28.01	--	83.24	33.47	--	83.24	35.57	--
Method-1	79.67	26.58	2.25	79.67	32.69	4.38	79.67	34.43	4.21
Method-2	79.33	25.90	6.20	79.33	31.17	7.92	79.33	33.58	12.69

Response with single dose-volume constraints

In this case, we considered our algorithm for one PTV (PTV-68) and one OAR (Bladder) problem. Here we use the initial OAR weight $\alpha_2^0 = 1$ and internal ending tolerance $\varepsilon^0 = 0.1$, with weight update factor $\tau = 2$, ending tolerance update factor $\sigma = 0.95$, and external ending tolerance $\varphi = 0.01$. For the problem formulated, a comparison-based analysis is made for the multiple doses as depicted in **Figure 3**. The final analysis shows that there is a minute deviation between the initial and final value of radiation dose for each analysis in terms of PTVs and the DVH. All the analyses have approximately minimized

the dosage to the bladder by approximately satisfying the dose-volume bounds, where iterative weighting yields a comparatively lesser dosage but at the cost of higher solution time.

In **Table 1** we have shown the numerical result of multiple dose-volume responses for PTV-68 and bladder. In the case of PTV-68 (prostate), we have calculated the common D95 dose therefore for each prostate case the response is the same but in the case of OAR (Bladder) we have selected three different values of dose-volume bounds (45 Gy, 40 Gy, and 38 Gy), therefore for each value of dose-volume bounds, there are certain changes in the value of response generated. Both the

methods formulated earlier are used for the generation of the result. The result shows that for the higher value of dose it clearly satisfies the dose-volume bounds but as the value of dose decreases response moves towards the outer region of the dose-volume bounds.

Multiple PTV and OARs with different dose-volume constraints

Now we consider our algorithm for multiple PTV and OAR problems. In this case, we are using two PTVs (PTV-68 and PTV-56) where we are delivering the maximum dose of 85 Gy across the PTV-68 and 70 Gy across the PTV-56 but due to the closeness between the volume of interest and the difference in doses across them it is much more challenging to satisfy all the dose-volume constraints across them. Various Geometric constraints and beamlet intensity pattern also make it complex

to satisfy competing objectives as shown in **Figure 4**, therefore, here it is advised to use the upper and lower limit on the prescribed dose. So that a sufficient amount of dose could be delivered across the PTVs and OARs

A complete analysis is converged after 35 iterations as depicted in **Figure 5**. Different Dose-volume bound for the multiple OARs we considered here is that maximum 50% of the rectum volume may overdose by 50 Gy, maximum 40% of the bladder volume may overdose by 40 Gy, and maximum 35% of the left and right femoral heads volume may overdose by 30 Gy. After the analysis, we found that all the OARs considered here are approximately met the dose-volume bounds as shown in **Figure 6**.

Figure 4. The optimal treatment plan obtained for beamlet intensity (MU) of five beams by ensuring to distribute an almost constant dosage of 85 Gy to the PTVs and nearly prescribed dose across the OARs: (a) Tumors in the prostate is exposed by five equally spread out beams with dose-volume bounds on the OARs. (b) Beamlet intensity of five beams

Figure 5. (a) Objective value convergence curve. (b) Convergence criteria curve

Figure 6. Dose-Volume constraint plot of multiple PTVs and OARs where dotted line indicates initial response and Solid line indicates optimized response

Conclusion

The prime work of IMRT and the other radiation-based treatment design is to distribute a recommended dosage to the malignancy cells without affecting surrounding healthy tissues. The fluence-mapping problem for IMRT is a broader area problem where we need to fulfill multiple objectives and bounds on the PTVs and OARs. Due to the non-convexity of the optimization problem, the clinically relevant DVH is NP-hard. Here we proposed a model-based methodology that can produce such treatment plans that meet the entire requirement

for the bounds on dose-volume for OARs without any tedious trial-and-error process. This suggested method can generate global minima for IMRT plans with reliable plan quality among diverse treatment planners and to provide better safety for significant dual OARs in an effective way. The whole methodology is having the capability to handles various objectives and to generate effective treatment procedures as validated with illustrations on the CORT dataset.

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