INTERACTIVE TREATMENT PLANNING IN CANCER RADIOTHERAPY

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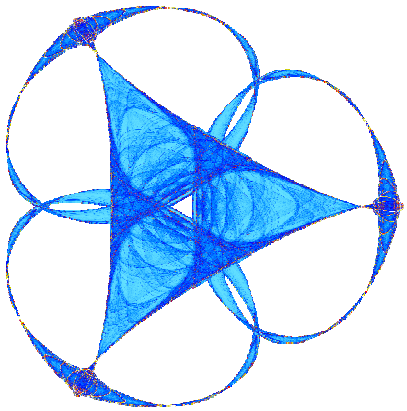

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Interactive Treatment Planning in Cancer Radiotherapy

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1 Introduction

Intensity modulated radiation therapy (IMRT) is a technique for treating patients affected by cancer. The goal is to deliver a given amount of radiation (prescribed by the physician) to the tumor while limiting the amount of radiation absorbed by the healthy organs in the proximity of the tumor. The prescribed amount of radiation is given in the form of a Dose-Volume-Histogram (DVH) specifying the percentage of volume of a given organ that can receive more than a given amount T of radiation.

The IMRT is accomplished by mean of the combination of a linear accelerator (LINAC) and a device called multi-leaf collimator (MLC). The radiation is modulated using a dynamic metallic filter that (blocking different parts of the beam) allows within a certain margin of error to localize the radiation on the region of interest.

The filter is modeled as a 2-dimensional grid whose elements are called *bixels*. Each bixel is associated with a certain value of the intensity passing through it. In the following we will denote the values of the intensity by the vector $x \in \mathbb{R}^n$ where n is the number of bixels.

In order to define the percentage of the volume receiving a certain amount of radiation it is convenient to discretized the region containing the target structure (the cancerous tumor) and the nearby healthy organs that may receive part of the radiation. This volume is divided into small cubes called *voxels* (see figure (1)).

If we let d_i be the radiation dose received by the i-th voxel, then the distribution of the dose absorbed by the treated region is described by a vector $d \in \mathbb{R}^m$ where m is the number of voxels.

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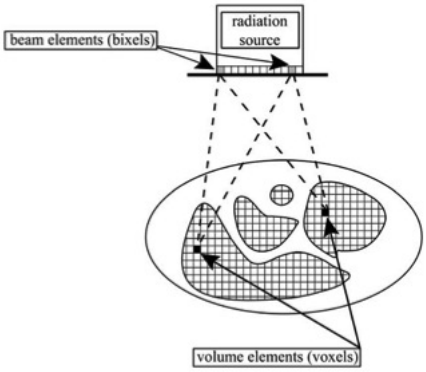

Figure 1: Representation of the multi-leaf collimator and the discretization of the target volume.

The standard model to describe the relation between the intensity of the radiation, x, and the dose received by the region of interest is given by,

$$\begin{cases} d = Dx, \\ x \geq 0, \end{cases} \tag{1}$$

where D is a given $m \times n$ matrix with positive real entries D_{ij}. In particular, D_{ij} represents the amount of dose absorbed by the i-th voxel per unit intensity emitted from the j-th bixel.

There are two main problems in solving the system (1). The first one deals with the fact that, since in general $m \gg n$, the system in eq. (1)is over determined. The second one is related with the information we have on the vector d. In order to describe the kind of information that is given about d is conveninet to assume a probabilistic point of view of the DVH.

If with $H_D(x)$ we indicate the histogram based on the values of the entries of d and with $C_D(x)$ the cumulative histogram corresponding to H_D, then the DVH curve is given by

$$DVH(x) = 1 - C_D(x). \tag{2}$$

Examples of DVH curves for healthy organs as well as the cancerous tumor (also called PTV: Planning Target Volume) are given in figure (2).

It is clearly seen from this probabilistic definition that a DVH curve associated with a distribution d is invariant under any permutation of the components of d. The treatment plans are determined using a collection of DVH curves associated with the organs constituting the region of interest (eg. spinal cord, lung, bladder). For simplicity, we will only consider regions comprising of two organs: one corresponding to the cancerous tumor and one associated with a healthy tissue. Our goal is to find the intensity x whose associated dose distribution d replicates the prescribed DVH curves. In the next section, we will introduce the so called "Moments based approach".

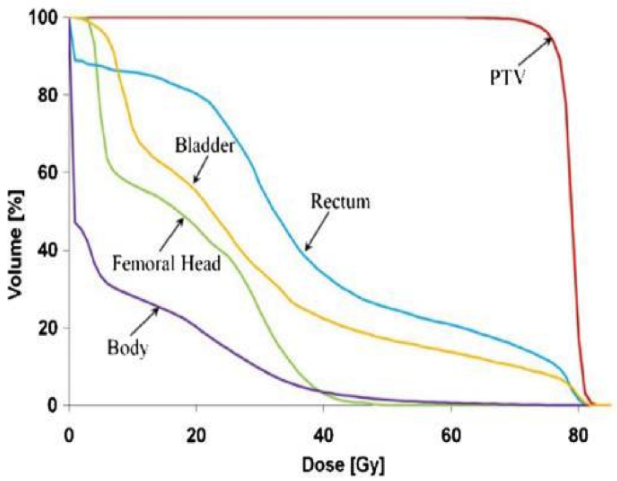

Figure 2: DVH curve for different organs and tumor (PVT)

2 Moment-based approach

The moment approach is based on the fact that there is a one to one correspondence between a given distribution function and the infinite set of moments of such distribution. Given this fact, we restrict the search space over all possible treatment plans to the ones corresponding to only the prescribed moments. In this manner, we are able to reproduce the desired DVH curves or alternatively certify that such plan does not exist.

In order to distinguish between the moments associated with the tumor (T) and critical structure (C), we define

$$D = \begin{bmatrix} D^T \\ D^C \end{bmatrix} \qquad \text{and} \qquad d = \begin{bmatrix} d^T \\ d^C \end{bmatrix} \tag{3}$$

and let

$$M_k(d^T) = \frac{1}{V}\sum_i (d_i^T)^k \tag{4}$$

$$M_k(d^C) = \frac{1}{V}\sum_i (d_i^C)^k \tag{5}$$

(where d_i^T represents the i-th component of the vector d^T) be the k-th moment of the dose distribution referring to the target and the critical structure respectively.

Our goal is to find a "least square" feasible solution with respect to the following constraints

$$\begin{cases} d = Dx, & x \geq 0 \\ M_k(d^C) = M_k^C(\overline{d^C}), & k = 1, ..., \infty \\ M_k(d^T) = M_k^T(\overline{d^T}), & k = 1, ..., \infty \end{cases} \tag{6}$$

where the vector $\bar{d}$ is constructed according to the given DVH curves and partitioned into $\overline{d^C}$ and $\overline{d^T}$ corresponding to critical organ and tumor respectively.

(6) deserves further comments:

1. Letting k ranges from 1 to ∞ in (6) implies that we need to impose infinitely many constraints. In practice, we limit the range of k only to finitely many values. This approximation is closely related to the well-known "moment problem" concept in statistics. It relies on the fact that a probability distribution can often be described accurately using only a finite number of its moments.

2. The moments defined in (6) are, for positive k, convex functions of their argument. This means that, even though the set of points specified by the equality constraints is not convex, relaxing the equalities to a set of inequalities will allow us to have a convex feasible region.

Based on the above comments, (6) can be relaxed in various ways. We found it most straightforward to consider the following form:

$$\begin{cases} d = Dx, & x \geq 0 \\ M_k(d^C) \leq \overline{M_k^C}, & k \in \mathbb{K} \\ lb \leq d^T \leq ub, \end{cases} \tag{7}$$

where $\mathbb{K}$ is a finite set of integers representing the set of moments used to approximate the DVH curve. The bounds lb and ub are used in order to prevent underdosing and overdosing the tumor area respectively.

We found it most useful and effective to incorporate the prescribed dose P for the tumor in the relaxed form of (6). This value is usually provided by the physician in addition to the DVH curve for the tumor and is used to further quantify the quality of the obtained DVH for the tumor. A feasibility approach based on the use of P value is as follows:

$$\begin{cases} M_k(D^C x) \leq M_k(\overline{d^C}), & k = 1, 2, \ldots, K \\ M_j(D^T x - P^T) \leq M_j(\overline{d^T} - P^T), & j = 2, 4, 6, \ldots, 2K \\ M_1(D^T x) = M_1(\overline{d^T}), \\ x \geq 0, \end{cases} \tag{8}$$

where K is a finite integer. Numerical results associated with this approach will be presented in section...

By Comparing (8) with the non-relaxed problem (6) we note that:

- We directly included the constraint $Dx = d$ in the formulation of the constraints for the moments.

- Since an equality constraint is convex, it does not present additional difficulties from the computational point of view. Therefore, we maintain the equality constraint on the first moment for the tumor.

- The equality constraints on the moments associated with the tumor are relaxed using the prescribed dose P. Note that in this case we used only even moments. This aims to minimize the distance (measured using the

moment norm) between d^T and P^T. In addition, since the discrepancy between $D^T x$ and P^T might result in negative values, using even moments ensures the convexity of the problem.

As a final remark of this section it is important to mention that the constraint moment approach outlined above can be made more flexible if instead of the moment of the distribution we consider to impose constraints on the generalized moment of it (see the analogous "generalized moment problem" in statistic). The simplest way of doing so at this point of the exposition is to allow the index k in (6) to assume all the possible values of the real line.

3 Beyond feasibility: Two-Phase Approach Algorithm

Despite its practical importance, the feasibility problem (8) admits several limitations. First, it does not consider an unachievable DVH, i.e., it assumes that associated with the given DVH curve, there exists an x satisfying $Dx = \bar{d}$ where $\bar{d}$ is constructed based on the given DVH. Second, it does not deliver the best possible solution for the achievable DVH. Third, it is prohibitively time-consuming when the size of the problem becomes large. In this section, we propose a novel approach in order to overcome the limitations concerned with the feasibility problem (8). Our aim is to present an algorithm that can be used as a black box by the physician in order to provide an optimal treatment plan for the patient. The only input to this algorithm is the DVH curve provided by the physician. We stress that our new algorithm is capable of handling both achievable and unachievable DVH curves as specified below:

1. In the case that the given DVH is unachievable, the algorithm provides the nearest plan (in the sense we are going to describe below) consistent with such DVH. This part of the algorithm is referred to as the Phase I.

2. In the case that the given DVH is achievable, the algorithm provides, among all feasible solutions, the one delivering the smallest amount of dose to the healthy organ. This part of the algorithm is referred to as the Phase II.

The main idea in implementing phases I and II is to change, in an adaptive way, the bounds on the higher moments described by (8).

3.1 Phase I

Suppose that the given DVH is unachievable. In this case, problem (6) does not admit any feasible solution, and its relaxed version (8) may or may not admit a feasible solution. In the latter case, the question that arises is that how to provide a treatment plan that is somehow close to the given DVH?

Consider the following optimization problem:

$$\begin{cases} \min_{\alpha,\beta} \sum_k \beta_k + \sum_j \alpha_j \\ M_k(D^C x) \leq M_k(\overline{d^C}) + \beta_k, & k = 1, 2, \ldots, K \\ M_j(D^T x - P^T) \leq M_j(\overline{d^T} - P^T) + \alpha_j, & j = 2, 4, 6, \ldots, 2K \\ M_1(D^T x) = M_1(\overline{d^T}), \\ x,\ \beta_k,\ \alpha_j \geq 0. \end{cases} \tag{9}$$

In this formulation, we loosen the bounds on both the moments and on the discrepancy between Dx and P by introducing the variables α and β respectively (compare with (8)). At the same time, we enforce these variables to be as small as possible by integrating them in the objective function. This formulation ensures that the optimal solution's moments are as close as possible to the prescribed moments.

3.2 Phase II

Suppose that, given the DVH curves, problem (8) admits one or more feasible solution (we remind that this may happen when problem (6) does not admit a feasible solution). In this case the natural question to address is how can we select, among the set of feasible solutions, the solution which is characterized by the smallest dose of radiation irradiated to the organs?

The idea is that feasible (in the sense of (8)) solutions characterized by a smaller dose to the healthy organs can be characterized by smaller values of $M_k(D^C x)$. This motivates the following formulation:

$$\begin{cases} \max_{\alpha,\beta} \sum_k \beta_k + \sum_j \alpha_j \\ M_k(D^C x) \leq M_k(\overline{d^C}) - \beta_k, & k = 1, 2, \ldots, K \\ M_j(D^T x - P^T) \leq M_j(\overline{d^T} - P^T) - \alpha_j, & j = 2, 4, 6, \ldots, 2K \\ M_1(D^T x) = M_1(\overline{d^T}), \\ x,\ \beta_k,\ \alpha_j \geq 0. \end{cases} \tag{10}$$

Nonnegative variables α and β are introduced in order to tighten the bounds on the moments' inequalities. Maximizing the objective function enforces these variables to become as small as possible.

3.3 Two-Phase Algorithm

In this section we will describe how, combining Phase I and II, we can devise a strategy for finding an optimal plan for cancer therapy. The strategy is illustrated by the following flow chart:

Given a DVH that can be either achievable or unachievable, we first runt phase I as described in section (3.1). If the objective function $\sum_k \beta_k + \sum_j \alpha_j$ reaches zero, we have found a solution that is feasible according to problem (8). [1] Thus, we run into the Phase II of the algorithm in order to find the intensity vector with the lowest amount of radiation to the healthy organs.

[1] In practical implementation the value of the function, even in the feasible case, does not

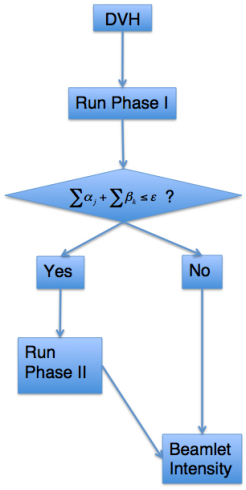

Figure 3: Two-phase approach algorithm

4 Numerical results

In this section, we illustrate the performance and reliability of our proposed approach on a prostate cancer patient. We use different number of moments and consider both achievable and unachievable DVH curves to justify the strategies and heuristics we have adopted in our implementation.

We implemented our two-phase algorithm in the well-known problem solving environment Matlab using the constrained minimization routine `fmincon`. We provided the gradient information to the fmincon, for both the constraints and objective function, which resulted in a significant improvement in the performance of the algorithm.

4.1 Using Achievable DVH

Figure (4) shows the results of our algorithm when using two ($k = 1, 2$ and $j = 2, 4$) and three moments ($k = 1, 2, 3$ and $j = 2, 4, 6$) respectively with achievable DVH curves. As can be seen in the figure, the result obtained using phase II is characterized by a minor dose delivered to healthy organs compared to what is obtained using phase I of the algorithm. In particular, the DVH curve for the femoral head ("green curve") is shifted considerably to the left. For the other organs (rectum, skin, bladder) we didn't achieve a comparable improvement. This is reasonable if we think that these organs are closely located to the prostate than the femoral head; therefore, it is more complicated to avoid these organs during the treatment.

4.2 Using Unachievable DVH

In this section, we report our results concerned with unachievable DVHs. In particular, we tested the robustness of our algorithm on three different unachiv-

reach zero. For this purpose we introduce a threshold ϵ to discriminate whether we have feasibility or not.

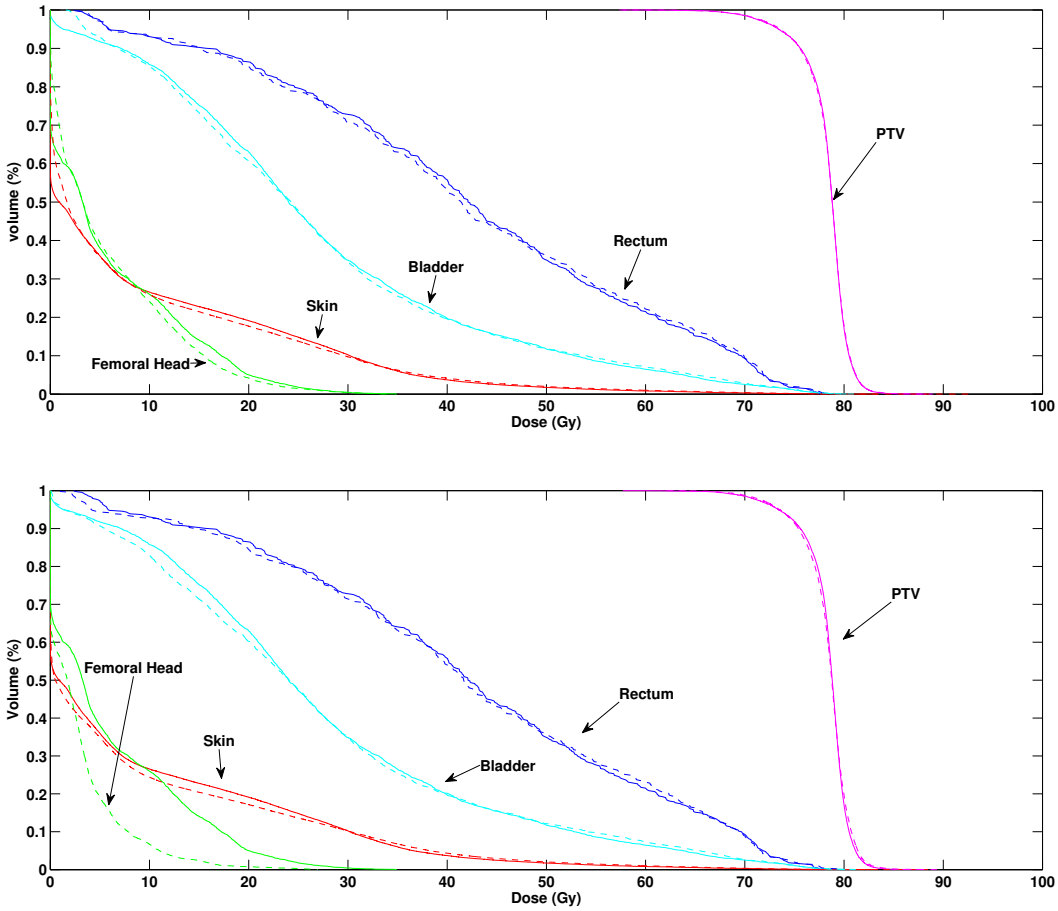

Figure 4: Results relative to Phase I (upper) and Phase II (lower) when using 2 moments. The solid and broken lines represent the given and computed DVH curves respectively.

able DVH curves (referring respectively to figures (6), (7) and (8)) obtained in the following way:

1. We started from the achievable DVH shown with the solid line in figure (4).

2. We obtained the DVH (solid lines) in figure (6) by shifting to the left only the DVH curve associated with the PVT until obtaining an unachievable DVH. The computed DVH is represented with broken lines.

3. We started from the DVH curves described in point 2 and obtained a new DVH (solid line in figure (7)) by shifting the DVH curve associated with the skin to the left (in red).

4. We started from the DVH curves described in point 3 and obtained a new DVH (solid line in figure (8)) by shifting the DVH curve corresponding to

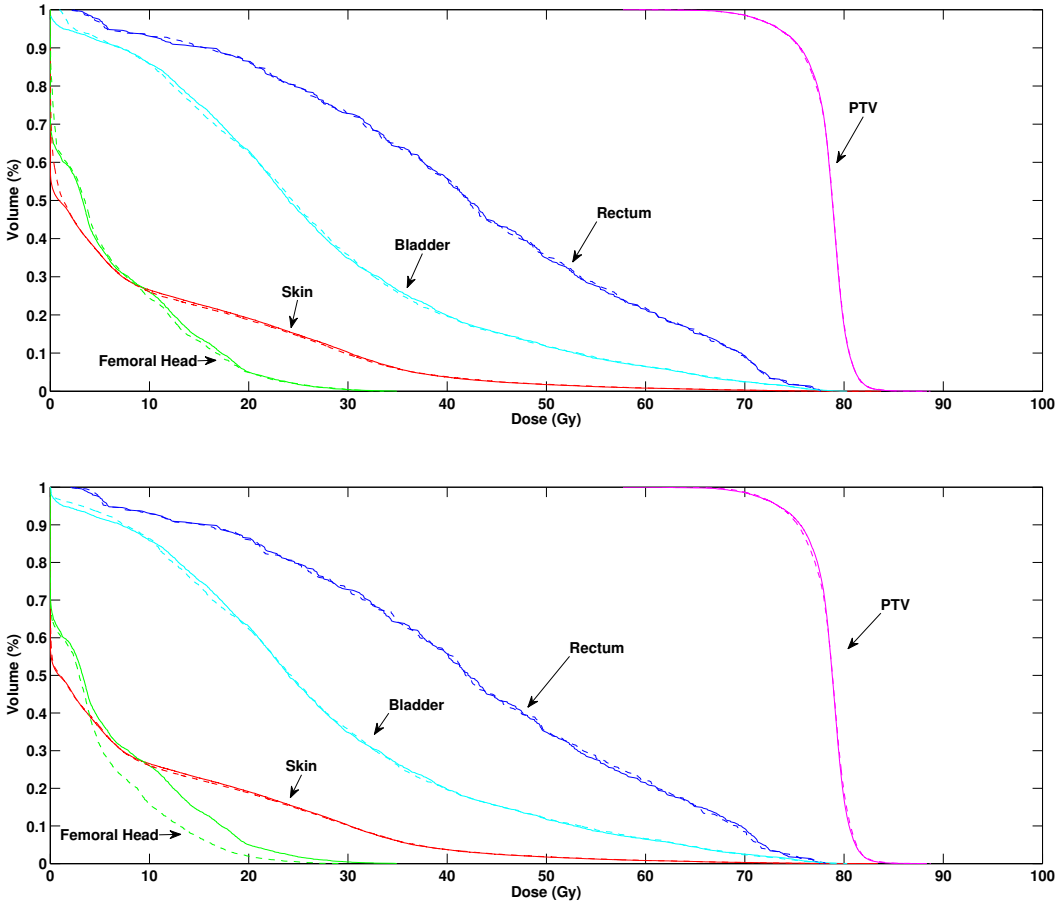

Figure 5: Results relative to Phase I (upper) and Phase II (lower) when using 3 moments. The solid and broken lines represent the given and computed DVH curves respectively.

the rectum to the left.

As we can see from figure (6), (7) and (8) the algorithm is still performing well with unachievable DVH. In particular the numerical solution that we obtained is not far from the given DVH, reflecting the fact that among the feasible solutions Phase I finds the solution that best approximate the DVH. Because we are using 3 moments, finding the best solution in this case means to find the solution whose mean, variance and skewness (the 3^{rd} moment) are closest to the given DVH curves.

5 Conclusion

We presented a new algorithm for the treatment planning of cancer radiotherapy. The algorithm is based on the so called moments approach in which a given

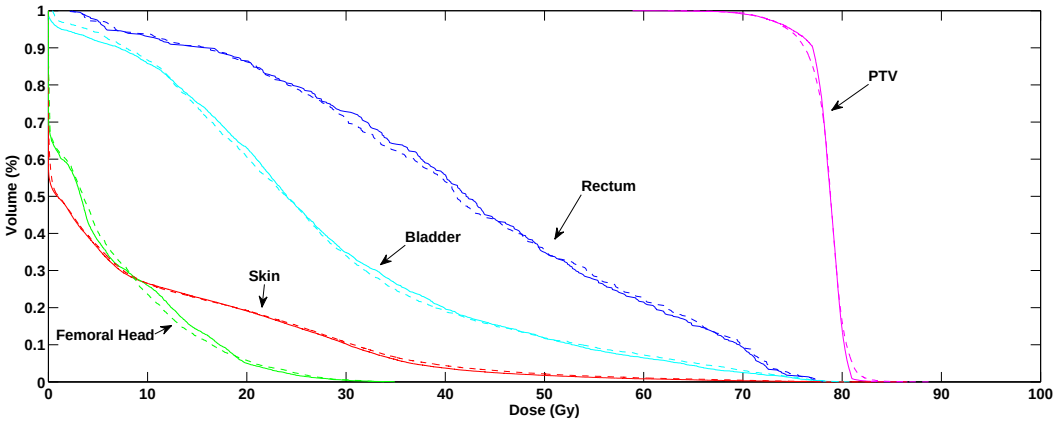

Figure 6: DVH curves obtained by shifting to the left only the DVH relative to the PVT

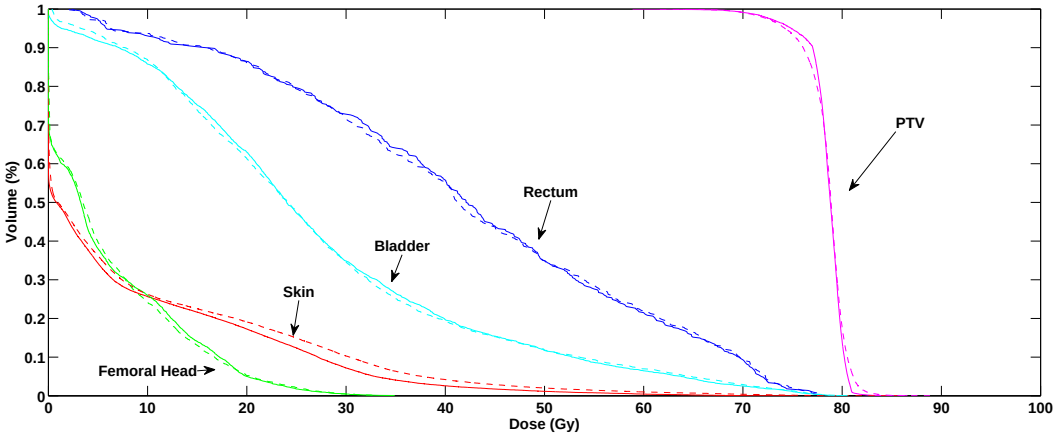

Figure 7: DVH curves obtained by shifting to the left only the DVH relative to the PVT and the skin

DVH is approximated with a set of constraints on the moments of the dose distribution. Because of the convex nature of our optimization problem, when compared to the traditional constrained voxel based approach, our two-phase algorithm presents several advantages. It is computationally more efficient than the usual mixed integer programming techniques and does not require external tuning of the weights characterizing multi-objective optimization kind of algorithms. As demonstrated by our numerical results our approach is promising to be used as a black box tool by the physician.

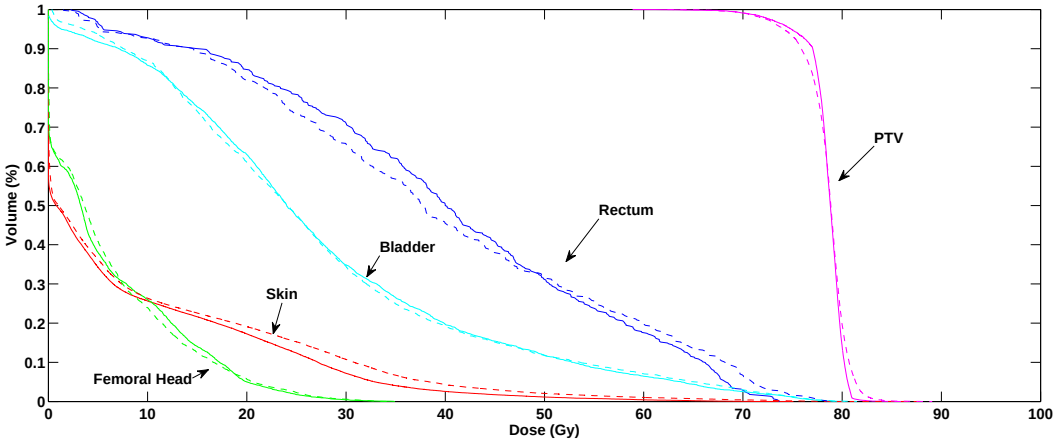

Figure 8: DVH curves obtained by shifting to the left only the DVH relative to the PVT the skin and the rectum