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RADIOTHERAPY TREATMENT PLANNING WITH DOSE VOLUME CONSTRAINTS BY LINEAR PROGRAMMING APPROACH

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ABSTRACT: Optimization has become an imperative tool in treatment scheduling for cancer radiation therapy. It may be used to determine beam weights, beam directions, and appropriate use of beam modifiers such as wedges and blocks, with the aim of delivering a required dose to the tumor while sparing critical structures and normal tissue in close proximity. Linear programming formulations are a core computation in many approaches to treatment planning, because of the abundance of highly developed linear programming software. Furthermore the choice of formulation, algorithm, and pivot rule that perform paramount computations are sometimes not obvious, and the software's default choices are sometimes pitiable. Here a number of linear programming formulations of treatment planning problem with dose volume constraints, conclusions are drawn about the formulations and variants.

KEYWORDS: Linear Programming, Simplex Method, Radiation Therapy.

1. INTRODUCTION:

Radiation therapy is a widely used technique for treatment many types of cancer. It works by depositing radiation into the body of the patient, so that prescribed amounts of radiation are delivered to the cancerous regions (tumors), while nearby non-cancerous tissues are spared to the extent possible. Radiation interferes with DNA of cells, impeding their ability to reproduce. It tends to affect fast-multiplying cells (such as found in tumors) preferentially, making them more likely to be eliminated.

In this paper we consider external beam radiotherapy, in which the radiation is delivered via beams fired into the patient's body from an external source. The linear accelerator that produces the beams is located in a gantry which can be moved around the patient, allowing the beams to be delivered from a number of different angles. Additionally, a collimator can be placed in front of the beam to change its shape, and wedges can be used to vary the intensity of the beam across the filed. In the "Step-and-Shoot" mode of treatment, the beam is aimed from a number of different angles (typically between 4 and 20), a wedge orientation and collimator shape is chosen for each angle, and the radiation beam is exposed for a certain amount of time (known as the beam weight). Two major variants of this approach includes conformal therapy in which the shape of the collimator at each angle is chosen to match the shape of the tumor as viewed from that angle, and intensity-modulated radiation therapy (IMRT) in which the beam field is divided for planning purposes into a rectangular array of "beamlets", which are then assigned individual weights.

For purposes of modeling and planning, that part of the patient's body to which radiation is applied is divided using a regular grid with orthogonal principal axes. The space is therefore partitioned into small rectangular volumes called "voxels". The treatment planning process starts by calculating the amount of radiation deposited by a unit weight from each beam into each voxel. These doses are assembled into a dose matrix. (Each entry A_{ij} in this matrix is the dose delivered to voxel *i* by a unit weight of beam *j*). Once the dose matrix is known, inverse treatment planning is applied to find a plan that optimizes a specified treatment objective while meeting certain constraints. The treatment plan consists of a specification of weights for all beams.

Linear programming is at the core of many approaches to treatment planning. It is a natural way to model the problem, because the amount of radiation deposited by a particular beam in each voxel of the treatment space is directly proportional to the beam weight, and because the restrictions placed on doses to different parts of the treatment space often take the form of bounds on the doses to the voxels.

We report in this paper on a computational study of linear programming formulations of the treatment planning problem, for data sets arising from both conformal radiotherapy and

IMRT. We aim to give some insight into the performance of the solvers on these various formulations, and as to which types of constraints cause significant increases in the runtime. We also give some general recommendations as to the best algorithms, pivot rules, and reduction techniques for each formulation.

The remainder of the paper is described as follows. Section 2 contains a linear programming model of treatment panning problem with dose volume constraints that we tested. The data sets used in the model are described in section 3; they include both data that is of conformal therapy and data that arises in IMRT planning. We interpret and discuss the computational results in section 4. Section 5 contains main conclusions.

2. A MODEL WITH DV (DOSE VOLUME) CONSTRAINTS

We now consider a linear programming formulation that arises when DV constrains are present. As mentioned earlier, such constraints typically have the form that "no more than a fraction *f* of the voxels in a critical region receives a dose higher than a specified threshold δ". This type of constraint was apparently first suggested by Langer and Leong in [2]. An exact formulation can be obtained by means of binary variables as follows. First we denote the critical region by C (with n_c voxels) and dose matrix for this region by A_c. Introducing the binary vector χ_c (with n_c components, each of which must be either 0 or 1), we formulate the constraint as

$$x_c = A_c w, \tag{2a}$$

$$x_c \le \delta e_c + M\chi_c, \tag{2b}$$

$$e_c^T \chi_c \le f n_c, \tag{2c}$$

$$\chi_c \in \{0,1\}^{n_c}, \tag{2d}$$

Where x_c the dose vector for the critical region, M is a large constant and e_c is the vector of all 1's and dimension n_c. The components for which χ_i =1 are those that are allowed to exceed the threshold. A typical linear programming problem arising in the course of the heuristic just described (and possibly others) is as follows:

$$\min_{w, x_T, x_N, x_C, x_\varepsilon} \quad C_N^T x_N + c_\varepsilon^T x_\varepsilon \tag{2.1a}$$

Subject to
$$x_T = A_T w, \tag{2.1b}$$
$$x_N = A_N w, \tag{2.1c}$$
$$x_C = A_C w, \tag{2.1d}$$
$$x_T^L \le x_T \le x_T^U, \tag{2.1e}$$
$$x_\varepsilon \ge x_C - b, \tag{2.1f}$$
$$w, x_\varepsilon \ge 0. \tag{2.1g}$$

Where b is a vector of thresholds for voxels in C (different thresholds may apply for different voxels in C), x_ε represents the dose to the critical voxels in excess of the doses specified in b. The cost vectors C_ε and C_N are the penalties applied to excess doses in the C voxels and to any non-negative dose in the N voxels. The threshold vector b and weight vector c_ε are the quantities that are manipulated between iterations of the heuristic in an attempt to satisfy the given DV constraints.

The vectors x_N and x_ε can be eliminated from (2.1) to obtain:

$$\min_{w, x_T, x_\varepsilon} \quad C_N^T A_N w + c_\varepsilon^T x_\varepsilon \tag{2.2a}$$

Subject to
$$x_T = A_T w, \tag{2.2b}$$
$$x_T^L \le x_T \le x_T^U, \tag{2.2c}$$
$$x_\varepsilon \ge A_C w - b, \tag{2.2d}$$
$$w, x_\varepsilon \ge o. \tag{2.2e}$$

Which we refer to as the reduced primal form.The dual of (2.2) can be written as follows: The standard primal form is

$$\min \quad C_N^T A_N w + c_\varepsilon^T x_\varepsilon \quad = \quad \max \quad -C_N^T A_N w - c_\varepsilon^T x_\varepsilon$$

Subject to
$$-A_T w \le -x_T^L,$$
$$A_T w \le x_T^U,$$
$$A_C w - x_\varepsilon \le b,$$

$$w, x_\varepsilon \geq 0.$$

Let the dual variables be μ_L , μ_U and μ_E

The dual of the above problem is

$$\min \quad -(x_T^L)^T \mu_L + (x_T^U)^T \mu_U + b^T \mu_E \quad = \quad \max \quad ((x_T^L)^T \mu_L - (x_T^U)^T \mu_U - b^T \mu_E \qquad (2.3a)$$

Subject to $\quad -A_T^T \mu_L + A_T^T \mu_U + A_C^T \mu_C \geq -A_N^T C_N$

$$-\mu_E \geq -c_E$$

$$\Rightarrow \quad A_T^T (\mu_U - \mu_L) + A_C^T \mu_C + A_N^T C_N \geq 0$$

$$-\mu_E + c_\varepsilon \geq 0$$

$$\Rightarrow \quad \mu_U - \mu_L \geq 0$$

$$\mu_C \geq 0$$

$$C_N \geq 0$$

$$\mu_E \leq 0, c_\varepsilon \geq 0$$

Introducing surplus variables $\mu_L, \mu_U, \mu_N, \mu_T, \mu_C, \mu_E,$

$$-\mu_U + \mu_L + \mu_T = 0 \qquad (2.3b)$$

$$\mu_N = C_N \qquad (2.3c)$$

$$\mu_C - \mu_E = 0 \qquad (2.3d)$$

$$\mu_E \leq C_E \qquad (2.3e)$$

$$-A_T^T \mu_T - A_C^T \mu_C - A_N^T \mu_N \geq 0 \qquad (2.3f)$$

$$\mu_L, \mu_U, \mu_E \geq 0. \qquad (2.3g)$$

By eliminating μ_C , μ_N , μ_T we obtain

$$\max \quad x_T^L \mu_L - x_T^U \mu_U - b^T \mu_E \qquad (2.4a)$$

Subject to $\quad 0 \leq \mu_E \leq c_\varepsilon,$ (2.4b)

$$A_T^T (\mu_L - \mu_U) - A_C^T \mu_E \leq A_N^T C_N, \qquad (2.4c)$$

$$\mu_L \ , \ \mu_U \ \geq o \qquad (2.4d)$$

Which we refer to as the reduced dual form. difference in runtime for the best choices of algorithm and pivot rule.

3.1 Data Sets. In this section we briefly describe the data sets used with the models of Section 2. For both conformal therapy data (with relatively few beams), and the IMRT case (which has many beams and a sparser dose matrix) we used only a real data set.

Conformal Therapy (Pancreatic Data Set): Our first data set was from a patient with pancreatic cancer (the same set used in Lim et al. [4]), which contained several critical structures (liver, spinal cord, and left and right kidney). Distribution of voxels between the target, critical regions, and normal regions is shown in Tab1.

Table-1

Pancreatic Data Set: Voxels per region

Region- Tissue	# of voxels
Target	1244
Normal	747667
Critical-Spinal Cord	514
Critical-liver	53244
Critical-Left Kidney	9406
Critical-Right kidney	6158
Total	818181

We used 36 beams in the model, where each beam is aimed from a different angle around the patient (angles separated by 10^0). The beam from each angle is shaped to match the profile of the tumor, as viewed from that angle. The full dose matrix has only 36 columns (one for each beam) but more than 800000 rows (one for each voxel). We set the entry in the dose matrix to zero if its dose was less than 10^{-5} of the maximum dose in the matrix. The dose matrix has many zeros but is still quite dense, since each of the 36 beams delivers dose to a large fraction of the voxels in the treatment region.

Table-2

IMRT Data Set: Voxels per Region

Region- Subclass	# of voxels
Target-Target	884
Target-Regional	4246
Critical-Spinal Cord	406
Critical-Parotids	692
Normal	17772
Total	24000

IMRT Data Set (Nasopharyngeal): In intensity modulated radiation therapy (IMRT), each beam is split into pencil beams or beamlets, usually by dividing its rectangular aperture by a rectangular mesh. A typical data set has 25-200 beamlets from each of 7-72 possible angles, where each beamlet has its own dose distribution. The solution of the model we describe in Section 2 yield a weight for each beamlet. Our data set for IMRT is a case of a Nasopharyngeal tumor, also used by Wu[5]. There are 51 beam angles, with 39 beamlets from each angle, giving a total of 1989 beamlets (that is, 1989 columns in the dose matrix). The 24000 voxels are divided into five regions, as shown in Table2. The target region is subdivided into a "target" region containing the actual tumor and a "regional" part, corresponding to voxels near the tumor that we wish to control in the same way as tumor voxels (by specifying target values on their doses, for instance). The critical region is subdivided into the spinal cord and the parotids. In summary, the dose matrix A has 24000 rows and 1989 columns.

4. COMPUTATIONAL RESULTS: We now give details of the computational results with the formulations of Section 2 on the data sets of Section 3. Our analysis of these results indicates that the most obvious formulations and the default algorithmic parameter selections often do not yield the best execution times. For this model we discuss separately the results for conformal radiotherapy and IMRT. In this formulation, we set the normal voxel penalty vector c_N to $e = (1, 1, \ldots, 1)^T$. For the pancreatic data set, we used x_T^L = 0.95e and x_T^U = 1.07e as bounds on the target voxel dose, and x_T^L = 50e and x_T^U = 75e for the IMRT data set.

4.1. Model Results: The parameter specific to model is the upper bound vector x_N^U on the normal voxel dose. To choose an appropriate value for this bound, we first solved the problem without these bounds. For the pancreatic data set, the highest doses to a voxel in each critical region (measured in relative units) were: .461 (spinal cord), .915 (liver), .111 (left kidney) and .612 (right kidney) (see Table 2 for a summary of the voxel distribution for this data set). For the IMRT data set, we set the bounds as follows: 75 Gy (target and normal tissue), 50 Gy (parotids), and 10 Gy (spinal cord).

Table-3

Problem Sizes and Effects of Preprocessing.

Data	Formulation	Before presolve		After presolve		Average presolve time (Sec)
		Rows	Columns	Rows	Columns	
Conf.	Full Primal	801815	801851	222690	222726	13.4
Conf.	Full Dual	801851	1025785	222726	446660	13.8
Conf.	Red.Primal	239058	1281	72496	1280	1.9
Conf.	Red Dual	37	819426	36	73740	4.1
IMRT	Full Primal	23999	25604	16260	17435	3.2
IMRT	Full Dual	25174	48820	17435	37651	3.8
IMRT	Red.Primal	16263	6736	16224	6305	2.7
IMRT	Red Dual	1606	29131	1175	21354	4.0

5. CONCLUSION:

We have performed a computational study of the linear programming approach to the radiation treatment planning problem with dose volume constraints. Our conclusions are that the choice of formulation, algorithm, and pivot rule can be crucial to the efficiency of the solution procedure, and that the default choices are sometimes not acceptable.

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