Optimization Under Uncertainty: Methods and Applications in Radiation Therapy

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Abstract

This research focuses on the methods and application of optimization under uncertainty to radiation therapy planning, where it is natural and useful to model the uncertainty of the problem directly. In particular, we present methods for optimization under uncertainty in radiation therapy of tumors and compare their results. Two themes are developed in this study: (1) the modeling of inherent uncertainty of the problems and (2) the application of uncertainty optimization.

1. Introduction

The use of particle beams to treat tumors is called the **radiation therapy problem** (RTP). Beams of particles, usually photons or electrons, are oriented at various angles and with varying intensities to deposit dose (energy/unit mass) to the tumor. The idea is to deposit as much dose as possible to the tumor while sparing normal tissue.

The process begins with the patient's computed tomography (CT) scan. Each image in the CT is examined to identify and contour the tumor and normal structures. The image is subsequently vectorized. Likewise candidate beams are discretized into **beamlets** where each beamlet is the width of a CT voxel. A voxel is the mathematical entity or structure (a cube) that is used to represent a unit volume of the body at a particular location. The identification of a set of beam angles and weights that provide a lethal dose to the tumor cells while sparing healthy tissue with a resulting dose distribution acceptable and approved by the attendant oncologist is called a **treatment plan**. A **dose transfer matrix** A (representing how one unit of radiation intensity in each beamlet is deposited in voxels), specific to the patient's geometry, is formed where columns of A corresponds to the beamlets and rows represent voxels. A component of column of the matrix A is non-zero if the corresponding beamlet intersects a voxel in which case it is the positive fraction of the volume of the intersection of the voxel with the beamlet (otherwise it is zero). Pre-multiplying matrix A by a characteristic vector, denoted α_i, extracts the structure of interest as the i^{th} constraint or as the objective function, $\alpha_i^T Ax$, where x represents the intensity vector of whose components are the intensities of the beamlets.

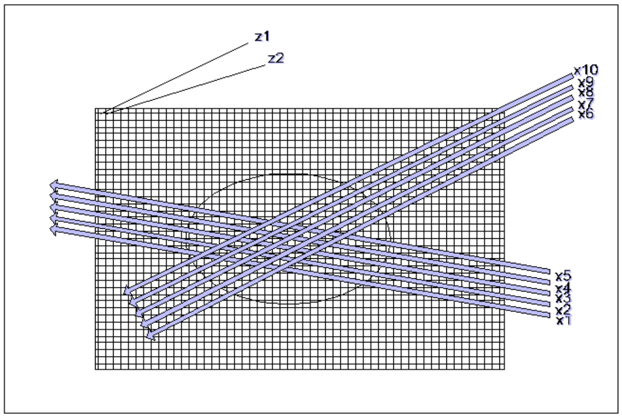
There are a variety of ways of treating this problem without uncertainty. Some voxels may be constrained separately, or groups of other voxels may be aggregated into one constraint. Under idealized assumptions (see [1], [3]) the problem without uncertainty takes the following form.

$$\min\ c^T x \qquad (1)$$

subject to:

$$Bx \le b, \quad 0 \le x \le \overline{x}, \qquad (2)$$

where B and b are defined by rewriting, in the form of (1), $T_{\min} \le \alpha_t^T Ax \le T_{\max}$ for each tumor voxel t and $\alpha_c^T Ax \le d_c$ for each group of other tissue with sharp bounds for critical organs; for example, the optic nerve, spinal cord, and liver. In the RTP literature there is no agreement on what the objective function should be. For example, one finds the following objective functions: minimize total radiation, maximize minimum tumor dosage, minimize radiation to critical structure(s), minimize the probability of healthy tissue complication, maximize the probability of delivering a tumoricidal dose, minimize maximum critical structure dose, etc. Typically, oncologists consider the RTP as one of attaining goals (or coming as close as possible to them). We return to this issue subsequently.



A typical CT scan with pencils

Mathematically, the RTP is a type of inverse computed tomography (CT) problem (see; for example, [1], [2], [3], and [6]). In this study, we use the discrete version of the inverse computed tomography problem since the method developed here is a way to identify a set of beam angles and beam weights that satisfy the constraints and goals (the oncologist).

This paper is organized in the following way. In section 2 we develop a mathematical model for the RTP that directly incorporates the fuzziness and uncertainty in the problem. Section 3 contains the explicit uncertainty optimization model formulation. The models developed in section 3 are applied to the RTP in section 4**.** Conclusions follow in section 5.

2. The Modeling of Uncertainty in the RTP

One may distinguish four sources of uncertainty and fuzziness in the RTP: (a) delineation of tumors and critical tissue, (b) radiation tolerances or critical dose levels for each tissue type or tumor, (c) the model for the delivered dose, that is the dose transfer matrix, and (d) the location of tissue at the time of radiation. Case (d) is the possible discrepancy between the identification of organs, tissues or tumor in the CT compared to where they are located in the patient at the time of radiation. Here we are primarily concerned with uncertainties of type (b); it is planned to extend the techniques to other cases.

The RTP in practice proceeds as follows. After the oncologist delineates the tumor and critical structures, a candidate set of beam intensities are obtained; for example by linear programming, fuzzy linear programming, simulated annealing, or purely human choice. These beam intensities are used as inputs to a FDA (Federal Drug Administration) approved dose calculator computer program to produce the graphical depiction of the dose deposition of each voxel (as color scales and dose-volume histograms, DVH's – see Figure 1). The objective function, in general, is never consulted; just the final distribution of dosage (as affected by the objective) is viewed. If the dose distribution is not satisfactory in the oncologist's judgment, the right-hand side is varied (by tightening or loosening tolerances consistent with the oncologist's expertise) until a set of beam weights that will give satisfactory DVH's are obtained. Thus, we will consider that all the fuzziness of the problem is in the right-hand side.

3. Optimization Under Uncertainty

Since the objective function is not precisely known and is chosen to suit the problem, we will specify it symbolically though we are thinking of it being the minimization of total dosage or minimization of radiation to critical structure or some other such objective.

We consider two categories of models of uncertainty. The first is based on fuzzy [10] and possibilistic theory [4], [5] [7] and the other on the theory of surprise [9].

a. The Fuzzy and Possibilistic Approach

The general fuzzy/possibilistic model considered here is:

$$\min \; c^T x \tag{3}$$

subject to:

$$Bx \le \tilde{b}, \;\; 0 \le x \le \bar{x}, \tag{4}$$

where now the bounds are fuzzy. The letters with the tilde denote vectors of fuzzy numbers. The fuzzy linear programming model (4) has the form considered by [10]. The fuzzy bounds are chosen to reflect expert judgment about the associated DVH's; c.f. section 4. The approach of [10] translates into the following real-valued linear program:

$$\begin{aligned} &\max \lambda \\ &\text{subject to: } \lambda p_i + \hat{B}_i \vec{x} \le \hat{b}_i + p_i \\ &\qquad\qquad \vec{x} \ge 0 \end{aligned} \tag{5}$$

From the point of view of [4], the RTP that incorporates the fuzzy right-hand side (from equation (4)) is:

$$\begin{aligned} &\tilde{F}(x) = f(x) + \tilde{d}^T \max\left\{0, Bx - \tilde{b}\right\} \\ &\textit{subject to}: \\ &0 \le x \le \bar{x}. \end{aligned} \tag{6}$$

Often, in the penalized fuzzy linear program, there may be no clear way to choose the fuzzy penalties $\tilde{d}$. The difference between (5) and (6) is that (6) considers the "interaction" among the variables. That is, the tradeoffs are more akin to stochastic programming tradeoffs since one allows violations (up to a point) at a cost that is simultaneously interacting with tradeoffs of violations of different constraints. Secondly, from a pure "morphological" point of view, the ensuing real-valued mathematical programming problem (5) is a linear programming problem while (6) is a non-linear programming problem.

For any x, the fuzzy function value, $\tilde{F}(x)$, is a fuzzy number, $\tilde{F}$, uniquely defined by its alpha-cuts (the proof can be found in [4]). The above problem is transformed into a deterministic optimization problem by optimizing the expected average of the resultant fuzzy number $\tilde{F}$. The expected average of a fuzzy number x is defined as

$$EA(\tilde{F}) = \frac{1}{2}\int_0^1 (F_\alpha^- + F_\alpha^+)d\alpha, \tag{7}$$

F_α^- and F_α^+ are the left (respectively right) endpoints of F_α. The motivation for using the expected average, its theory and associated proofs are found in [4]. There it is shown that this approach is useful since among other properties, it transforms the range space into a Banach space for most applications. This means that a convergence theory for algorithms exists and in particular, this is true for the fuzzy RTP. The penalized optimization problem is a nonlinear programming problem with simple bound constraints. The objective function is convex and smooth, $C^{(1)}$, so that, at least in principle, it can be solved using conventional nonlinear optimization packages.

b. Uncertainty Optimization Based on Surprise Functions

A goal satisfaction problem is one in which a set of goals is to be attained. When the goals are in fact uncertain (fuzzy), then the best compromise can be found by a minimization of the surprise function (see [9]) associated with the fuzzy goal total. Each fuzzy constraint

$$(Ax)_i \le \tilde{b}_i \tag{8}$$

is translated into a fuzzy equality constraint

$$(Ax)_i = \tilde{\xi}_i, \tag{9}$$

where the membership function $\mu_i(\xi)$ of $\tilde{\xi}_i$ is the possibility $Pos_i(\tilde{b}_i \ge \xi)$. Each membership function is translated into a surprise function by

$$s_i(\xi) = (\mu_i(\xi)^{-1} - 1)^2; \tag{10}$$

and the contribution of all constraints are added to give the total surprise,

$$\sum_i s_i(\xi)) = \sum_i s_i((Ax)_i). \tag{11}$$

Thus, the best compromise is the solution of

$$\begin{aligned} &\min \sum_i s_i((Ax)_i) \\ &subject\ to: \quad 0 \le x \le \bar{x}. \end{aligned} \tag{12}$$

For triangular and trapezoidal fuzzy numbers, the surprise function is simple, smooth and convex. Hence, the optimization problem is tractable with standard optimization software, even for very large problems.

4. The Application to the RTP Problem

Since the RTP has no clear generally accepted objective function, most objective functions are really (fuzzy) goals. Thus, the problem will be stated simply as a set of goals. In fact, this is in the spirit of [10]. The objective then, is to find the "best" compromise among all constraints. By "best" we mean the one that most likely leads to a viable treatment plan as defined by an oncologist. In particular, it is a plan that most closely produces a DVH that, for the tumor cells, is close to maximum dose until the value of a tumoricidal dose is reached after which it is zero (the white line below) and for critical structures and healthy tissues is a close to possible zero dose (see the black lines below). The oncologist considers plans based on the shape of these curves so that the fuzzy right-hand side values to the constraints are functions that reflect the ideal DVH.

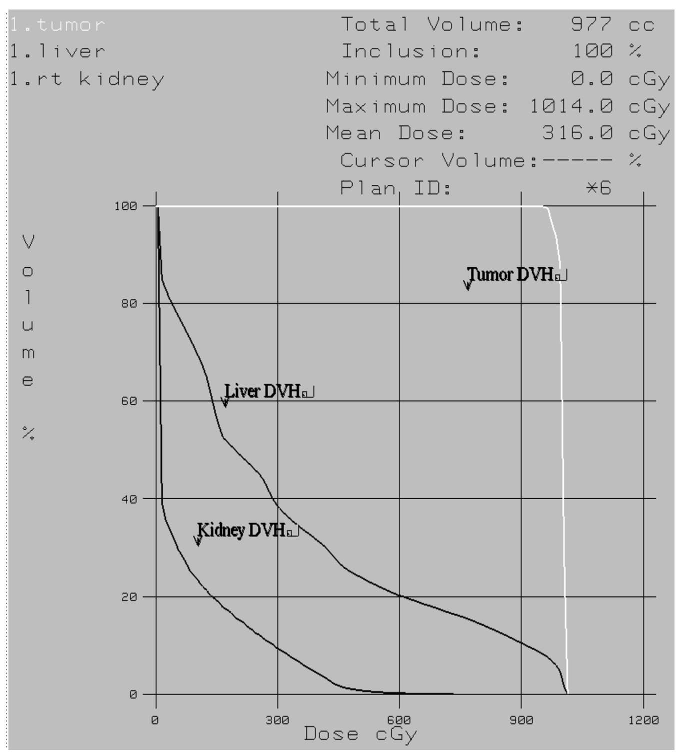


Figure 1: Dose Volume Histogram (DVH)

Thus, from the desired shapes of the DVH's we create fuzzy right-hand side constraints $\tilde{b}$. In particular, the more "square" the DVH looks, the more likely it is that it will be a treatment plan. Thus, this is reflected in the creation of the membership functions associated with the constraints.

For the fuzzy optimization problem [10], the fuzzy right-hand sides, defined by the DVH's, are fed into (3), (4). For the possibilistic optimization approach [4], the same fuzzy right-hand sides are inserted into (7). For the surprise approach [9], the fuzzy constraints are translated into nonlinear programming problem with simple bound constraints (12).

5. Conclusion

We have demonstrated how to use fuzzy optimization to solve the RTP in its most natural setting by directly accounting for and modeling its inherent uncertainties. The three approaches presented are computationally tractable since they are linear programs in fuzzy optimization (3), (4) or nonlinear convex programming with simple bound constraints in the case (6) or (12). Thus, large problems that arise from the RTP are, in principle, straight forward to solve.

6. References

[1] Y. Censor, M. Altschuler, and W. Powlis, "A computational solution of the inverse problem in radiation-therapy treatment planning," *Applied Mathematics and Computation*, 25: 57-87, 1988.

[2] A. M. Cormack, "Some early radiotherapy optimization work," *International Journal of Imaging Systems and Technology*, 6: 2-5, 1995.

[3] A. M. Cormack and E. T. Quinto, "The mathematics and physics of radiation dose planning using x-rays," *Contemporary Mathematics*, 113: 41-55, 1990.

[4] K. D. Jamison and W. A. Lodwick, "Fuzzy linear programming using a penalty function," *Fuzzy Sets and Systems*, 119:97-110, 2001.

[5] K. D. Jamison and W. A. Lodwick, "Constrcution of consistent possibility and necessity measures," *UCD/CCM Report No. 171*, Feb. 2001.

[6] B. Lind and A. Brahme, "Development of treatment techniques for radiotherapy optimization," *International Journal of Imaging Systems and Technology*, 6: 33-42, 1995.

[7] W. A. Lodwick and K. D. Jamison, "Interval methods in fuzzy optimization," *International Journal of Uncertainty, Fuzziness and Knowledge-Based Systems* 5(3): 239-249, 1997.

[8] W. A. Lodwick, S. McCourt, F. Newman and S. Humphries, "Optimization methods for radiation therapy plans," in C. Borgers and F. Natterer (editors) *IMA Volumes in Mathematics and its Applications, Computational Radiology and Imaging: Therapy and Diagnosis*, Springer-Verlag, 1998.

[9] A. Neumaier, "Fuzzy modeling in terms of surprise," (submitted).

[10] Zimmermann, H.-J, "Description and optimization of fuzzy systems," *International Journal of General Systems*, 2:209-217, 1976.