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Constraint generation methods for robust optimization in radiation therapy

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ABSTRACT

We develop a constraint generation solution method for robust optimization problems in radiation therapy in which the problems include a large number of robust constraints. Each robust constraint must hold for any realization of an uncertain parameter within a given uncertainty set. Because the problems are large scale, the robust counterpart is computationally challenging to solve. To address this challenge, we explore different strategies of adding constraints in a constraint generation solution approach. We motivate and demonstrate our approach using robust intensity-modulated radiation therapy treatment planning for breast cancer. We use clinical data to compare the computational efficiency of our constraint generation strategies with that of directly solving the robust counterpart.

1. Introduction

Robust Optimization (RO) deals with optimization problems in which some problem parameters are uncertain and modeled as belonging to an "uncertainty set" [1,2]. One of the areas in which robust optimization has been applied is radiation therapy (RT) treatment planning. In RT, the goal is to deliver radiation beams from different angles to a cancer patient so that the beams intersect at the cancerous target (i.e., a tumor), while sparing as much of the surrounding healthy tissue as possible. Robust optimization has been used to manage uncertainties in RT treatment planning problems including uncertainties in patient geometry [3], dose calculations [4], breathing motion [5–10], and range and setup errors in proton therapy [11–14].

Much effort in RO is placed on deriving tractable robust counterparts, which are finite-sized deterministic equivalents to the original RO problem. However, the resulting robust counterpart can still be quite large and computationally challenging to solve for real-world problem instances. In radiation therapy treatment planning for example, the original problem is often of a very large scale and the robust counterpart is even larger. Therefore, there is a need for specialized solution methods to solve these problems.

Decomposition methods, which have a long history [15,16], represent a wide range of methods that can be used to solve large-scale optimization problems. Constraint generation is one type of decomposition method that has been used extensively to solve large-scale optimization problems in applications such as timetable scheduling [17], network reliability [18], network design [19], facility location [20], and network interdiction [21,22]. Oskoorouchi et al. [23] developed an interior point constraint generation algorithm for semi-infinite problems that was applied to radiation therapy.

In this paper, we develop a family of constraint generation strategies to solve large-scale robust optimization problems in radiation therapy. We focus on problems with multiple sets of robust constraints, which necessitates exploring different strategies for choosing constraints to be added at each iteration. We test several strategies for finding and adding constraints efficiently. We also compare the computational efficiency of the constraint generation methods with that of directly solving the robust counterpart. Our solution approach is motivated by the robust intensity-modulated radiation therapy (IMRT) treatment planning problem for breast cancer, in which there exists a large number of robust constraints [8].

2. Breast cancer IMRT treatment planning

Previously, a robust optimization model that incorporated conditional value-at-risk (CVaR) [24,25] was developed for breast

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cancer IMRT to control the tail dose to the tumor and organs-at-risk under breathing motion uncertainty [8]. In this section, we first introduce this problem and then briefly describe the optimization model in order to motivate the development of our constraint generation strategies.

2.1. Background

In IMRT, the radiation beams can be modeled as a collection of small *beamlets* whose intensities are optimized. An optimization problem is to find the intensity of each beamlet such that sufficient dose is delivered to the tumor while minimizing the dose to the surrounding healthy tissue. Our approach to breast cancer IMRT follows the clinical protocol at the Princess Margaret Cancer Centre [26,27]. There are two opposed beams that are tangent to the body and deliver radiation to a target volume in the breast tissue. In left-sided breast cancer, parts of the left lung and the heart are usually inside the treatment field and are considered to be organs-at-risk (OAR). Since the radiation is delivered to the patient while the patient is breathing, the organs move and deform throughout the course of the treatment. In particular, the heart may move inside the treatment field and become exposed to excessive radiation. Four-dimensional computed tomography (4D-CT) images are used to obtain geometrical information about the organs over the phases of the patient's breathing cycle from inhale to exhale. The uncertain parameter in this problem is the patient's breathing pattern, which is modeled as a probability mass function (PMF) that captures the fraction of time that the patient spends in each breathing phase. We construct the uncertainty set by including upper and lower error bounds on a nominal breathing pattern[8].

2.2. A robust-CVaR optimization model for breast cancer IMRT

Here, we briefly introduce the optimization model from Chan et al. [8], which proposes the robust optimization model that we consider. Let w_b be the intensity of beamlet $b \in \mathcal{B}$, where $\mathcal{B}$ is the set of all beamlets. The body is discretized into small volumetric pixels called "voxels". Let $\mathcal{V}^T$ and $\mathcal{V}^H$ be the set of all voxels in the clinical target volume (inside the breast) and the heart, respectively. A breathing PMF is defined over the set of breathing phases $\mathcal{I}$.

The total dose to each voxel is the sum of the dose accumulated over all breathing phases and depends on the uncertain fraction of the time spent at each phase. Let $\Delta_{v,i,b}$ be the *influence matrix*, which quantifies the amount of dose that voxel v receives when the patient is in phase i per unit intensity of beamlet b. A robust upper β-CVaR constraint on the target can be formulated as:

$$\bar{\zeta}^T_\beta + \frac{1}{1-\beta}\sum_{v\in\mathcal{V}^T}\max\left\{0, \sum_{i\in\mathcal{I}}\sum_{b\in\mathcal{B}}\Delta_{v,i,b}\tilde{p}(i)w_b - \bar{\zeta}^T_\beta\right\} \le U^T_\beta, \quad \forall\tilde{\mathbf{p}}\in\mathcal{P}. \tag{1}$$

The variable ζ is the value-at-risk (VaR) of the dose distribution, which captures the β percent of an organ that is receiving the highest amount of dose. Parameter U^T_β is the upper bound on the conditional-value-at-risk (CVaR) which is the average β% of the tail of the dose distribution. Constraint (1) is a β-CVaR constraint and must be met for all breathing patterns $\tilde{\mathbf{p}}$ in the given uncertainty set $\mathcal{P}$, which is a polyhedral set. Lower CVaR constraints can be formulated similarly. Model (2) shows the robust-CVaR IMRT model with one set of upper and lower β-CVaR constraints for limiting overdose and underdose to the target.

$$\text{minimize} \quad \frac{1}{|\mathcal{V}^H|}\sum_{v\in\mathcal{V}^H}\sum_{i\in\mathcal{I}}\sum_{b\in\mathcal{B}}\Delta_{v,i,b}p(i)w_b \tag{2a}$$

$$\text{subject to} \quad \bar{\zeta}^T_\beta + \frac{1}{(1-\beta)|\mathcal{V}^T|}\sum_{v\in\mathcal{V}^T}\bar{d}^T_{v,\beta} \le U^T_\beta, \quad \forall\beta\in\bar{A}^T, \tag{2b}$$

$$\bar{d}^T_{v,\beta} \ge \sum_{i\in\mathcal{I}}\sum_{b\in\mathcal{B}}\Delta_{v,i,b}\tilde{p}(i)w_b - \bar{\zeta}^T_\beta, \quad \forall v\in\mathcal{V}^T,\ \beta\in\bar{A}^T,\ \tilde{\mathbf{p}}\in\mathcal{P}, \tag{2c}$$

$$\underline{\zeta}^T_\beta - \frac{1}{(1-\beta)|\mathcal{V}^T|}\sum_{v\in\mathcal{V}^T}\bar{d}^T_{v,\beta} \ge L^T_\beta, \quad \forall\beta\in\bar{A}^T, \tag{2d}$$

$$\bar{d}^T_{v,\beta} \ge \bar{\zeta}^T_\beta - \sum_{i\in\mathcal{I}}\sum_{b\in\mathcal{B}}\Delta_{v,i,b}\tilde{p}(i)w_b, \quad \forall v\in\mathcal{V}^T,\ \beta\in\bar{A}^T,\ \tilde{\mathbf{p}}\in\mathcal{P}, \tag{2e}$$

$$\bar{\zeta}^T_\beta \ge 0, \quad \forall\beta\in\bar{A}^T, \tag{2f}$$

$$\underline{\zeta}^T_\beta \ge 0, \quad \forall\beta\in\underline{A}^T, \tag{2g}$$

$$\bar{d}^T_{v,\beta} \ge 0, \quad \forall v\in\mathcal{V}^T,\ \beta\in\bar{A}^T, \tag{2h}$$

$$\underline{d}^T_{v,\beta} \ge 0, \quad \forall v\in\mathcal{V}^T,\ \beta\in\underline{A}^T, \tag{2i}$$

$$w_b \ge 0, \quad \forall b\in\mathcal{B}. \tag{2j}$$

In a robust IMRT problem, there may exist multiple CVaR constraints on an organ for different values of β. Notice that constraint (2c) and (2e) must hold for all voxels in the tumor. We define a *type* of robust constraint as one that must hold for the same set of voxels for the same β value and in the same inequality direction (i.e., upper or lower CVaR constraints) for all $\tilde{\mathbf{p}} \in \mathcal{P}$. For example, all the upper β-CVaR constraints in (2c) are of the same type, although they are separate constraints for each voxel on the tumor. On the other hand, the sets of robust constraints (2c) and (2e) are of different types. Similarly, constraints for different β values or for different organs would be of different types.

Because the original problem is linear and the uncertainty set is polyhedral, the robust counterpart of this problem is linear. However, the large number of robust constraints make the robust counterpart very large. Alternatively, because the uncertainty set is polyhedral, an equivalent reformulation exists by simply enumerating the vertices of $\mathcal{P}$. In general though, enumerating all the vertices of a polyhedron is NP-hard [28] and could lead to an exponential number of constraints. Thus, we consider constraint generation as an alternative solution method.

3. A constraint generation solution method

In this section, we first formulate a general form of the previous RO problem with multiple uncertain constraints. Then, we define the steps of the constraint generation algorithm and develop several constraint addition strategies.

3.1. A robust optimization problem with uncertain constraints

Consider a robust optimization problem with uncertain constraints of different types $k \in \mathcal{K}$ that must hold for every $v \in \mathcal{V}(k)$. Let $\mathbf{w}$ be the decision vector. The uncertainty is in the vector $\tilde{\mathbf{p}} \in \mathcal{P}$, which is a parameter that affects all robust constraints. In other words, all robust constraints must hold for all values of $\tilde{\mathbf{p}}$ in the uncertainty set $\mathcal{P}$. Let $\mathbf{c}$ be the vector of objective function coefficients and $\mathbf{A}_{v,k}$ be the constraint coefficient matrix for constraint type $k \in \mathcal{K}$ for every $v \in \mathcal{V}(k)$. Given that $|\mathcal{I}|$ and $|\mathcal{B}|$ are the sizes of the vectors $\tilde{\mathbf{p}}$ and $\mathbf{w}$, respectively, the size of the matrix $\mathbf{A}_{v,k}$ is $|\mathcal{I}| \times |\mathcal{B}|$ for each v, k. The parameter $a_{v,k}$ is the right hand side