Combinatorial Benders Cuts for Decomposing IMRT Fluence Maps

Using Rectangular Apertures

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Abstract

We consider the problem of decomposing Intensity Modulated Radiation Therapy (IMRT) fluence maps using rectangular apertures. A fluence map can be represented as an integer matrix, which denotes the intensity profile to be delivered to a patient through a given beam angle. We consider IMRT treatment machinery that can form rectangular apertures using conventional jaws, and hence, do not need sophisticated multi-leaf collimator (MLC) devices. The number of apertures used to deliver the fluence map needs to be minimized in order to treat the patient efficiently. From a mathematical point of view, the problem is equivalent to a minimum cardinality matrix decomposition problem. We propose a combinatorial Benders decomposition approach to solve this problem to optimality. We demonstrate the efficacy of our approach on a set of test instances derived from actual clinical data. We also compare our results with the literature and solutions obtained by solving a mixed-integer programming formulation of the problem.

Keywords: IMRT; mixed-integer programming; combinatorial Benders decomposition; matrix segmentation by rectangles

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1 Introduction

Cancer is one of the leading causes of death throughout the world, and is the biggest killer of people aged 45-64 in Europe [32]. Today, approximately two-thirds of all newly diagnosed cancer patients receive radiation therapy for treatment. Over the past decade, Intensity Modulated Radiation Therapy (IMRT) has developed into the most successful external-beam radiation therapy delivery technique for many forms of cancer. This is due to its ability to deliver highly complex dose distributions to cancer patients, which enables the eradication of cancerous cells while limiting damage to nearby healthy organs and tissues. Patients treated with IMRT often experience a higher chance of cure while simultaneously suffering from fewer side effects of the treatment [39]. However, since the radiation beams employed in radiation therapy damage all cells traversed by the beams, both in targeted areas that contain cancerous cells and surrounding healthy organs and tissues, treatment must be carefully designed. Without a well-designed and properly executed treatment plan, patients can suffer from several side effects of treatment such as loss of hearing, inability to swallow, nerve damage and even death.

Excessive data and computational resource requirements make it impractical to solve the IMRT treatment planning problem at once. Instead, IMRT treatment planning is usually performed in three phases. The first phase determines a set of beam angles through which radiation is delivered. Beam angle optimization problem, which determines the best set of beam angles, is well studied in the literature and there exist several heuristics and optimization approaches for this problem (see [28, 29, 34]). In the second phase, an optimal radiation intensity profile (or fluence map) for each beam angle is determined, where the fluence map takes the form of a matrix of intensity values. The goal of fluence map optimization is to ensure that cancerous tissues receive the required amount of dose while functional organs are spared. Different approaches for fluence map optimization problem can be found in Lee et al. [25, 26, 27] and Romeijn et al. [36]. In order to deliver the fluence maps to the patient, a third phase decomposes them into a collection of deliverable aperture shapes and corresponding intensities. This last phase is called the leaf sequencing problem (or segmentation problem) and it is the problem that this paper focuses on. We refer the reader to [35] for a thorough review of optimization-based approaches to IMRT treatment planning.

Many IMRT devices use multi-leaf collimator (MLC) systems to form complex apertures by independently moving leaf pairs that block part of the radiation beam. Several variants of the leaf sequencing problem for IMRT devices using MLC devices have been studied in the literature. The problem of finding the minimum beam-on-time (defined as the total amount of time that the machine is actually delivering radiation) required to decompose a given fluence map is polynomially solvable (see [1, 21, 38]). However, the problem of finding the minimum number of apertures required for the decomposition is NP-hard in the strong sense [2]. While earlier studies have proposed various heuristic approaches for minimizing the number of apertures (e.g. [2, 11, 38, 43]), more recent studies have focused on generating optimal solutions. Langer et al. [24] and Wake et al. [42] developed mixed integer programming formulations of the problem, while Kalinowski [19] proposed an exact dynamic programming approach with the objective of minimizing total number of apertures used under the condition that the total treatment time is minimum. Baatar et al. [3], Ernst et al. [14] and Cambazard et al. [5] utilized constraint programming approaches to minimize the total number of apertures used. Recently, Taskin et al. [40] considered the problem of minimizing total treatment time, which is measured as a weighted combination of the beam-on-time and the number of apertures, and proposed a hybrid integer programming / constraint programming algorithm. Their results show that clinical problem instances can be solved to optimality within clinically acceptable computational time limits. On a related line of research, Engel and Kiesel [13] and Kiesel [22] considered a variant of the leaf sequencing problem in which the fluence map does not have to be decomposed exactly, but an approximate decomposition that can be delivered efficiently is sought.

While MLC devices allow for a high degree of flexibility in forming apertures, they are expensive to manufacture, operate and maintain. Therefore, researchers have recently started investigating the possibility of designing machinery that operates by using conventional jaws that are already integrated into radiation delivery devices, hence generating only rectangular aperture shapes (see [10, 30, 23, 31, 44]). Formally, a fluence map is represented as an $m \times n$ nonnegative integer matrix B. An aperture is represented as an $m \times n$ binary matrix, in which bixels that are blocked by jaws are represented by 0, exposed bixels are represented by 1 and we need the set of ones to form a rectangular shape. A feasible decomposition is one in which the original desired fluence map is equal to the summation of a number of feasible binary matrices multiplied by corresponding intensity values. For instance, the fluence map below is decomposed using four rectangular apertures, whose intensities are respectively chosen to be 4, 2, 3 and 6, yielding a total beam-on-time of 15.

$$
\begin{bmatrix} 4 & 0 & 2 \ 3 & 9 & 5 \end{bmatrix} = 4 \begin{bmatrix} 1 & 0 & 0 \ 0 & 0 & 0 \end{bmatrix} + 2 \begin{bmatrix} 0 & 0 & 1 \ 0 & 0 & 1 \end{bmatrix} + 3 \begin{bmatrix} 0 & 0 & 0 \ 1 & 1 & 1 \end{bmatrix} + 6 \begin{bmatrix} 0 & 0 & 0 \ 0 & 1 & 0 \end{bmatrix}
$$

Note that there are $O(m^2n^2)$ rectangular apertures that can be used for decomposing an $m \times n$ fluence map. Also note that a feasible decomposition is guaranteed to exist since the intensity requirements of bixels can be satisfied individually by unit rectangles. Dai and Hu [9] proposed two heuristics for finding a feasible decomposition. Engel [12] proposed an integer programming formulation, which aims to minimize beamon-time under the constraint that intensity values take on integer values. More recently, Taskin et al. [39] proposed a mixed-integer programming formulation to minimize the number of rectangular apertures and the total treatment time, and derived several valid inequalities and a partitioning approach for the problem. Their computational results show that even though their approach can be used to derive good bounds on the minimum number of rectangular apertures, only few clinical problem instances can be solved to optimality.

In this paper, we extend Taskin et al. [39]'s work by devising a solution methodology based on combinatorial Benders decomposition, which is a relatively new technique for solving a class of mixed-integer linear programming problems containing "big-M" type formulations [7]. Even though such formulations typically have poor linear programming relaxations, they are often used to model logical implications. Similar to the traditional Benders decomposition method, combinatorial Benders decomposition partitions the problem into an integer programming master problem and a linear programming subproblem. The key difference between the two methods is the way cuts are derived: traditional Benders cuts are based on linear programming duality, while combinatorial Benders cuts are based on minimal infeasible subsystems (MIS) associated with the subproblem. Given an infeasible linear system of equations, an MIS is defined as an infeasible subset of the system with the property that removal of any element yields a feasible subsystem (hence the term minimal). Generated cuts are combinatorial in nature and do not contain any big-M coefficients, which can result in significantly tighter bounds and improved solvability of the problem [7].

There are several successful applications of combinatorial Benders decomposition in the literature. Bai and Rubin [4] used combinatorial Benders cuts in order to solve a toll pricing problem and reported that their approach can find optimal solutions for small to medium size problems in a short amount of time. Cortes et al. [8] utilized combinatorial Benders decomposition for a large-scale pick-up and delivery problem with transfers and reported 90% savings on the average in terms of CPU times. Sawaya and Elhedhli [37] used combinatorial Benders decomposition and classical Benders decomposition in a nested way to solve a telecommunication network planning problem. Tanner and Ntaimo [41] proposed a variant of combinatorial Benders cuts to solve a vaccine allocation problem. Their computational results show that these cuts significantly reduce solution times and the number of nodes searched in the branch and bound tree for their problem.

The rest of this paper is organized as follows. In Section 2, we review Taskin et al. [39]'s formulation and demonstrate how to derive combinatorial Benders cuts for solving it. In Section 3, we discuss some strategies for improving the solution process. We present the results of our tests on clinical problem instances in Section 4. Finally, we provide concluding remarks in Section 5.

2 Combinatorial Benders Cuts for IMRT Fluence Map Decomposition

Taskin et al. [39] formulate the problem of minimizing the number of rectangular apertures as follows. Let R denote the set of all rectangular apertures that can be formed. Define a continuous variable x_r to denote the amount of intensity delivered through aperture $r \in R$, and a binary variable y_r to denote whether aperture r is used (that is $y_r = 1$ if and only if $x_r > 0$). Denoting the amount of required intensity to be delivered to bixel (i, j) by b_{ij} , the set of bixels that aperture r covers by $C(r)$ and the set of apertures that cover bixel (i, j) by $R(i, j)$, the rectangular decomposition problem (RDP) can be formulated as:

RDP: Minimize
$$
\sum_{r \in R} y_r
$$
 (1a)

subject to:
$$
\sum_{r \in R(i,j)} x_r = b_{ij} \quad \forall i = 1, ..., m, j = 1, ..., n
$$
 (1b)

$$
x_r \le M_r y_r \quad \forall r \in R \tag{1c}
$$

$$
x_r \ge 0, y_r \in \{0, 1\} \quad \forall r \in R,\tag{1d}
$$

where $M_r = \min_{(i,j) \in C(r)} b_{ij}$ denotes the minimum required intensity value among the bixels covered by aperture r. The objective (1a) minimizes the number of rectangles used in the decomposition. Constraints (1b) guarantee that each bixel receives the exact amount of intensity needed. Constraints (1c) form the relationship between x_r and y_r . Finally, constraints (1d) state logical conditions on variables. Note that the objective (1a) guarantees that $y_r = 0$ when $x_r = 0$ in an optimal solution.

We observe that the structure of RDP is suitable for the application of combinatorial Benders decomposition. In particular, the objective function (1a) contains only the y-variables, which are binary, and the constraints (1b) contain only the x-variables, which are continuous. Constraints (1c) relate the x- and y-

variables using a big-M type formulation. In alignment with Codato and Fischetti [7], it can be argued that the x-variables are "artificial" variables introduced in order to enforce some feasibility conditions that the y-variables have to satisfy. Furthermore, constraints (1c) reduce to $x_r \le 0$ if $y_r = 0$, and are redundant otherwise. Therefore, they can be interpreted as "conditional" constraints enforcing the logical condition $y_r = 0 \Rightarrow x_r = 0$. In the spirit of combinatorial Benders decomposition, RDP can be formulated in terms of the y-variables as:

$$
\textbf{MP:} \text{Minimize } \sum_{r \in R} y_r \tag{2a}
$$

 y corresponds to a feasible decomposition $(2b)$

$$
y_r \in \{0, 1\} \quad \forall r \in R,\tag{2c}
$$

where feasibility of a given \hat{y} -vector can be checked by seeking a feasible solution of the linear system:

$$
\mathbf{SP}(\hat{y}) \mathbf{:} \sum_{r \in R(i,j)} x_r = b_{ij} \quad \forall i = 1, \dots, m, \ j = 1, \dots, n \tag{3a}
$$

$$
x_r \le M_r \hat{y}_r \quad \forall r \in R \tag{3b}
$$

$$
x_r \ge 0 \quad \forall r \in R. \tag{3c}
$$

If $SP(\hat{y})$ has a feasible solution \hat{x} , then (\hat{y}, \hat{x}) is a feasible solution of RDP. Otherwise, the value of at least one y-variable has to be different in all feasible solutions of RDP. Therefore, in principle, (2b) can be written as a collection of inequalities of form

$$
\sum_{r \in R: \hat{y}_r = 0} y_r + \sum_{r \in R: \hat{y}_r = 1} (1 - y_r) \ge 1,
$$
\n(4)

one for each \hat{y} such that SP(\hat{y}) has no feasible solution. However, for our problem it can be seen that if \hat{y} does not yield a feasible solution, then any \bar{y} such that $\bar{y}_r \leq \hat{y}_r$, $\forall r \in R$ does not yield a feasible solution either. (Note that the value of an x-variable can be zero even if the value of the corresponding y -variable is one. Therefore, all feasible solutions of $SP(\bar{y})$ are also feasible for $SP(\hat{y})$ if $\bar{y}_r \leq \hat{y}_r \,\forall r \in R$, which implies that if $SP(\hat{y})$ is infeasible then $SP(\bar{y})$ is also infeasible.) Hence, at least one aperture r having $\hat{y}_r = 0$ has to be allowed in a feasible solution. Therefore, the following cut is valid:

$$
\sum_{r \in R: \hat{y}_r = 0} y_r \ge 1. \tag{5}
$$

Constraint (5) is clearly stronger than (4). However, only few of the $O(n^2m^2)$ apertures have their $y_r = 1$, and the rest have $y_r = 0$ in an optimal solution. Therefore, (5) is often very weak. In order to generate a stronger cut, Codato and Fischetti [7] propose finding a minimal (or irreducible) infeasible subsystem (MIS or IIS) of SP (\hat{y}) . In particular, let \hat{y} be a vector such that SP (\hat{y}) is infeasible and consider an associated MIS. Recall that MIS is an infeasible subset of $SP(\hat{y})$ with the property that the removal of any constraint from MIS yields a feasible system of equations. By definition, the MIS consists of a subset of (3a), (3b) and possibly (3c). The critical observation in combinatorial Benders decomposition is that the value of at least one y-variable corresponding to a constraint of type $(3b)$ that is a member of the MIS has to be changed in order to "repair" the infeasibility associated with the MIS. Let $\tilde{R} \subseteq R$ be the subset of rectangles that are associated with an MIS corresponding to \hat{y} . Then, the combinatorial Benders cut proposed by Codato and Fischetti [7] is:

$$
\sum_{r \in \hat{R} : \hat{y}_r = 0} y_r + \sum_{r \in \hat{R} : \hat{y}_r = 1} (1 - y_r) \ge 1.
$$
 (6)

As before, second term of (6) is not needed in our problem since if $y_r = 1$, then the corresponding constraint of type (3b) is redundant and is never included in an MIS. Therefore, we instead add the following cut whenever an MIS is identified:

$$
\sum_{r \in \hat{R} : \hat{y}_r = 0} y_r \ge 1. \tag{7}
$$

We next discuss how to obtain MISs associated with an infeasible set of constraints. There are several studies about locating an MIS of an infeasible system in the literature (e.g., Chinneck [6], Guieu and Chinneck [17]). Some of these methods have been implemented in modern mixed-integer programming solvers (for instance RefineConflict function of CPLEX and computeIIS in Gurobi). However, solver implementations are geared towards finding a single MIS efficiently (see [18]) while there can be an exponential number of MISs associated with an infeasible system (see [16, 33]). Since a different, non-dominated cut of type (7) can be written for each MIS, we are interested in generating multiple MISs corresponding to a \hat{y} -vector yielding no feasible solution for $SP(\hat{y})$. Gleeson and Ryan [16] showed that there is a one-to-one correspondence between MISs of an infeasible linear system and the supports of vertices of a related polyhedron. Inspired by this study, Parker and Ryan [33] proposed different methods to locate MISs of infeasible linear systems. We develop an MIS search heuristic based on these methods. According to the key results found in Parker and Ryan [33], the indices of the MISs of the linear system consisting of (3a)–(3c) correspond to supports of the extreme points of the following polyhedron:

$$
\mathbf{P}(\hat{y}) = \begin{cases} \sum_{(i,j)\in C(r)} w_{ij} + u_r \ge 0 & \forall r \in R \\ \end{cases}
$$
 (8a)

$$
\sum_{i=1}^{m} \sum_{j=1}^{n} b_{ij} w_{ij} + \sum_{r \in R} M_r \hat{y}_r u_r = -1
$$
 (8b)

$$
w_{ij} \text{ unrestricted } \forall i = 1, \dots, m, \ j = 1, \dots, n \tag{8c}
$$

$$
u_r \ge 0 \quad \forall r \in R \bigg\},\tag{8d}
$$

where w_{ij} and u_r are dual multipliers associated with constraints (3a) and (3b), respectively, and $C(r)$ denotes the set of bixels covered by rectangle $r \in R$. Note that (8b) is the Gleeson-Ryan normalization constraint. We add the following objective function to $P(\hat{y})$

Minimize
$$
\sum_{r \in R} u_r
$$
 (9a)

in order to obtain an MIS that contains few constraints of type $(3b)$ (see also [4]). Note that nonzero u-values in the solution of this problem form the index set of MISs and low cardinality MISs will produce stronger cut of type (7). In order to encourage detection of different MISs, we iteratively set u-variables that are included in previous MISs to zero and re-solve resulting problem (see also [7]). This process continues until $P(\hat{y})$ becomes empty due to these zero-valued *u*-variables.

3 Model Improvements

In this section, we discuss how the basic combinatorial Benders decomposition framework can be improved within the context of our problem. In particular we describe some valid inequalities in Section 3.1 and propose heuristic procedures for obtaining an initial feasible solution in Section 3.2. We discuss ways of "repairing" MISs in Section 3.3 and devise a local search algorithm for improving solution quality in Section 3.4. Finally, we discuss how to implement the algorithm in a branch-and-cut setting in Section 3.5.

3.1 Valid Inequalities

Consider the initial iteration that MP is solved for the first time, when no inequalities of type (7) have yet been generated. The initial optimal solution of MP assigns all y-variables to zero, which clearly yields no feasible solution for SP. In this section we discuss how some characteristics of all feasible solutions of RDP can be used to derive some valid inequalities, which can be added to MP before the initial execution of the master problem in order to improve the convergence rate of the decomposition algorithm.

Taskin et al. [39] propose several valid inequalities for the rectangular problem. Their computational results show that a class of valid inequalities called "bounding box inequalities" are particularly useful for our problem. A bounding box associated with bixel (i, j) is characterized by four integers (l, u, r, d) such that $b_{ij} > b_{il} + b_{uj} + b_{ir} + b_{dj}$. In this case, (l, u, r, d) correspond to the left-hand-side, upper, right-handside and lower borders of a box, respectively, such that at least one aperture that is contained within the bounding box has to be used in any feasible decomposition. In the example below, the bixels marked in gray correspond to the borders of a bounding box associated with bixel (2,2), which is marked in bold text.

Note that all apertures that cover at least one of the bixels marked in gray can deliver a cumulative intensity of $1+3+4+1=9<10$. Therefore, at least one aperture that covers bixel $(2, 2)$ but none of the gray bixels has to be selected in any feasible solution. Let BB_{ij} denote a bounding box associated with bixel (i, j) and $R(BB_{ij})$ denote the set of rectangles that cover (i, j) and that are contained within BB_{ij} . Then, the following inequality is valid:

$$
\sum_{r \in R(BB_{ij})} y_r \ge 1. \tag{10}
$$

Taskin et al. [39] show that there can be multiple bounding boxes for each bixel, and propose an algorithm for finding all non-dominated bounding boxes, which we use to generate valid inequalities of type (10) and add to MP.

Another class of valid inequalities can be derived by observing that the total intensity that can be delivered to each bixel needs to be greater than or equal to its required intensity.

$$
\sum_{r \in R(i,j)} M_r y_r \ge b_{ij}, \quad \forall i = 1, \dots, m, \ j = 1, \dots, n. \tag{11}
$$

Note that these inequalities are implied by (1b) and (1c) in RDP. However, in the decomposition framework MP does not contain any constraints that imply (11). Therefore, we add (11) to MP after processing them with the tightening procedure described in [39].

3.2 Generating an Initial Feasible Solution

The availability of a high-quality initial feasible solution can help improve the performance of MP because it provides a good upper bound, which allows the solver to fathom more nodes by bound and apply strategies

such as reduced cost fixing. Engel [12] proposed a heuristic for the problem and compared it with two heuristics proposed by Dai and Hu [9]. Engel [12]'s results show that while their heuristic, which is aimed at minimizing beam-on-time, yields better solutions than Dai and Hu [9]'s heuristics for beam-on-time, on average Dai and Hu [9]'s heuristics find solutions using fewer apertures for most instances. Therefore, we focus on Dai and Hu [9]'s heuristics for our problem. We also propose two additional approaches, a straightforward greedy algorithm and a Lagrangian relaxation algorithm, for generating initial feasible solutions for our problem. We review these three approaches below, and compare them empirically in Section 4.

- Greedy Heuristic: The first heuristic proposed by Dai and Hu [9] selects a rectangle covering the largest area (that is having maximum $|C(r)|$) in each iteration. It then assigns the aperture's intensity as the minimum intensity among the bixels covered by the rectangular aperture (M_r) , removes the resulting rectangle from the original matrix and updates M_r for each rectangle. This process continues until the zero-matrix is obtained. We refine this heuristic as follows. Instead of choosing a rectangle covering the largest area, we choose a rectangle whose area times the minimum intensity (i.e. $|C(r)|M_r$) is maximum. In this manner, we greedily reduce the total amount of intensity to be delivered as much as possible in each iteration. In our computational tests, we observed that this simple refinement significantly improves solution quality.
- DAIHU: The second algorithm proposed by Dai and Hu [9] first finds the maximum intensity value in the input matrix. Among the rectangles that cover this maximum intensity value, the one whose removal makes the complexity of the remaining matrix minimum is selected. Complexity of a matrix is defined as the number of blocks in it, where a block is defined as the largest rectangular area formed by bixels having equal intensity level. The algorithm then assigns the selected aperture's intensity as

the minimum intensity among the bixels covered by the aperture and removes the resulting rectangle from the original matrix. The same operations are carried out until zero-matrix is obtained.

• Lagrangian Relaxation: Lagrangian relaxation is a widely used technique to obtain simultaneous upper and lower bounds for computationally difficult optimization problems. In Lagrangian relaxation constraints are divided into "nice" constraints, which can easily be handled, and "complicating" constraints, which make the problem difficult to solve. In Lagrangian relaxation complicating constraints are removed from the constraint set and their violations are penalized by adding them to the objective function. The resulting problem is often separable, and it can be used to obtain upper and lower bounds for the original problem (see Fisher [15]).

Examining the structure of RDP, we observe that constraints (1b) contain only continuous variables while (1c) contain continuous and binary variables as well as big-M coefficients. Therefore, (1b) can be thought of as nice constraints and (1c) can be regarded as complicating constraints. Associating $\lambda_r \geq 0$ with each constraint of type (1c) and dualizing them, the Lagrangian problem can be obtained as:

$$
\mathbf{LR}(\lambda): \text{Minimize } \sum_{r \in R} y_r + \sum_{r \in R} \lambda_r (x_r - M_r y_r) \tag{12a}
$$

subject to:
$$
\sum_{r \in R(i,j)} x_r = b_{ij} \quad \forall i = 1, ..., m, j = 1, ..., n
$$
 (12b)

$$
x_r \ge 0, \ y_r \in \{0, 1\} \quad \forall r \in R. \tag{12c}
$$

We observe that $LR(\lambda)$ is separable with respect to x-variables and individual y-variables. The sub-

problem with respect to x -variables can be written as:

$$
\mathbf{LR}x(\lambda): \text{Minimize } \sum_{r \in R} \lambda_r x_r \tag{13a}
$$

subject to:
$$
\sum_{r \in R(i,j)} x_r = b_{ij} \quad \forall i = 1, ..., m, j = 1, ..., n
$$
 (13b)

$$
x_r \ge 0 \quad \forall r \in R,\tag{13c}
$$

which is a linear programming problem that can be solved efficiently. Similarly, the subproblem with respect to y_r , for each $r \in R$, can be written as

$$
LRy_r(\lambda_r): \text{Minimize } (1 - \lambda_r M_r)y_r \tag{14a}
$$

$$
subject to: y_r \in \{0, 1\},\tag{14b}
$$

which can trivially be solved by inspection. Then, the Lagrangian dual problem can be written as

LR: Maximize
$$
LRx(\lambda) + \sum_{r \in R} LRy_r(\lambda_r)
$$
 (15a)

$$
subject to: \lambda_r \ge 0 \quad \forall r \in R. \tag{15b}
$$

In our computational tests we observed that the lower bound obtained by solving the Lagrangian problem is weak. This is not surprising since the Lagrangian problem has the integrality property, and hence the best lower bound that can be obtained by solving LR is equal to the bound induced by the linear programming relaxation of RDP [15]. In principle, the lower bound can be improved by adding valid inequalities (10) and (11) to formulation $LRy(\lambda)$. However, once these valid inequalities are added, the problem is no longer separable with respect to individual y_r -variables and can no longer be solved by inspection. Furthermore, we are primarily interested in obtaining a good upper bound quickly as opposed to improving lower bounds. Note that an upper bound can be obtained for some $\lambda \geq 0$ simply by choosing $y_r = 1$ for all rectangular apertures r having $x_r > 0$ in an optimal solution

of $LRx(\lambda)$. In our implementation we use a standard subgradient optimization algorithm to solve the Lagrangian dual problem (15), seeking an improved upper bound at each iteration.

3.3 Repairing Infeasible Solutions

During execution of the algorithm, we get several solutions \hat{y} from the master problem MP that do not yield any feasible solutions for the subproblem $SP(\hat{y})$. In this section we propose two heuristics for "repairing" such solutions in order to obtain feasible solutions for RDP. Our first algorithm delivers as much intensity as possible by using the allowed rectangular apertures, which have $\hat{y}_r = 1$. Then it decomposes the remaining fluence map heuristically. Our second algorithm uses implications of the detected MISs to construct a feasible solution. We discuss details of the two methods below.

• Method 1 : Let \hat{y} denote a solution of MP that does not yield a feasible solution for SP(\hat{y}). Let $R_1(\hat{y}) = \{r : r \in R, \hat{y}_r = 1\}$ denote the set of rectangles allowed by \hat{y} . We formulate the following linear program in order to calculate the maximum amount of intensity that can be delivered by using the rectangles in $R_1(\hat{y})$.

$$
\text{SSP}(\hat{y}) : \text{Maximize} \sum_{r \in R_1(\hat{y})} |C(r)| x_r \tag{16a}
$$

subject to:
$$
\sum_{r \in R(i,j) \cap R_1(j)} x_r \le b_{ij} \quad \forall i = 1, ..., m, j = 1, ..., n
$$
 (16b)

$$
x_r \ge 0, \quad \forall r \in R_1(\hat{y}).\tag{16c}
$$

Note that SSP (\hat{y}) is guaranteed to be feasible since the zero-vector is a trivial feasible solution. Let x' denote an optimal solution of SSP (y) and let $y'_r = 1$ for $x'_r > 0$. Note that y' is not necessarily equal to \hat{y} since some allowed rectangles may be left unused. We update B by subtracting the intensity delivered by x' . Let B' denote the residual fluence map. Formally,

$$
b'_{ij} = b_{ij} - \sum_{r \in R(i,j) \cap R_1(j)} x'_r \quad \forall i = 1, ..., m, \ j = 1, ..., n.
$$
 (17)

 B' can be decomposed approximately using our Lagrangian relaxation procedure or optimally using formulation RDP. However, we decompose B' by applying our greedy algorithm described in Section 3.2 so that the repair heuristic terminates quickly. Let $y_r'' = 1$ if rectangle r is used in the decomposition of B' . A feasible solution of the original problem can be found by combining the two (disjoint) sets of rectangles, that is $\tilde{y} = y' + y''$ yields a feasible solution for our problem.

- Method 2 : Feasible solutions can also be generated by iteratively eliminating detected MISs. We use the following algorithm to construct a feasible solution starting with a \hat{y} -vector for which SP(\hat{y}) is infeasible:
	- Step 1: Use a method described in Section 2 to obtain an MIS. Let \hat{R} denote the set of rectangles contained in the MIS.
	- Step 2: Add the corresponding combinatorial Benders cut (7) to MP.
	- **Step 3:** Pick some $r \in \hat{R}$ having maximum $|C(r)|M_r$ such that $\hat{y}_r = 0$. Set $\hat{y}_r = 1$.
	- Step 4: Solve SP (\hat{y}) . If a feasible solution \hat{x} exists, then stop. Else go back to Step 1.

This algorithm finds an MIS in each iteration and adds a new rectangle that can potentially eliminate the infeasibility associated with the identified MIS. Since RDP is guaranteed to be feasible and a distinct rectangle is added in each iteration, the algorithm eventually generates a feasible solution. As previously stated, \hat{x}_r might be equal to zero for some $r \in R$. We disregard those rectangles while calculating the upper bound obtained by the algorithm. An important advantage of this method is that it allows us to generate several combinatorial Benders cuts, which significantly improves the lower bound associated with MP.

3.4 Solution Improvement Algorithm

In this section we devise a simple local search algorithm that attempts to improve a given feasible solution. Our local search algorithm iterates over the set of allowed rectangles and disallows them one by one. If the problem still yields a feasible solution, then the new solution has a better objective function value. Formally, let \hat{y} denote a vector such that SP(\hat{y}) is feasible. Such a vector may have been found by any one of the algorithms discussed in Sections 3.2 or 3.3. Starting with \hat{y} , the following algorithm seeks an improved solution \bar{y} :

- Step 1: Initialize $\bar{y} = \hat{y}$. Label all rectangles as untried.
- Step 2: Pick an untried rectangle r having $\bar{y}_r = 1$. If no such r exists, then return \bar{y} . Else continue to Step 3.
- Step 3: Set $\bar{y}_r = 0$. If SP(\bar{y}) yields no feasible solution, then set $\bar{y}_r = 1$.
- Step 4: Mark r as tried and go back to Step 2.

We execute our solution improvement algorithm whenever a feasible solution \hat{y} is found.

3.5 Single Branch-and-Bound Tree

Repeatedly solving MP (which is an integer programming problem) to optimality, adding a cut and resolving it can be very expensive from a computational point of view. In order to improve efficiency of the algorithm we can interrupt the branch-and-bound solution process of MP each time the solver finds an integer solution \hat{y} , and check whether SP(\hat{y}) yields a feasible solution. If a feasible solution exists, then we accept \hat{y} as the new incumbent and resume solving MP. Otherwise, we reject \hat{y} , generate a combinatorial Benders cut (7), apply our solution repair heuristics and again resume the solution process of MP. In our computational tests, this approach consistently outperformed solving MP to optimality in each iteration, adding a cut, and re-optimizing it. This is because this refinement allows us to solve MP through the solution of a single branch-and-bound tree that is tightened as necessary, as opposed to generating a branch-and-bound tree in each iteration. A similar approach was used in several studies including Codato and Fischetti [7], Bai and Rubin [4] and Taskin et al. [40].

We also use the single branch-and-bound tree approach for generating upper bounds based on fractional \hat{y} -vectors generated by the solver while solving linear programming relaxations. Given a fractional \hat{y} -vector, we first round values greater than some parameter θ up to one and the remaining values down to zero to obtain an integer vector \tilde{y} . We then check whether SP(\tilde{y}) yields a feasible solution that can be used as an improved incumbent. If it does not, then we use Method 1 described in Section 3.3 to construct a feasible solution starting with \tilde{y} . This approach allows us to obtain high quality solutions for problem instances that are too difficult to solve to optimality.

4 Computational Results

We implemented our algorithm using CPLEX 12.2 running on a Windows XP PC with a 2.13 GHz Intel Core 2 CPU and 2 GB RAM. Our test data consists of 25 clinical problem instances used in Taskin et al. [39]. Each instance is characterized by the patient and the beam angle corresponding to the instance ("Name"), number of rows (m) , number of columns (n) and the maximum required intensity $(L = \max_{(i,j)} b_{ij})$ of the input matrix. We used RefineConflict function of CPLEX to find an MIS associated with infeasible subproblem instances in addition to our heuristic MIS search procedure described in Section 2. In particular, we used RefineConflict to efficiently obtain a single MIS in each iteration of our repair heuristic discussed in Section 3.3, and we used our heuristic MIS search algorithm to obtain multiple cuts of type (7) associated with infeasible solutions. In our tests we observed that the simultaneous use of these methods is computationally

beneficial, where on average approximately 35% of the cuts were generated by our MIS heuristic. We also used CPLEX's callback functions to solve our model in a single branch and bound tree as described in Section 3.5, where we used $\theta = 0.6$ as the threshold value for rounding fractional solutions.

In our first experiment, we analyzed the performances of various heuristics and exact approaches for our problem. Table 1 presents the results of this experiment. The set of columns titled "Heuristics" show the number of rectangles used in solutions generated by the three heuristics for obtaining an initial feasible solution discussed in Section 3.2. In particular, columns titled as "GH," "DH" and "LR" correspond to our greedy heuristic, DAIHU [9] and our Lagrangian relaxation algorithm, respectively. DAIHU is able to generate the best upper bounds in 20 problem instances. However, in most instances there is no significant improvement in the solution quality compared to the other heuristics. Furthermore, our greedy heuristic executes much faster than DAIHU and Lagrangian relaxation algorithms. Therefore, we used our greedy heuristic to generate feasible solutions that we use as initial upper bounds in our combinatorial Benders decomposition algorithm. Comparing heuristic solutions with the best upper bounds generated by our algorithm, which are presented in the "UB" column under the set of columns titled "CBC," we observe that our algorithm is able to improve heuristic solutions in all problem instances.

The set of columns titled "Literature" in Table 1 shows the results obtained by Taskin et al. [39] on the same data set using CPLEX 11 running on a Windows XP PC with a 3.4 GHz CPU and 2 GB RAM. We present the best solution reported in [39] for each problem instance in terms of the solution time ("CPU"), upper bound ("UB"), lower bound ("LB") and percentage optimality gap ("GAP"). The set of columns titled "CBC" represents values of the same performance measures obtained by our algorithm based on combinatorial Benders cuts. We enforced a time limit of 1800 seconds, which is equal to the time limit enforced in [39], for each problem instance. We rounded all lower bounds up since the objective function is guaranteed to have an integral value. Bold numbers in Table 1 mark the best optimality gaps found for

Data				Heuristics				Literature		CBC					
Name	$\,m$	\boldsymbol{n}	L	GH	D _H	LR	CPU	UB	\mathbf{LB}	GAP	CPU	UB	LB	GAP	
case1 beam1	15	14	20	71	67	67	1800	63	62	1.6%	130	63	63	0.0%	
case1 beam2	11	15	20	53	53	53	138	48	48	0.0%	20	48	48	$0.0\,\%$	
case1 beam3	15	15	20	63	62	63	1800	57	54	5.3%	373	56	56	$0.0\,\%$	
case1 beam4	15	15	20	67	65	69	1800	59	55	6.8%	1800	59	55	$6.8\,\%$	
case1 beam5	11	15	20	51	51	52	1800	46	45	2.2%	$80\,$	45	45	$0.0\,\%$	
case2 beam1	18	20	20	121	111	117	1800	103	87	15.5%	1800	102	92	9.8%	
case2 beam2	17	19	20	107	106	102	1800	94	82	12.8%	1800	95	84	11.6%	
case2 beam3	18	18	20	109	97	105	1800	94	77	18.1%	1800	95	81	14.7%	
case2 beam4	18	18	20	115	110	115	1800	105	88	16.2%	1800	109	88	19.3%	
case2 beam5	17	18	20	100	97	101	1800	91	72	20.9%	1800	88	76	13.6%	
case3 beam1	22	17	20	126	123	124	1800	119	79	33.6%	1800	117	82	29.9%	
case3 beam2	15	19	20	77	75	74	1800	70	52	25.7%	1800	68	58	14.7%	
case3 beam3	20	17	20	121	114	119	1800	107	77	28.0%	1800	112	82	26.8%	
case3 beam4	19	17	20	109	107	107	1800	99	78	21.2%	1800	103	79	23.3%	
case3 beam5	15	19	20	76	76	76	1800	71	58	18.3%	1800	71	61	14.1%	
case4 beam1	19	22	20	120	117	115	1800	107	89	16.8%	1800	106	92	13.2%	
case4 beam2	13	24	20	88	87	92	1800	91	58	36.3%	1800	84	63	$25.0\,\%$	
case4 beam3	18	23	20	100	99	101	1800	93	77	17.2%	1800	90	82	$8.9\,\%$	
case4 beam4	17	23	20	105	103	110	1800	98	83	15.3%	1800	101	85	15.8%	
case4 beam5	12	24	20	96	95	92	1800	87	67	23.0%	1800	86	72	16.3%	
case5 beam1	15	16	20	72	70	71	1800	66	65	1.5%	217	66	66	$0.0\,\%$	
case5 beam2	13	17	20	66	61	60	102	58	58	0.0%	15	58	58	$0.0\,\%$	
case5 beam3	14	16	20	74	70	70	1800	65	57	12.3%	1800	63	58	7.9%	
case5 beam4	14	16	20	78	65	69	1800	64	59	7.8%	1800	62	60	3.2%	
case5 beam5	12	17	20	57	54	54	36	49	49	0.0%	81	49	49	$0.0\,\%$	
Average gap								14.3%				11.0%			
# of optimally solved instances										3				τ	
	# of best solutions					11				$\overline{7}$				22	

Table 1: Results obtained by heuristics, combinatorial Benders decomposition and best results in literature

Parameter	Description	Value
mip cuts cliques	Clique cuts	2 (Generate aggressively)
mip cuts covers	Cover cuts	2 (Generate aggressively)
mip cuts flowcovers	Flow cover cuts	2 (Generate aggressively)
mip cuts gomory	Gomory fractional cuts	2 (Generate aggressively)
mip cuts gubcovers	Generalized upperbound cover cuts	2 (Generate aggressively)
mip cuts implied	Implied bound cuts	2 (Generate aggressively)
mip cuts mircut	Mixed integer rounding cuts	2 (Generate aggressively)
mip cuts pathcut	Flow path cuts	2 (Generate aggressively)
mip limits cutsfactor	Row multiplier factor for cuts	30
mip strategy backtrack	Backtracking tolerance	0.1
mip strategy heuristicfreq	Heuristic frequency	100
mip strategy probe	Probing level	2 (Aggressive Probing)

Table 2: Tuned parameter settings used in solving RDP model

each instance. Note that Taskin et al. [39]'s approach found optimal solutions for three problem instances (case1 beam2, case5 beam2 and case5 beam5) while our algorithm is able to find optimal solutions for four additional problem instances (case1 beam1, case1 beam3, case1 beam5 and case5 beam1). Furthermore, comparing optimality gaps obtained by these two approaches we observe that our approach is able to find equivalent or improved solutions in 22 out of 25 problem instances (with the notable exceptions of case2 beam4, case3 beam4 and case4 beam4) and reduce average optimality gap from 14.3% to 11.0%.

Our second experiment compares the performance of our algorithm with the direct solution of the underlying mixed-integer programming formulation RDP discussed in Section 2. For this aim, we first used CPLEX's automated tuning tool to find a parameter set that closes optimality gap as quickly as possible. Table 2 lists the parameters that were switched from their default values. Table 3 presents the results obtained on the same data set by directly solving RDP with default CPLEX parameters ("Default CPLEX"), with tuned CPLEX parameters ("Tuned CPLEX") and our algorithm ("CBC"). Table 3 shows that tuning CPLEX parameters as presented in Table 2 is quite effective in closing optimality gaps for our problem. We observe that while the average optimality gap is reduced from 15.6% to 12.9%, tuning parameters deteriorates solution quality for several problem instances and it decreases the number of instances that can be

solved to optimality from three to one. We also repeat the results obtained by our algorithm under the set of columns titled "CBC" for ease of comparison. Similar to Table 1, numbers marked in bold correspond to best optimality gaps found by the three approaches. We observe that our algorithm is able to provide the best optimality gaps in 17 instances. Furthermore, our algorithm finds provably optimal solutions in seven problem instances, which is significantly higher than the number of instances that CPLEX can solve to optimality using both default and tuned parameters. These results show that our solution approach significantly improves the solvability of the problem.

Our last experiment focuses on testing the effect of the maximum intensity level L on the performance of our algorithm and the generated solution. In IMRT treatment planning process, fluence maps are often generated by solving a nonlinear optimization problem and then rounding the intensity levels assigned to bixels to integers in order to limit the delivery time. Higher values of L yield less round-off errors, and more precise fluence maps that typically require a higher number of apertures to be delivered. Table 4 shows the results obtained by our combinatorial Benders decomposition algorithm for problem instances that are scaled such that $L \in \{5, 10, 15\}$ in addition to $L = 20$, which corresponds to our algorithm's results presented in Tables 1 and 3. In Table 4, bold numbers denote the problem instances that could be solved optimally. As expected, our algorithm provides tighter optimality gaps and finds optimal solutions for more problem instances as L decreases. In particular, our approach is able to find provably optimal solutions of 7 instances for $L = 20$, 8 instances for $L = 15$, 14 instances for $L = 10$ and for all 25 instances for $L = 5$. This is not surprising since the problem naturally gets easier to solve as L decreases, and is polynomially solvable for $L = 1$ [20].

Data		Default CPLEX				Tuned CPLEX			CBC						
Name	\boldsymbol{m}	\boldsymbol{n}	L	CPU	UB	LB	GAP	CPU	UB	LB	GAP	CPU	UB	LB	GAP
case1 beam1	15	14	20	1800	63	61	3.2%	1800	64	61	4.7%	130	63	63	0.0%
case1 beam2	11	15	20	675	48	48	0.0%	1800	48	47	2.1%	20	48	48	0.0%
case1 beam3	15	15	20	1800	57	54	5.3%	1800	58	54	6.9%	373	56	56	0.0%
case1 beam4	15	15	20	1800	60	55	8.3%	1800	60	55	8.3%	1800	59	55	6.8%
case1 beam5	11	15	20	1800	46	43	6.5%	1800	49	44	10.2%	80	45	45	0.0%
case2 beam1	18	20	20	1800	101	87	13.9%	1800	105	91	13.3%	1800	102	92	9.8%
case2 beam2	17	19	20	1800	96	79	17.7%	1800	98	83	15.3%	1800	95	84	11.6%
case2 beam3	18	18	20	1800	96	76	20.8%	1800	96	80	16.7%	1800	95	81	14.7%
case2 beam4	18	18	20	1800	109	85	22.0%	1800	107	88	17.8%	1800	109	88	19.3%
case2 beam5	17	18	20	1800	95	70	26.3%	1800	89	74	16.9%	1800	88	76	13.6%
case3 beam1	22	17	20	1800	122	81	33.6%	1800	114	87	23.7%	1800	117	82	29.9%
case3 beam2	15	19	20	1800	67	52	22.4%	1800	70	57	18.6%	1800	68	58	14.7%
case3 beam3	20	17	20	1800	115	75	34.8%	1800	110	81	26.4%	1800	112	82	26.8%
case3 beam4	19	17	20	1800	103	75	27.2%	1800	99	78	21.2%	1800	103	79	23.3%
case3 beam5	15	19	20	1800	71	57	19.7%	1800	71	59	16.9%	1800	71	61	14.1%
case4 beam1	19	22	20	1800	105	88	16.2%	1800	105	93	11.4%	1800	106	92	13.2%
case4 beam2	13	24	20	1800	86	60	30.2%	1800	85	66	22.4%	1800	84	63	25.0%
case4 beam3	18	23	20	1800	89	76	14.6%	1800	91	80	12.1%	1800	90	82	8.9%
case4 beam4	17	23	20	1800	99	80	19.2%	1800	98	85	13.3%	1800	101	85	15.8%
case4 beam5	12	24	20	1800	85	66	22.4%	1800	85	71	16.5%	1800	86	72	16.3%
case5 beam1	15	16	20	1800	66	63	4.5%	1800	66	65	1.5%	217	66	66	0.0%
case5 beam2	13	17	20	875	58	58	0.0%	447	58	58	0.0%	15	58	58	0.0%
case5 beam3	14	16	20	1800	64	55	14.1%	1800	65	57	12.3%	1800	63	58	7.9%
case5 beam4	14	16	20	1800	63	58	7.9%	1800	64	59	7.8%	1800	62	60	3.2%
case5 beam5	12	17	20	180	49	49	0.0%	1800	52	49	5.8%	81	49	49	0.0%
Average gap							15.6%				12.9%				11.0%
# of optimally solved instances							3				1				7
# of best solutions							3				$\overline{7}$				18

Table 3: Results obtained by default CPLEX, tuned CPLEX and combinatorial Benders decomposition

Data					$L=5$						$L=15$		$L=20$					
Name	$\,m$	\boldsymbol{n}	CPU	UB	\mathbf{LB}	GAP	CPU	UB	LB	GAP	CPU	UB	LB	GAP	CPU	UB	LB	GAP
case1 beam1	15	14	$\mathbf{2}$	37	37	0.0%	5.9	50	50	0.0%	19.1	57	57	0.0%	130	63	63	0.0%
case1 beam2	11	15	1.3	29	29	0.0%	3.3	37	37	0.0%	12.3	42	42	0.0%	20	48	48	0.0%
case1 beam3	15	15	3.2	35	35	0.0%	13	43	43	0.0%	106.7	54	54	0.0%	373	56	56	0.0%
case1 beam4	15	15	7.4	33	33	0.0%	1017.9	45	45	0.0%	1800	57	53	7.0%	1800	59	55	6.8%
case1 beam5	11	15	1.9	26	26	0.0%	5.7	37	37	0.0%	24.2	45	45	0.0%	80	45	45	0.0%
case2 beam1	18	20	156.1	54	54	0.0%	1074.6	76	76	0.0%	1800	95	86	9.5%	1800	102	92	9.8%
case2 beam2	17	19	33.6	55	55	0.0%	1266.6	71	71	0.0%	1800	81	79	2.5%	1800	95	84	11.6%
case2 beam3	18	18	42.5	52	52	0.0%	1800	73	70	4.1%	1800	85	76	10.6%	1800	95	81	14.7%
case2 beam4	18	18	155.5	59	59	0.0%	1800	87	81	6.9%	1800	100	84	16.0%	1800	109	88	19.3%
case2 beam5	17	18	34.6	52	52	0.0%	1800	69	64	7.2%	1800	77	69	10.4%	1800	88	76	13.6%
case3 beam1	22	17	467.5	57	57	0.0%	1800	90	73	18.9%	1800	117	79	32.5%	1800	117	82	29.9%
case3 beam2	15	19	59.9	34	34	0.0%	837.8	46	46	0.0%	1800	58	53	8.6%	1800	68	58	14.7%
case3 beam3	20	17	516.8	55	55	0.0%	1800	81	72	11.1%	1800	97	79	18.6%	1800	112	82	26.8%
case3 beam4	19	17	499.3	55	55	0.0%	1800	81	70	13.6%	1800	96	75	21.9%	1800	103	79	23.3%
case3 beam5	15	19	30.2	40	40	0.0%	310.6	54	54	0.0%	1800	63	57	9.5%	1800	71	61	14.1%
case4 beam1	19	22	69.5	64	64	0.0%	1800	85	83	2.4%	1800	98	90	8.2%	1800	106	92	13.2%
case4 beam2	13	24	293	50	50	0.0%	1800	67	59	11.9%	1800	76	61	19.7%	1800	84	63	25.0%
case4 beam3	18	23	57.8	50	50	0.0%	1800	68	67	1.5%	1800	79	74	6.3%	1800	90	82	8.9%
case4 beam4	17	23	127.2	54	54	0.0%	1800	75	74	1.3%	1800	90	79	12.2%	1800	101	85	15.8%
case4 beam5	12	24	94.8	49	49	0.0%	1800	66	64	3.0%	1800	78	69	11.5%	1800	86	72	16.3%
case5 beam1	15	16	1.9	42	42	0.0%	3.6	51	51	0.0%	7.1	64	64	0.0%	217	66	66	0.0%
case5 beam2	13	17	1.6	35	35	0.0%	4.5	49	49	0.0%	7.5	54	54	0.0%	15	58	58	0.0%
case5 beam3	14	16	23.4	35	35	0.0%	232	50	50	0.0%	1800	60	56	6.7%	1800	63	58	7.9%
case5 beam4	14	16	3.8	29	29	0.0%	48.9	56	56	0.0%	297.8	59	59	0.0%	1800	62	60	3.2%
case5 beam5	12	17	1.8	30	30	0.0%	4.3	39	39	0.0%	12.5	46	46	0.0%	81	49	49	0.0%
Average gap						0.0%				3.3%				8.5%				11.0%
# of optimally solved instances					25				14				8				$\overline{7}$	

Table 4: Results obtained by combinatorial Benders decomposition for different maximum intensity values

5 Conclusion

In this paper, we described two heuristics and an exact algorithm for the problem of finding optimal decomposition of IMRT fluence maps using rectangular apertures. Rectangular apertures can be formed by conventional jaws already integrated in IMRT devices and these devices do not need costly multi-leaf collimator (MLC) systems to be used in radiation therapy. Our algorithm is based on combinatorial Benders decomposition and it can be used to analyze the delivery efficiency of jaws-only treatment machinery. We tested the efficacy of our approach on a set of clinical problem instances and compared our results against the literature. Our results show that our approach is able to find higher quality solutions for most problem instances. We also compared our algorithm's results with direct solution of a mixed-integer programming formulation of the problem using both default solver parameters and a parameter set that is tuned for our set of problem instances. Our results reveal that solvability of the problem is significantly enhanced with our combinatorial Benders decomposition scheme.

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