Stochastic Local Search Algorithms for the Direct Aperture Optimisation Problem in IMRT

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Abstract. In this paper, two heuristic algorithms are proposed to solve the direct aperture optimisation problem (DAO) in radiation therapy for cancer treatment. In the DAO problem, the goal is to find a set of deliverable aperture shapes and intensities so we can irradiate the tumor according to a medical prescription without producing any harm to the surrounding healthy tissues. Unlike the traditional two-step approach used in intensity modulated radiation therapy (IMRT) where the intensities are computed and then the apertures shapes are determined by solving a sequencing problem, in the DAO problem, constraints associated to the number of deliverable aperture shapes as well as physical constraints are taken into account during the intensities optimisation process. Thus, we do not longer need any leaves sequencing procedure after solving the DAO problem. We try our heuristic algorithms on a prostate case and compare the obtained treatment plan to the one obtained using the traditional two-step approach. Results show that our algorithms are able to find treatment plans that are very competitive when considering the number of deliverable aperture shapes.

Keywords: Intensity modulated radiation therapy
Direct Aperture Optimisation · Multi-leaf collimator sequencing

1 Introduction

Intensity modulated radiation therapy (IMRT) is one of the most common techniques in radiation therapy for cancer treatment. Unfortunately, the IMRT planning problem is an extremely complex optimisation problem. Because of that, the problem is usually divided into three sequential sub-problems, namely, beam angle optimisation (BAO), fluence map optimisation (FMO) and multi-leaf collimator (MLC) sequencing. In the BAO problem, the aim is to find the optimal beam angle configuration (BAC), i.e. the BAC that leads to the optimal treatment plan. To find this optimal treatment plan, the intensities for the given

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BAC, need to be computed (FMO problem). Finally, the MCL sequencing problem must be solved to find the set of deliverable aperture shapes and intensities of the MLC during the delivery process [10].

One problem of this sequential approach is that, once the FMO problem is solved, i.e., we have computed the optimal intensities for a given BAC, we need to determine a set of apertures for the MLC such that the optimal intensities can be delivered to the patient. Although there exist exact approaches that minimise the time a patient is exposed to the radiation (*beam-on time*) and heuristic algorithms that are very efficient minimising the number of apertures (*decomposition time*), solutions of the MLC sequencing problem usually require too many deliverable aperture shapes and long beam-on times, which is something that we want to avoid as it means patients should stay longer on the treatment couch and fewer patients can be treated per day. In order to reduce the number of apertures and the beam-on time, treatment planners usually simplify the treatment plan by rounding the intensities at each beam angle to some predefined values. Although this (over-)simplification of the optimal plan allows us to deliver a treatment plan using fewer deliverable aperture shapes and shorter beam-on times, the quality of the treatment plan is impaired w.r.t. the optimal one. Thus, it seems reasonable to incorporate some MLC sequencing considerations into the FMO problem such that the optimal intensities found during its optimisation process can be directly delivered to the patient without needing any 'adjustment' process.

In this paper we focus on solving the *direct aperture optimisation* problem (DAO), that is, the problem of optimising the intensities and shapes of the apertures simultaneously, for a specific BAC. In other words, we aim to solve the FMO problem taking into account a constraint on the number of deliverable apertures and the physical constraints associated with the MLC sequencing. In this way, any post-processing on the intensities found by the solver is needed.

First, let us introduce the mathematical model of the FMO problem [3]. Consider that each beam angle is associated with a series of sub-beams or *beamlets* and n is the total number of beamlets summed over all the possible beam angles. Let $\mathscr{A}$ be a BAC and $x \in \mathbb{R}^n$ be an intensity vector or *fluence map* solution. Each component x_i of a solution represents the length of time that a patient is exposed to the *beamlet* i. The set $\mathcal{X}(\mathscr{A}) \subseteq \mathbb{R}^n$ is the set of all feasible solutions of the FMO problem when the BAC $\mathscr{A}$ is considered[1]. Finally, $z(x) : \mathbb{R}^n \to \mathbb{R}^*_+ := \{v \in \mathbb{R} : v \geq 0\} \cup \{\infty\}$ is a function that attempts to penalize both: (1) zones where the tumor would not be properly irradiated according to the medical prescription and (2) healthy tissues that would be harmed by the fluence map x. Thus, solving the FMO problem for a given BAC $\mathscr{A}$ consists on finding the fluence map $x \in \mathcal{X}(\mathscr{A})$ that minimises the penalty $z(x)$.

The main difference of DAO w.r.t. the FMO problem is related to the set of feasible intensity vectors $\mathcal{X}(\mathscr{A})$. For the DAO problem we need to add some additional constraints to the set $\mathcal{X}(\mathscr{A})$. In particular, we first need to set the

[1] i.e., only beamlets x_i that belong to a beam angle in $\mathscr{A}$ are allowed to be greater than zero.

number of apertures $\Theta_{\mathscr{A}_i}$ for each beam $\mathscr{A}_i \in \mathscr{A}$ with $i = \{1, \ldots, N\}$. Then, we have to ensure that the beamlets intensities can be delivered given the number of apertures for each beam angle $\theta^{\mathscr{A}_i}$. We denote this new set of feasible intensity vectors as $\mathcal{X}(\mathscr{A}, \Theta)$.

The DAO problem was first introduced by [13]. In their paper, the authors identify as input for the DAO problem the beam angles, the beam energies and the number of apertures per beam angle, while the decision variables are the leaf positions for each aperture and the weight assigned to each aperture. They propose to solve the problem by adjusting the leaf position at each iteration following a set of rules that determine, using a probabilistic function, which pair of leaves should be adjusted next. Authors consider a function similar to the one we use in this paper. The DAO problem is also considered in [15]. Unlike previous approaches, [15] proposes a "rapid" DAO algorithm which replaces the traditional Monte Carlo method for dose calculation by what they call a dose influence matrix based piece-wise aperture dose model. The authors claim that their approach is faster than traditional approaches based on Monte Carlo as well as able to find treatment plans that result in more precise dose conformality. In [2], authors focus on the DAO problem as a mean of reducing the complexity of IMRT. Authors define the complexity of a treatment plan in IMRT in terms of the number of *monitor units* (MU) a plan needs to be delivered. Since the DAO problem gives control over the number of apertures (and therefore over the number of MUs), authors claim that they can reduce the complexity of treatment plans without any major impairment on the overall quality of the delivered treatment plan. A similar conclusion is drawn by [8,11,13,15].

The main goal of our work is to study and evaluate the design and application of hybrid algorithms combining the best features of local search techniques and FMO models to generate high-quality treatment plans that exhibit characteristics that make them candidates to be applied in real cases. As a first step towards this goal, the work presented in this paper studies the application of two simple stochastic local search algorithms to solve the DAO problem. We apply these algorithms on a simple prostate case considering two organs at risk, namely, the bladder and the rectum. We compare treatment plans obtained by our algorithms with those obtained by well-known FMO models. We compare these treatment plans in terms of their corresponding dose-volume-histograms as well as in terms of their objective function value in order to evaluate their quality and their practical desirability.

The remaining of this paper is organized as follows: Sect. 1.1 introduces the general concepts of IMRT as well as the mathematical models we will consider in this study. In Sect. 2 the algorithms we implement in this paper are presented and their main features discussed. Section 3 presents the prostate case algorithms are applied on and the obtained results. A discussion on these results is also included in this section. Finally, in Sect. 4 we draw the main conclusions of our work as well as outline future work.

1.1 IMRT: An Overview

In this section we briefly introduce some key concept in IMRT. This section is mainly based on the IMRT description given in [3–6,10].

In IMRT, each organ is discretised into small sub-volumes called *voxels*. The radiation dose deposited by a fluence map x into each voxel j, denoted by d_j^r, of the tumor and each organ at risk (OAR), is calculated using expression (1) [10].

$$d_j^r(x) = \sum_{i=1}^{n} A_{ji}^r x_i \quad \forall j = 1, 2, \ldots, m^r, \tag{1}$$

where $r \in R = \{O_1, \ldots, O_Q, T\}$ is an element of the index set of regions, with the tumor indexed by $r = T$ and the organs at risk and normal tissue indexed by $r = O_q$ with $q = 1, \ldots, Q$. m^r is the total number of voxels in region r, j corresponds to a specific voxel in region r, $d^r \in \mathbb{R}^{m^r}$ is a dose vector and its elements d_j^r give the total dose delivered to voxel j in region r by the fluence map $x \in X(\mathscr{A}, \theta)$. Here, dose deposition matrix $A^r \in \mathbb{R}^{m^r \times n}$ is a given matrix where $A_{ji}^r \geqq 0$ defines the rate at which radiation dose along beamlet i is deposited into voxel j in region r.

Based on the dose distribution in (1), both physical (*dose-volume*) and biological (*dose-response*) models have been proposed (see [10] for a survey). Here, the following dose-volume model of the FMO problem is considered:

$$\min_{x \in X(\mathscr{A}, \Theta)} z(x) = \sum_{q=1}^{Q} \left(\frac{1}{m^{O_q}} \times \sum_{j=1}^{m^{O_q}} (\max(d_j^{O_q} - D^{O_q}, 0)^2)\right) + \left(\frac{1}{m^T} \times \sum_{j=1}^{m^T} (\max(D^T - d_j^T, 0)^2)\right) \tag{2}$$

where parameters D^T and D^{O_q} correspond to the prescribed dose values for tumor and OARs, respectively. This problem is a convex optimisation problem and, thus, optimal fluence maps can be obtained using mathematical programming techniques.

2 Stochastic Local Search Algorithms for DAO

In this section we present two stochastic local search algorithms to solve DAO. For a given BAC $\mathscr{A}$, and subject to a maximum number of apertures for each beam angle, the algorithms attempt to find a set of aperture shapes for each angle in $\mathscr{A}$ such that the corresponding fluence map x minimizes $z(x)$. Both algorithms follow an iterative improvement scheme and they diverge in the representation they use to search the aperture shapes and intensities.

The algorithmic scheme followed by the proposed techniques is outlined in Algorithm 1. The algorithm receives as input the maximum number of apertures per beam angle (ASIZE), the number of target beamlets (BSIZE), the number of target voxels (VSIZE), the perturbation size (PSIZE), the number of steps without improvement to perform a perturbation (N_RESTART), the aperture pattern initial setup (AP_SETUP), the budget available for the search (BUDGET), and other parameters related to the search strategy instantiated in the algorithm (...).

The idea of the algorithm is simple. An initial configuration or plan S of aperture shapes and intensities for each beam angle is generated (line 2). x_S denotes the fluence map generated by the plan S. Then the algorithm identifies one of the BSIZE beamlets b impacting the most to a subset of the VSIZE *worst* voxels of the organ (resp. tumor) (line 8), i.e., a subset of the voxels with the largest (resp. smallest) deposited doses of radiation. Then, we attempt to improve the current plan by modifying the apertures and intensities related to the selected beamlet (line 9). If the change improves the quality of S, then it is accepted, otherwise we try with another beamlet and the process is repeated. When all selected beamlet modifications have been evaluated without finding an improvement to the current plan or when N_RESTART iterations without an improvement have been reached, a perturbation of size PSIZE is applied (line 7 and line 17). Finally, the best plan found is returned.

```
1  IterativeImprovement (ASIZE,BSIZE, VSIZE,PSIZE, N_RESTART,AP_SETUP,
   BUDGET, ...); out: Sbest
2  S ← initializeangles (AP_SETUP);
3  Sbest ← S;
4  no_improvement ← 0;
5  while !termination(BUDGET) do
6      while improvementExhauted(BSIZE,VSIZE,S) do
7          S ← perturbation(S, PSIZE);
8      (b, angle) ← select_promising_beamlet (S, BSIZE, VSIZE);
9      S' ← search(b, angle, S, ...);
10     no_improvement ← no_improvement + 1;
11     if z(x_S') < z(x_S) then
12         no_improvement ← 0;
13         S ← S';
14     if z(x_S) < z(x_Sbest) then
15         Sbest ← S;
16     if no_improvement ≥ N_RESTART then
17         S ← perturbation(S, PSIZE) ;
18 return Sbest
```

Algorithm 1. Iterated improvement outline of the proposed techniques.

2.1 Selecting a Promising Beamlet

The procedure select_promising_beamlet(S, BSIZE,VSIZE) returns one of the BSIZE beamlets impacting the most to a subset of VSIZE voxels of the organs/tumor. In the following, we give details about how these beamlets (and voxels) are selected.

Consider a current fluence map x. From Eqs. (1) and (2) we can deduce that the change in the evaluation of $z(x)$ provided by increasing or decreasing the intensity of a beamlet i in 1 is approximately:

$$\Delta_z(i) = \sum_{(j,r)\in V} A^r_{ji} \frac{\partial z}{\partial d^r_j}(x)$$

where V is the set of all the pairs (voxel, organ) of the problem. Thus, we consider that the most promising beamlets are those beamlets maximizing $|\Delta_z(i)|$. However, given that computing $\Delta_z(i)$ is expensive, mainly due to $|V|$ is very large (of the order of tens of thousands), we only consider a subset of VSIZE representative voxels.

We rank the voxels according to how much the objective function changes if we increase (or decrease) the radiation dose deposited in the voxel. The rate of change is given by $\left|\frac{\partial z}{\partial d^r_j}(x)\right|$, and the voxels are kept sorted by this value in a set V. The procedure select_promising_beamlet then uses the first VSIZE voxels from V for identifying the BSIZE beamlets maximizing $|\Delta_z(i)|$. Finally, one of these beamlets is randomly selected and returned by the procedure.

2.2 Representation of the DAO Search Space

We propose two different approaches for representing the search space of the problem. An *intensity-based representation* which defines a matrix of intensities for each angle maintaining the constraints related to the apertures. And an *aperture-based representation* which defines a set of aperture shapes for each angle and assigns an intensity to each of these shapes. In the following we provide more details for each representation.

Intensity-Based Representation: The set of aperture shapes of each angle is represented by a single intensity integer matrix I. Each value I_{xy} in the matrix corresponds to the total intensity delivered by the corresponding beamlet and the set of apertures. In order to respect the limit of allowed aperture shapes we force the matrix to respect two conditions:

- The number of different intensities n in the matrix cannot be greater than the maximum number of allowed aperture shapes.
- For each row, consider that the k-th beamlet has the greatest intensity. Then, the intensities of beamlets $\{1, 2, .., k\}$ should increase monotonically and the intensities of beamlets $\{k, k+1, .., x_{max}\}$ should decrease monotonically.

If the intensity matrix I satisfies the two conditions, it is easy to map I to a set of n aperture shapes. Consider the intensity matrix of Fig. 1. It has $n = 5$ different intensities: $\mathcal{Y} = \{1, 2, 4, 7, 8\}$ and each row satisfies the second condition. In order to obtain the intensities of the matrix we can consider the following five aperture shapes:

– An aperture of intensity 1 considering every beamlet (x, y) such that $I_{xy} \geq 1$.
– An aperture of intensity 1 considering every beamlet (x, y) such that $I_{xy} \geq 2$.
– An aperture of intensity 2 considering every beamlet (x, y) such that $I_{xy} \geq 4$.
– An aperture of intensity 3 considering every beamlet (x, y) such that $I_{xy} \geq 7$.
– An aperture of intensity 1 considering every beamlet (x, y) such that $I_{xy} \geq 8$.

Note that, in general, we should consider every aperture with intensity $\mathcal{Y}_i - \mathcal{Y}_{i-1}$ and beamlets (x, y) such that $I_{xy} \geq \mathcal{Y}_i$. Also note that the sum of intensities of the apertures (beam-on time) is equal to the maximum intensity in the matrix $(1 + 1 + 2 + 3 + 1 = 8$ in the example).

0	0	1	1	7	7	7	8	7	2	1	0	0	0
0	0	0	0	0	1	4	4	7	7	7	7	8	0
0	0	0	1	4	7	7	7	8	8	1	0	0	0
1	1	1	1	1	2	2	2	2	2	2	2	7	7
8	7	4	2	2	1	0	0	0	0	0	0	0	0

Fig. 1. An intensity matrix representing a set of five aperture shapes.

Aperture-Based Representation: We directly represent the aperture shapes of an angle as a set of n apertures $A = \{a_1, \ldots, a_n\}$, where each element is a list $a_i = \{(x_1, y_1), \ldots, (x_r, y_r)\}$, $x_j, y_j \in \{1, \ldots, c_j\}$, and $x_j \leq y_j, \forall j \in \{1, \ldots, r\}$, r is the number of rows in a beam of the MLC, and c_j is the number of active beamlets in row j. The set a indicates the range of beamlets that are open per each row of the beam. An intensity value $I[i] \in \{1, \ldots, \text{max\_}i\}$ is assigned to each of these aperture shapes, where max_i is the maximum intensity allowed for a beam/aperture. All open beamlets in an aperture a_i emit radiation with the same intensity $I[i]$. Figure 2 shows an example of this representation using 5 aperture shapes for the matrix presented in Fig. 1. Searching this representation has the benefit that the generated solutions inherently satisfy the constraints associated to the number of apertures. Nevertheless, the complex dependencies of the aperture shapes and the delivered radiation dose difficult the optimisation and thus, effectively searching the solution space depends greatly of the technique applied.

2.3 Intensity-Based Beamlet Targeted Search

When the intensity-based representation is used, the search method of the algorithm attempts to increase (or decrease) the intensity of a subset of contiguous beamlets of the angle. Algorithm 2 shows the procedure. Note that, in addition to the angle, the beamlet and the current solution, the procedure also gets some user-defined parameters as input. First, the values *delta_intensity*

```
a1 = {( 3,10), ( 6,13), (4, 4), ( 1, 5), (1,1)}, I[1]=1
a2 = {( 5, 9), ( 7,13), (6,10), ( 6,14), (1,3)}, I[2]=2
a3 = {( 5, 9), ( 9,13), (5,10), (13,14), (1,2)}, I[3]=4
a4 = {(10,11), (13,13), (6,11), (14,14), (1,6)}, I[4]=1
a5 = {( 8, 8), ( 7, 8), (9,10), (13,13), (3,5)}, I[5]=1
```

Fig. 2. Aperture-based representation for angle intensity matrix in Fig 1.

and a are randomly selected from an uniform distribution). Then, the procedure increaseIntensity attempts to increase in *delta_intensity* the intensity of a square $a \times a$, including the beamlet, and its surrounding beamlets. Note that if $a = 1$ the intensity of only one beamlet will be modified.

Note that the values of the parameters MAX_A and MAX_D progressively decrease as the search goes on (providing that $\alpha < 1$). This mechanism forces larger changes at the beginning of the search and smaller changes at the end. The procedure returns the new modified solution S'.

search $(b, angle, S, \alpha$,MAX_D,MAX_R,); **out:** S'
delta_intensity $\leftarrow$ random(1,MAX_D);
MAX_D $\leftarrow$ α*MAX_D;
$a \leftarrow$ random(1,MAX_R);
MAX_R $\leftarrow$ α*MAX_R;
$S' \leftarrow$ increaseIntensity$(S, b, angle, delta_intensity, a)$;
return S';

Algorithm 2. Search procedure for the intensity-based representation.

Increasing/Decreasing Intensities in the Matrix: In Algorithm 2, the procedure increaseIntensity *attempts* to increase the intensity of a square of beamlets in *delta_intensity* units. The procedure increases the intensities directly in the intensity matrix and then it runs a two-phase reparation mechanism for re-satisfying the conditions of the intensity-based representation.

In the first phase we perform a reparation related to the second condition. The procedure repairs each row independently. If *delta_intensity* is positive we may arrive to a situation as in Fig. 3-left. The figure shows the intensities (y axis) of all the beamlets of a row (x axis). The intensity of red beamlets has increased violating the second condition. For repairing the row we first identify the beamlet with the largest intensity b. Then we *increase* the intensities of some beamlets (green beamlets in Fig. 3-right) to force the intensities on the left side of b to increase monotonically and the intensities on the right side of b to decrease monotonically. As a result we obtain the intensity distribution in Fig. 3-right.

In the case that *delta_intensity* is negative we also identify the beamlet b with the largest intensity and force the intensities of the left and the right side of b to increase or decrease monotonically depending on the case. However, in this case this is achieved by *reducing* the intensities of some beamlets.

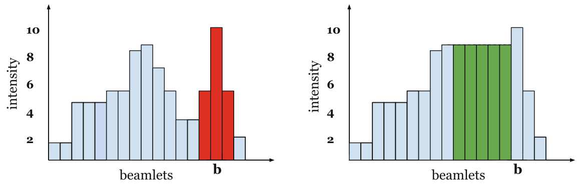

Fig. 3. Example of the reparation mechanism when the intensity of some beamlets *increases*. (left) The intensities in red increased. (right) The reparation mechanism modified the intensities in green. (Color figure online)

In the second phase of the reparation mechanism, called *aperture-reduction*, the first condition is treated. If the number of different intensity values is larger than the maximal number of aperture shapes allowed then we try to reduce this number with the following procedure:

– We consider the set of different intensities $\mathcal{Y}$, where $\mathcal{Y}_0 = 0$.
– We consider that changing an intensity I_{xy} in c units has a cost of c.
– For each value $\mathcal{Y}_i$ ($i \geq 1$), we compute the cost of changing all the intensities $I_{xy} = \mathcal{Y}_i$ by $\mathcal{Y}_{i-1}$ and by $\mathcal{Y}_{i+1}$.
– We perform the change with the minimum cost.
– The process is repeated until the number of different intensities is equal to the number of maximal number of apertures allowed.

Consider the intensity matrix of Fig. 1 and suppose that the maximal number of apertures allowed is 4. The set of intensities is $\mathcal{Y} = \{0, 1, 2, 4, 7, 8\}$. There are 11 beamlets with intensity equal to 1, thus changing its intensities to 0 (or 2) has a cost of 11. Changing the 2s to 1s has a cost of 10. Changing the 4s to 2s has a cost of $4 \cdot 2 = 8$. Changing the 7s to 8s has a cost of 14 and changing the 8s to 7s has a cost of 5. Thus, we will prefer to perform the last change transforming the matrix into the intensity matrix of Fig. 4.

0	0	1	1	7	7	7	7	7	2	1	0	0	0
0	0	0	0	0	1	4	4	7	7	7	7	7	0
0	0	0	1	4	7	7	7	7	7	1	0	0	0
1	1	1	1	1	2	2	2	2	2	2	2	7	7
7	7	4	2	2	1	0	0	0	0	0	0	0	0

Fig. 4. The matrix of Fig. 1 reduced to a set of four aperture shapes.

Perturbation: In the case of the intensity-based representation, the perturbation method performs PSIZE times the following two steps:

– Select a random angle

– Reduce the number of intensities in the angle matrix by performing the aperture-reduction procedure.

This method has a two-fold objective: one is to perturb the current solution in order to explore other regions in the search space, the other to reduce the number of apertures without affecting too much the cost of the objective function.

2.4 Aperture-Based Beamlet Targeted Search

When searching the aperture-based representation the proposed algorithm attempts to either increase or decrease the contribution of radiation of the targeted beamlet by (1) opening/closing the beamlet in the apertures of the angle, or (2) by modifying the intensity of the apertures in which the beamlet is active (not closed). Algorithm 3 gives the outline of the search procedure for the aperture-based representation. The procedure starts by obtaining the minimum delta allowed to modify the intensity of an aperture (line 1). Each iteration, a random aperture of the selected angle is targeted in order to attempt improving the objective function of the treatment plan by either modifying its aperture shape or its intensity. When it is possible to perform both operations, the modification of the aperture intensity is selected with probability P_INT (line 8). As soon an improving solution is obtained, the algorithm returns it to re-start the process with a different beamlet. The aperture shapes are modified in line 11 and line 17. When the radiation must be reduced for the selected beamlet, if possible, we evaluate to close the beamlet by moving the right and the left leaf. Note that this implies that the procedure evaluates two modifications in some cases.

```
1  search (angle, beamlet, S); out: S′ δ ← getMinDelta(angle, beamlet, S);
2  S′ ← S;
3  for a in randomOrder(angle.A) do
4      open ← isOpen(angle, beamlet, a);
5      if δ < 0 then
6          if !open then next;
7          if S.I[a][beamlet] + δ < 0 then  δ = −S.I[a][beamlet];
8          if rand() <P_INT  then
9              S′ ← modifyIntensity(angle, S, a, δ);
10         else
11             S′ ← modifyAperture(angle, beamlet, S, a, δ);
12     else
13         if S.I[a][beamlet] + δ > MAX_P then  δ =MAX_P−S.I[a][beamlet] ;
14         if  open then
15             S′ ← modifyIntensity(angle, S, a, δ);
16         else
17             S′ ← modifyAperture(angle, beamlet, S, a, δ);
18     if z(x_S′) < z(x_S) then  return (S′);
19     ;
20     S′ = S;
21 return S′
```

Algorithm 3. Search procedure for the aperture-based representation.

Fig. 5. Prostate case considered in this study. Two OARs (bladder and rectum) are considered. (Color figure online)

Perturbation: The perturbation procedure implements an operator that changes PSIZE times the initial solution S by randomly choosing, with probability 0.5, to modify the intensity of a randomly selected aperture a or modifying the aperture shape in a by opening or closing a randomly selected beamlet.

3 Experiments

A clinical prostate case obtained from the CERR package [7] has been considered in this study. Figure 5 shows a transversal view of this case. Boundaries of the target volume (tumor + margin in green), rectum (in light blue) and bladder (in yellow) are highlighted as the regions of interest in this study. We label the rectum and the bladder as *organs at risk* (OARs). The total number of voxels is about 56,000. The number of decision variables (beamlets) depends on the BAC and ranges between 320 and 380. The number of beam angles N considered in a BAC is equal to 5. The dose deposition matrix A^r is given for each BAC. We consider 72 beam angles, all of which are on the same plane. Just as in [4,6], we consider a set of 14 equidistant BACs to make our experiments.

We compare the algorithms described before to the sequential approach commonly used in clinical practice. That is, we first optimise the intensities (i.e. to solve the FMO problem) and then we find the set of deliverable apertures corresponding to the optimal intensities (i.e. to solve the MLC sequencing problem). While to solve the FMO problem we use the IPOPT solver [14], to solve the MLC sequencing problem we use the algorithm proposed in [1]. This algorithm finds a set of apertures delivering the optimal intensities and minimizing the beam-on time.

3.1 Parameter Configuration

In order to properly compare the proposed algorithms, we configure the parameter values of the intensity-based and aperture-based approaches using irace [12]. Each DAO algorithm run is allowed 60 seconds of execution time. The budget provided to irace for searching the parameter space of the algorithms was 1 000 evaluations and the configuration process was performed over 7 equidistant IMRT instances using default irace settings. The parameter settings obtained by irace, and used in the following experiments, are given in Table 1.

Table 1. Parameters settings obtained by irace (With the exception of N_RESTART which was set manually to 100 iterations) for the aperture-based algorithm (ABLS) and the intensity-based algorithm (IBLS).

Parameter	ABLS	IBLS	Parameter	ABLS	IBLS
BSIZE	7	45	P_INT	0.01	–
VSIZE	34	92	MAX_DELTA	–	15
PSIZE	6	6	α	–	0.99
Initial setup	`open-min`	`open-min`	MAX_RATIO	–	5
N_RESTART*	100	100			

3.2 Initialisation Method

The proposed algorithms have an intensifying nature due to the beamlet selection heuristic and the acceptance of only improving solutions. The initialisation setup of the aperture shapes and the intensities can influence the performance of the algorithms given that they provide the initial point from which solutions are repaired and improved. In the following experiments we evaluate the effect of the initialisation strategy on the performance of the proposed algorithms. For the aperture shapes we define 3 types of initial setup: (`open`, `closed`, `random`). The `open` setup initialises all the beamlets in the apertures open, `closed` does the opposite by initialising all beamlets as closed, and `random` initialises the aperture shapes randomly. The intensities can be initialised to the minimum intensity allowed (`min`), the maximum intensity (`max`), or a random (`rand`) value between the permitted minimum and maximum intensity. Table 2 gives the mean results obtained using the different initialisation approaches. In both algorithms the best mean results are obtained by the `open-min` strategy and the worst results are obtained by `open-max`. We note that the results of the `closed-min` strategy are not significantly different from the results of `open-min` for the intensity-based algorithm (p-value = 0.54). This hints that the selection of the most promising beamlet heuristic and the proposed search procedures benefit of a low initial intensity that will be iteratively increased during the search. Oppositely, repairing a treatment plan initialized with high intensities appears to be a more difficult scenario to tackle for these techniques.

Table 2. Mean value of $z(x)$ obtained by 30 repetitions of the algorithms using different initialisation strategies across the set of 14 BACs. The best mean results are shown in bold and results that are not significantly different to the bests mean results are shown in cursive (Wilcoxon signed-rank test with Bonferroni correction, $\alpha = 0.05$).

	`open-min`	`open-max`	`closed-min`	`rand`
IBLS	**55.2**	85.1	*55.6*	56.2
ABLS	**70.3**	137	98.8	91.0

3.3 Comparison of Performance

Table 3 shows a comparison between the different proposed strategies and the IPOPT solver which solves the FMO problem to optimality. The first column shows the BAC for which the intensities and deliverable apertures are computed. Columns 2–7 show the mean cost, the standard deviation (SD) and the mean beam-on time (BOT) found by the proposed intensity-based (IBLS) and aperture-based (ABLS) strategies considering a maximum of 5 apertures per beam angle, that is, a total of 25 deliverable aperture shapes per BAC. Each heuristic algorithm was run 30 times with a budget of 40 seconds on each instance. Columns 8–10 show the optimal cost for the FMO problem found by the IPOPT solver, the minimal beam-on time of the optimal solution found and a *lower bound* for the number of the aperture shapes required. The latter two values were reported by the MLC sequencing algorithm proposed in [1].

The results obtained by the proposed techniques are worst, in terms of the evaluation function, when compared to the optimal solution of the FMO problem. Nevertheless, the average beam-on time and number of aperture shapes required by this optimal solution are considerable larger. Large number of apertures and large beam-on times result in long treatment times which are undesirable from a practical perspective[2]. In particular, the significantly better beam-on time reported by IBLS is mainly due to the conditions imposed by the matrix representation of the intensities. For each angle, this matrix can be easily mapped to a small set of apertures with a total beam-on time equal to the maximum beamlet intensity in the matrix.

The solutions obtained by the intensity-based algorithm are competitive w.r.t the rounded solutions as they further reduce the beam-on time and number of aperture shapes increasing the applicability of the treatment plan and producing a smaller worsening of the evaluation function compared to the aperture-based technique. An important aspect of the desirability of treatment plans is the radiation dose distribution in the organs and tumours.

Figure 6 shows an example of dose distributions for an instance and the three strategies using their best configurations. Each curve represents an organ (the

[2] Even disregarding the impact on the clinical schedule, long treatment times are uncomfortable for the patients and carry an increased risk of intra-fraction motion, which may compromise plan quality [9].

Table 3. Mean results ($z(x)$), standard deviation (SD) and beam-on time (BOT) obtained by the intensity-based and aperture-based algorithms (IBLS and ABLS resp.), the FMO problem optimal solution evaluation (IPOPT, $z(x^*)$), the corresponding beam-on time and a lower bound for the required number of apertures (#ap).

Instances	IBLS			ABLS			IPOPT		
	$z(x)$	SD	BOT	$z(x)$	SD	BOT	$z(x^*)$	BOT	$\#ap$
0-70-140-210-280	55.2	2.16	85	77.6	7.46	114	41.3	204	40
5-75-145-215-285	55.8	2.78	85	73.8	5.28	148	41.6	188	39
10-80-150-220-290	55.7	3.84	88	73.7	7.37	148	41.8	216	39
15-85-155-225-295	54.9	2.96	87	69.1	6.73	143	41.7	220	39
20-90-160-230-300	55.5	2.98	87	68.6	5.4	111	41.8	194	37
25-95-165-235-305	54.4	2.51	85	67.4	6.24	116	42.3	242	38
30-100-170-240-310	54.2	2.71	84	64.6	3.67	120	42.4	218	40
35-105-175-245-315	55.3	2.22	84	68.3	5.69	125	42.0	206	38
40-110-180-250-320	55.6	3.24	87	72.4	5.61	136	42.3	222	39
45-115-185-255-325	56.2	2.76	86	70.7	5.32	156	43.0	208	41
50-120-190-260-330	55.6	3.26	84	72.8	6.6	131	42.9	222	41
55-125-195-265-335	55.3	2.74	85	69.7	5.38	130	42.4	210	40
60-130-200-270-340	54.2	2.44	83	68.1	5.84	138	42.7	238	39
65-135-205-275-345	54.8	2.6	86	67.3	4.99	119	41.4	236	39
Average	**55.2**	**2.8**	**86**	**70.3**	**5.83**	**131**	**42.1**	**216**	**39.2**

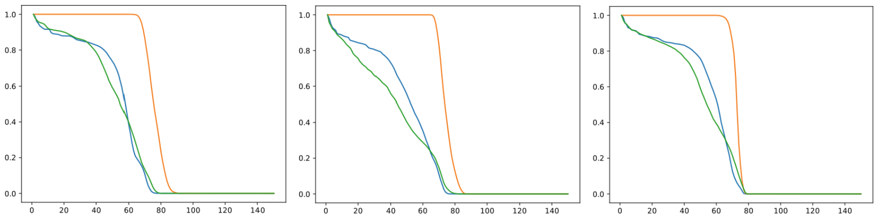

Fig. 6. Dose distributions of the instance 0-70-140-210-280 obtained by using IPOPT (left) the intensity-based strategy (middle) and the aperture-based one (right). (Color figure online)

yellow one corresponds to the tumor). Points (x, y) in each curve indicate that, related to the organ (or tumor), the $y\%$ of its voxels receive a radiation dose of at most x. Thus, it is desirable that the organ curves quickly decline to $y = 0$, while the tumor curve should remain high until the prescribed dose is reached.

Note that the dose distribution curves of the intensity-based strategy are quite similar to the ones reached by IPOPT. While, the tumor curve is slightly to the left, the organs clearly receive smaller radiation doses. On the other hand, in the aperture-based strategy the tumor reaches a dose closer to the prescribed dose but, as a result, the organs are affected to a greater extent by the radiation. Finally, highlight that, as our methods are stochastic, they may be able to offer different alternative treatments depending on the random number sequence.

4 Conclusions

In this paper we have introduced two novel heuristic algorithms to solve the DAO problem in radiation therapy for cancer treatment. Proposed heuristics are able to find a set of deliverable aperture shapes and intensities for each beam angle of a given BAC within a clinically acceptable time. Further, despite the heuristic algorithms were allowed to use only 5 apertures shapes per beam angle, they were able to find very competitive treatment plans.

We compare the heuristic algorithms to the traditional two-step approach where the optimisation of the intensities is performed first and then the sequencing problem is solved given an optimal intensity map. Results show that delivering the optimal plan would require more than two times the number of deliverable aperture shapes than our heuristic methods. These promising preliminary results encourage us to keep working on this research field.

As future work we want to include other criteria within our proposed framework, such as clinical markers. The collaboration of both techniques to solve DAO and the integration of the FMO problem model to use the optimal solution to guide this search is also part of our future work. Moreover, we also want to integrate to the proposed framework the beam angle optimisation problem, so we can (approximately) solve the whole IMRT problem in an integrated way.

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