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Radiation Therapy Treatment of Breast Cancer

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## Table of Contents

Cover.....	1
SF 298.....	2
Table of Contents.....	3
Introduction.....	4
Key Research Accomplishments.....	4
References.....	9
Appendices.....	

## **I Introduction:**

The implementation of inverse planning technique is essential to the realization of the potential of intensity modulated radiation therapy (IMRT). The most popular inverse planning techniques currently used fall into two distinct categories: 1) beamlet-based inverse planning and 2) aperture-based inverse planning. In beamlet-based planning, each field (a gantry angle – energy combination) is divided into a matrix of beamlets whose weights are optimized independently. The optimization therefore yields an intensity map which is then translated into a sequence of leaf aperture shapes before being delivered. There are several problems associated with beamlet-based inverse planning. First, optimized intensity maps are often converted into a series of discrete levels in an attempt to make the sequencing easier. However this step also introduces some quantization errors and therefore results in loss of treatment plan quality. Second, leaf sequencing is constrained by hardware-related factors and therefore often requires a large number of complex field shapes to deliver a given intensity map, thereby decreasing the overall efficiency. Third, since the leaf sequencing step is excluded from the intensity-map optimization therefore all the delivery-related effects such as leakage, the tongue-and-groove design and head scatter are not taken into account when choosing an intensity map. Efforts to include these effects have also introduced significant additional complexity. Aperture-based optimization is designed to reduce the complexity of IMRT treatment plans and is flexible enough to easily include delivery-related effects. In particular, aperture optimization requires no leaf sequencing and apertures are guaranteed to satisfy delivery constraints. It is therefore a promising alternative to beamlet-based IMRT. In this work, we consider a method of contour-based treatment planning in which, unlike in Direct Aperture Optimization (DAO), the aperture shapes are initially chosen to be the Beam Eye's View (BEV) of the target and the critical structures, and therefore are given as constants in the optimization process. The obvious advantage of this method with regard to DAO is that the only parameters that need be optimized are the fields' weights, and the plan is not optimized over all the possible aperture shapes. Our hope is naturally that optimal aperture shapes are somewhat close to the BEV and that making this choice will save a significant amount of computation time.

## **II Research and Accomplishments**

We now turn to the description of the optimization algorithm. The point of the following optimization scheme is to find the beamlet weights that will deliver a dose conformation that is as close to the prescription as possible. A natural way is to use an iterative approach in order to find the optimal plan: an initial plan is evaluated, adjustments are made, the plan is reevaluated, further adjustments are made, and so on until some convergence criterion is met. In order to evaluate a treatment plan, we need to be able to assess 'how far' it is from the prescription. This evaluation can be made by condensing the quality of a plan into a single value. This value is referred to as the objective function and naturally depends on the choice of criteria that was made to compute it. The objective function is therefore a mathematical function that takes as its input the dose distribution of both the evaluated plan and the prescription. Once we have determined the criteria that define the objective function, we can easily compare two possible treatment plans by comparing the values of their respective objective functions.

In the following approach, the objective function is chosen to be roughly the sum of the squared differences between the prescription and the delivered doses at different measurement points in different structures. We naturally want to achieve a plan whose objective function is as small as possible (since a small objective function indicates that the delivered doses are close to the prescription ones). In order to derive the expression of the objective function, we first need to introduce some notations.

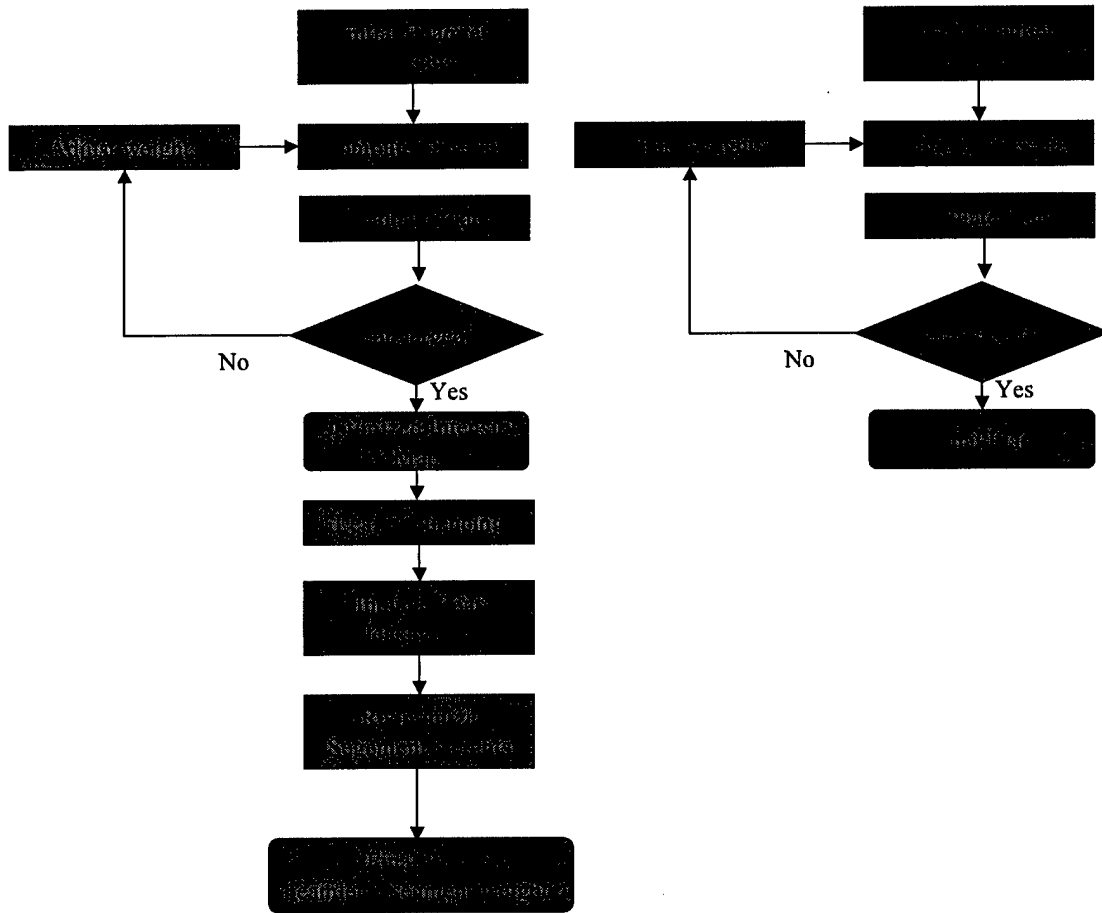


Figure 1: Comparison of flowcharts for beamlet-based and aperture-based IMRT. The segment weights optimization is not detailed here for clarity.

## 2.1 Notations for Plan Size Parameters, Doses and Constraints

We begin with a CT dataset containing structures of interest that are manually contoured. There are  $A$  structures (organs). Index  $a=0$  refers to the target structures while other structures are indexed from 1 to  $A-1$ . Each structure  $a$  contains  $N_a$  measurement points, for  $a=0, K, A-1$ . We also assume that organs do not overlap, which means that every measurement point belongs to one and only one structure.

As we discussed earlier, beam geometries and energies are specified before the optimization. Each (beam angle/energy) combination is called a field; a port refers to a single beam geometry. Just like in beamlet-based optimization, each field is divided into beamlets, and we denote  $B$  the total number of beamlets. All the beamlets belong to a total number of  $G$  fields (every beamlet only belongs to one single fields).  $b_g$  is the number of beamlets in field  $g$ , and we thus have that  $B = \sum_{g=1}^G b_g$ .

For each beamlet  $b$  (where  $b \in [1, B]$ ) and each structure  $a$ , we define the dose kernel  $d_b^{(a)}$  as the array of doses received by each point  $n$  in structure  $a$  when only beamlet  $b$  is given weight 1 and all the other

beamlets are given zero weights. Since structure  $a$  contains  $N_a$  points, we have  $d_b^{(a)} = \{d_{b,1}^{(a)}, K, d_{b,N_a}^{(a)}\}$ . Using accurate values for the beamlet kernels is critical to the final treatment plan quality, and this is why dose kernels are computed via Monte-Carlo simulation in this work.

The weight given to beamlet  $b$  is denoted  $w_b$ , and we are trying to determine the set of weights that best matches the prescription. Once the dose kernels are computed (and they are only computed once prior to the optimization), the doses received at each point in each structure at any time depend only on the beamlet weights at that time. This is why the vector  $w = \{w_1, K, w_B\}$  that contains all the beamlet weights is referred to as the state-vector.

Indeed, knowing the dose kernels and the state vector, we can easily compute the accumulated dose at every measurement point (or voxel). We denote  $D_n^{(a)}$  as the total accumulated dose at point  $n$  in organ  $a$ .

In particular, we have that  $D_n^{(a)} = \sum_{b=1}^B w_b d_{b,n}^{(a)}$ , which is just a mathematical way to express that the total accumulated dose at point  $n$  in organ  $a$  is simply the sum of the doses delivered by each individual beamlet.

We now need to specify our conventions regarding prescription doses, which are defined as follows. A prescribed dose is specified for the target, and then dose-volume constraints are defined for both the target and critical structures. We denote  $\hat{D}_0^{(0)}$  as the prescribed dose for the target. Besides this prescribed dose, there are two additional dose-volume constraints that apply to the target. The upper dose-volume constraint is of the form: “no more than  $v_1^{(0)}\%$  of organ 0 (i.e. the target) should receive a dose *greater* than  $D_1^{(0)}$ ”, whereas the lower dose-volume constraint is of the form “no more than  $v_1^{(0)}\%$  of organ 0 should receive a dose *less* than  $D_1^{(0)}$ ”.

For each other structure  $a$ , there are  $C_a$  dose-volume constraints, each one of them of the form “no more than  $v_c^{(a)}\%$  of organ  $a$  should receive a dose *greater* than  $D_c^{(a)}$ ”. Eventually each constraint  $c$  that apply to organ  $a$  (including the target) is given a relative weight factor  $\alpha_c^{(a)}$ .

## 2.2 Objective Function and Gradient for Beamlet-Based IMRT

In these conditions, the objective function is the sum of term that represents the target prescription dose, plus other terms that represent violations to all the constraints that apply:

$$F = F_c^{(0)} + \sum_{a=0}^{A-1} \sum_{c=1}^{C_a} (F_c^{(a)})$$

The term for the target prescription dose has the following quadratic form:

$$F_0^{(0)} = \frac{\alpha_0}{N_0} \sum_{n=1}^{N_0} [\hat{D}_0^{(0)} - D_0^{(0)}(w)]^2.$$

It can be shown (see Appendix for details) that the gradient of the objective function has the following form:

$$\frac{\partial F}{\partial w_b} = -2 \cdot \sum_{a=1}^{A-1} \frac{1}{N_a} \sum_{n=1}^{N_a} d_{w_b,n}^{(a)} \sum_{c,a} [\zeta_{c,n}^{(a)} \alpha_c^{(a)} (\hat{D}_c^{(a)} - D_n^{(a)}(w))] \quad (4)$$

Once we have computed a gradient, we can move along its direction (departing from the initial state) and find the step size that minimizes the objective function. This step is referred to as the line-minimization, and comes down to finding step size  $t$  such that  $F(w + t \nabla F)$  is minimal. We first turn to the adaptation of this method to aperture-based optimization before tackling the additional difficulties that pertain to the line minimization step.

### 2.3 Objective Function and Gradient for Aperture-Based IMRT

In aperture-based optimization, we want to express this function in terms of the weights of each field. In other words, we want to set the weights of all the beamlets, within each field, equal. We must also make sure that this simplification remains throughout the optimization process, and thus, that the gradient direction along which we evolve imposes the same changes in weights for all the beamlets that belong to the same field.

In order to achieve this, we need to modify the gradient computation. We thus can consider a modification of expression (3) in which we incorporate the fact that all beamlets from the same field have the same weights. This yields the following expression of the objective function:

$$F = \sum_{a=1}^{A-1} \frac{1}{N_a} \sum_{c,a} \sum_{n=1}^{N_a} \left[ \zeta_{c,n}^{(a)} \alpha_c^{(a)} \left( \hat{D}_c^{(a)} - \sum_{g=1}^G w_g \sum_{b=1}^{B_g} d_{w_b, x_n}^{(a)} \right) \right]^2 \quad (5)$$

where  $G$  is the number of ports,  $B_g$  is the number of beamlets in port  $g$ .

If we duplicate the proof through which we derived (4) from (3), we get a modified version of expression (4) that incorporates the fact that the objective function must only be differentiated with respect to all the beamlet weights that belong to the same field. This naturally dramatically reduces the number of differentiations, thus limiting the dimension of the space over which we have to optimize. The new gradient expression is now:

$$\frac{\partial F}{\partial w_g} = -2 \cdot \sum_{a=1}^{A-1} \frac{1}{N_a} \sum_{n=1}^{N_a} \left( \sum_{b=1}^{B_g} d_{w_b, n}^{(a)} \right) \sum_{c,a} \left[ \zeta_{c,n}^{(a)} \alpha_c^{(a)} \left( \hat{D}_c^{(a)} - D_n^{(a)}(w) \right) \right]$$

We must now take into account the effect of the non-negativity constraints, which already existed, in the original process. These constraints simply account for the fact that beamlet weights must remain non-negative since a negative weight has no physical meaning, even though we can conceptually imagine that 'removing' dose from the patient would reduce the objective function. Negative coefficients can occur for instance if we depart from a valid initial state, i.e. such that  $w_b \geq 0$ , for all  $b$ , and then perform a line minimization along the gradient direction, which yields a step size of  $t$ . If there is a  $b$  such that  $th_b < -w_b$ , then the new weight for beamlet  $b$  will become negative. In order to avoid such aberration, we must find a  $t$  that is such that  $th_b \geq -w_b$  for all beamlets, and this can be done by performing a loop through all the beamlets and scaling  $t$  down to  $-w_b / h_b$  whenever  $th_b < -w_b$ . By scaling the initial  $t$  down to the  $t'$  yielded by this loop, we are actually guaranteed (under technical yet general conditions) that the new step will result in some reduction of the objective function since we are still moving in the direction of the minimum. This loop is made clear in the following pseudo-code:

---

```

t'=t;
for b = 1 to B,
    w'_b = w_b + th_b;
    if w'_b < 0 then

```

```

        t' = - wb / hb
    end if
end for

```

---

Alg. 1: Scaling step in order to avoid negative weights.

However, several problems arise from such scaling. If there is a beamlet  $b$  for which  $w_b = 0$  and  $th_b < 0$ , then  $t$  will be scaled down to zero. One way to solve this problem is to modify the search direction before looping through beamlets, and in particular to set to zero the negative  $h_b$  that correspond to zero-weighted beamlets since we know that these beamlets will scale the step size down to zero if nothing is done preventively. However, by doing this we modify the search and we therefore have no other guaranty that the step size will be negative. We therefore need to come up with two search directions (one for positive steps  $t$ , one for negative steps  $t$ ) along which the step size can be scaled down. This method is detailed in algorithm 2.

Eventually, once we have the two search directions, we just need to find  $t$  that minimizes the following function:  $G(t) = \begin{cases} F(t+h^-) & \text{if } t \leq 0 \\ F(t+h^+) & \text{if } t > 0 \end{cases}$ , and numerical techniques to bracket the minimum are employed but not discussed here.

---

```

for b = 1 to B,
    if (wb = 0 and hb > 0) then
        hb- = 0
        hb+ = hb
    else if (wb = 0 and hb < 0)
        hb- = hb
        hb+ = 0
    else
        hb- = hb
        hb+ = hb
    end if
end for

```

---

Alg. 1: Modification of the search direction in order to avoid zero-length steps

The optimization algorithm for the simplified objective function was only tested on a simple plan of one single port made 20\*12 beamlets. As one would expect, the number of steps in the optimization process was dramatically reduced, from 1500 down to 1 single step. This makes sense since, for a single port, the aperture-based optimization is reduced to a single-variable function optimization. No further testing of the algorithm could be performed before expiration of the grant.

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