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Abstract

The paper considers the intensity modulated radiation therapy (inverse) treatment planning. An approach to determine the trajectories of the leaves of the multileaf collimator (MLC) in order to produce the prescribed intensity distribution is developed. The paper concentrates on the multiple static delivery technique. A mathematical model for calculating the intensity distribution with the help of locations of the leafheads of subsequent subfields is constructed. Furthermore an optimization model in which the decision variables are the locations of leafheads is developed. The relevant constraints are considered as well. The optimization problem is a large dimensional constrained nonlinear global extremum problem. It is solved by the LGO (Lipschitz (Continuous) Global Optimizer) program system. Comparisons with other optimization method (Hooke-Jeeves iteration) are included. Numerical experiments are presented to confirm the functionality of the method.

AMS-classification: 49-04, 92C50, 93-04

1 Introduction

Development of new accessories for the linear accelerators, especially the multileaf collimator (MLC), have provided new potentials in dose delivery for patients. One of the most promising dose delivery techniques is intensity modulated radiation therapy, allowing the construction of sharp dose gradients between tumor and healthy tissue and dose distributions with better deformity of planning target volume. However, these new techniques set new demands also for the treatment planning. Significant research is focused nowadays in developing new algorithms for this purpose (for reviews see e.g. [3, 5, 6, 29]).

In intensity modulated radiation therapy treatment planning, there are traditionally two basic problems. The first one is to determine the intensity distribution in the treatment domain in such a way that it generates as well as possible the dose distribution in the patient domain prescribed by the oncologist. The second problem is to determine the trajectories of the leaves of the multileaf collimator to produce the obtained intensity distribution. Both of these are inverse problems. For the first problem, there have been developed various kind of inverse treatment planning algorithms (e.g. [15, 7, 19, 16, 24, 11, 31, 18, 27]). In the second problem the methods to control the collimator leaves can be divided into dynamic collimation and multiple static collimation. In dynamic collimation the leaves are be moved during the irradiation and so the dose is delivered continuously corresponding to each individual field. The radiation is interrupted only during the selection of the subsequent fields. For the implementation of this method several techniques have been applied ([23, 8, 26, 25]). In multiple static collimation the leaves are moved only in a series of discrete steps and the radiation is always interrupted during the motion of the leaves ([2, 28, 12, 13]). Each field is, then, divided in a series of discrete subfields with own static MLC configuration for each subfield.

In this study, our aim is to introduce an approach for the control of the multileaf collimation which is based on the use of an explicit (physical) objective function where the decision variables are the locations of the leafheads or closely related to them . This enables us more easily to determine the real restrictions which the multileaves must satisfy. The modelling is based on the use of modified Heaviside function (cf. [2, 14]). The model does not take into account the so called "groove and tongue effect" ([30]) and the beam divergence. The result is optimal in a sense that the method minimizes the chosen objective function. Here our main interest lies in the multiple static collimation. The method is, however, applicable also to dynamic treatment schemes. The optimization of leaf trajectories with this method is a large dimensional constrained multiextremal problem. We have applied the optimizing algorithm built into the Lipschitzian global optimization (LGO) program ([21, 22, 20]) to solve the problem. In addition we have used local optimization algorithm, Hooke-Jeeves iteration.

2 Mathematical model for leaf position control

2.1 Model without head scattering

We assume that the intensity distributions of fields are given. It suffices to consider one field since the precalculated intensity distributions of separate fields are independent of each other. Let the collimator plane (treatment head) be a rectangle $U = [-a, a] \times [-b, b] \subset \mathbf{R}^2$. Denote the point of U by $u = (u_1, u_2)$. The collimator leaves are orthogonal to the u_2-axis.

The leaves have a positive width d. Assume that there are N leaf pairs $(B_i, A_i),\ i = 1, ..., N$. This means that $2b = Nd$. Let $U_i := [-a, a] \times]u_{2,i-1}, u_{2,i}[,\ i = 1, ..., N$ be the strips (along u_1-axis) determined by the leaf pairs (B_i, A_i). Figure 1 explains more in detail these notational conventions.

Let $\Psi = \Psi(u)$ be the prescribed intensity distribution (related to the monitor unit distribution). We assume that Ψ is a piecewise continuous function $U \mapsto \mathbf{R}$ such that $\Psi(u)$ is constant $\Psi_i(u_1)$ for $u_2 \in]u_{2,i-1}, u_{2,i}[$ that is, $\Psi(u)$=$\Psi_i(u_1)$ for $u \in U_i$. This will be e.g. the case when in the calculation of intensities (in the inverse problem of treatment planning) we subdivide the treatment domain into bixels in such a way that the partition points in u_2- direction are exactly the points $u_{2,i}$.

Let Ψ_0 be the uniform flux density per unit area incident on the MLC.

The leaf control problem can be stated as follows:

Problem A. *Suppose that Ψ is given. Let T be a positive number (the total treatment time) . Let the right hand head of leaf A_i be in a point $a_i(t) \in [-a, a]$ at the moment t and let the left hand head of leaf B_i be in a point $b_i(t) \in [-a, a]$ at the moment t.*

For any $i = 1, ..., N$ determine the leaf trajectories $a_i = a_i(t),\ b_i = b_i(t)$ such that there exist a finite number of time intervals $\Delta T_j \subset [0, T],\ j = 1, ..., n_{u_1,i}$ for which

$$\sum_{j=1}^{n_{u_1,i}} \Psi_0 |\Delta T_j| = \Psi_i(u_1),\ i = 1, ..., N, \tag{1}$$

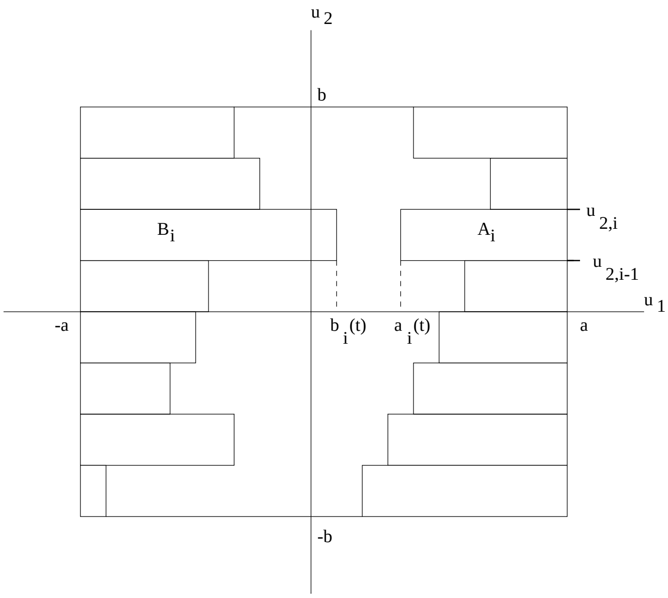

Figure 1: The geometrical setting of the treatment head. The number of leaf pairs is $N = 8$. A_i is the right hand leaf and B_i is the left hand leaf.

$$b_i(t) \leq u_1 \leq a_i(t), \ t \in \cup_{j=1}^{n_{u_1,i}} \Delta T_j \tag{2}$$

$$u_1 \leq b_i(t) \text{ or } u_1 \geq a_i(t) \ t \in [0,T] \setminus \cup_{j=1}^{n_{u_1,i}} \Delta T_j, \tag{3}$$

$$b_i(t) \leq a_i(t), \ t \in [0,T], \tag{4}$$

$$-a \leq b_i(t) \text{ and } a_i(t) \leq a, \ t \in [0,T]. \tag{5}$$

The above criteria (1-3) for the trajectories a_i and b_i means that the total time during which the field is open at the point $u \in U$ will exactly be the prescribed value $\Psi_i(u_1)/\Psi_0$, as desired. The criteria (4-6) are needed since the leaves can not overlap and the values of $a_i(t)$ and $b_i(t)$ are limited to the interval $[-a, a]$. In practice there may also be some other limitations for the leaves which can be added to the above restrictions (cf. section 3.3). We remark that our assumption here is that the number $n_{u_1,i}$ *is finite.* The figure 2 will visualize the evolution of leaf heads for one particular leaf pair (B_i, A_i). The time intervals where the field is open at $u_1 \in [-a, a]$ are marked in Figure 2.

We shall formulate the stated problem in a more compact, analytical way. Let $H : [-a, a] \mapsto \mathbf{R}$ be the Heaviside function

$$H(x) = \begin{cases} 1, & x \geq 0 \\ 0, & x < 0 \end{cases}.$$

Then we see that

$$H(a_i(t) - u_1)H(u_1 - b_i(t)) = \begin{cases} 1, & b_i(t) \leq u_1 \leq a_i(t) \\ 0, & u_1 \leq b_i(t) \text{ or } u_1 \geq a_i(t) \end{cases}.$$

Hence we observe that (see figure 2)

$$\int_0^T H(a_i(t) - u_1)H(u_1 - b_i(t))dt = \sum_{j=1}^{n_{u_1,i}} |\Delta T_j|, \tag{6}$$

where $\Delta T_j, \ j = 1, ..., n_{u_1,i}$ are the subintervals of $[0,T]$ for which the conditions (2) and (3) are valid (in Figure 2 the number $n_{u_1,i} = 2$).

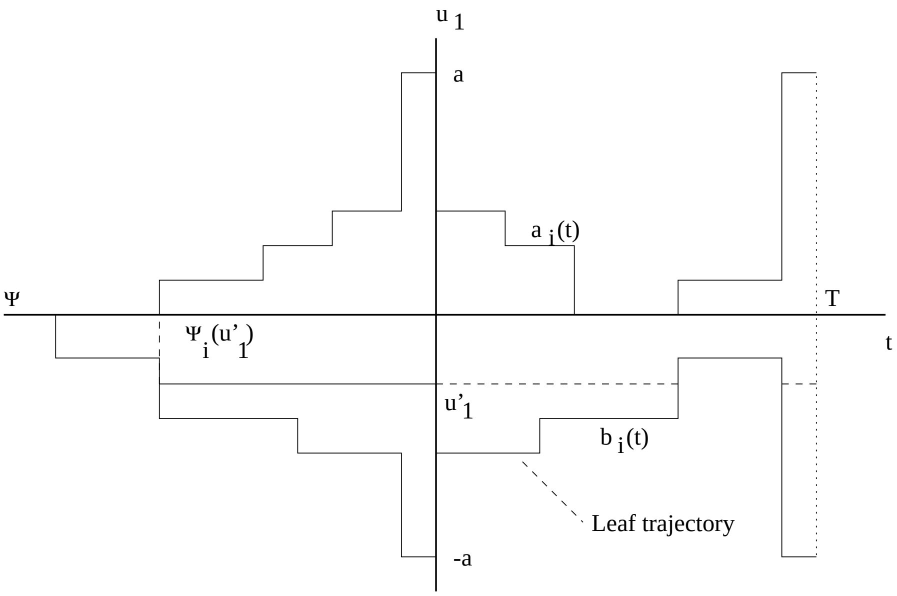

Figure 2: At right: Evolution of leaf trajectories when they are step functions. At left: The corresponding intensity distribution in the case where Ψ_0= 1. For example, at u_1' (marked in the picture) $\Psi_i(u_1)$ is the sum of the lengths of dashed lines.

Hence we are able to reformulate the leaf control problem as follows:

Problem B. *Suppose that* Ψ *is given as in Problem A. Let* T *be a positive number (the treatment time) . For any* $i = 1, ..., N$ *determine the leaf trajectories* $a_i : [0, T] \mapsto [-a, a],\ b_i : [0, T] \mapsto [-a, a]$ *such that*

$$\Psi_0 \int_0^T H(a_i(t) - u_1) H(u_1 - b_i(t)) dt = \Psi_i(u_1),\ u \in U_i \tag{7}$$

and

$$b_i(t) \le a_i(t),\ t \in [0, T]. \tag{8}$$

Denote

$$q(a_i, b_i)(u_1) = \Psi_0 \int_0^T H(a_i(t) - u_1) H(u_1 - b_i(t)) dt.$$

Then the equation (7) can be written as

$$q(a_i, b_i)(u_1) = \Psi_i(u_1),\ u \in U_i. \tag{9}$$

Remark 1 *A. Since for the Heaviside function (for* $x_1 > x_2$*)*

$$H(x_1 - x) H(x - x_2) = H(x_1 - x) - H(x_2 - x)$$

we can rewrite the integral $q(a_i, b_i)(u_1)$ *as*

$$q(a_i, b_i)(u_1) = \Psi_0 \int_0^T [H(a_i(t) - u_1) - H(b_i(t) - u_1)] dt.$$

This substitution can be approximately also made in the context of the corrected model considered below. It may simplify the computations.

B. In the above problems the minimization of the treatment time T *is also important, besides the determination of the trajectories.*

2.2 Model correction due to head scattering

The above model assumes that the leaves do not produce scattered radiation and that there is no leakage through or between the leaves. In practice there exist scattering and leakage in the leaves and so the Heaviside function must be replaced with a modified (steplike) function. These effects are possible to take into account in the modelling. We shall consider model corrections (for Problem B) due to scattering and leakage here.

We can replace the Heaviside function e.g. by one of the functions

$$\tilde{H}(x) = \mathrm{erf}_\tau(x) = \frac{1}{\sqrt{\pi}\tau}\int_{-\infty}^{x} e^{-s^2/\tau^2} ds \tag{10}$$

or

$$\tilde{H}(x) = C_1 + C_2 \overline{\mathrm{arc}}\tan(C_3 x) \tag{11}$$

or

$$\tilde{H}(x) = C_1 + C_2(1 - \tanh(C_3 x)). \tag{12}$$

Such replacements of the Heaviside function yield some more "soft" function which takes into account the head scattering *from the tops of leaves* in the modelling. In addition, leakage through the leaves can also be modelled with this substitution. By choosing the modification $\tilde{H}(x)$ appropriately, the computations become simple. The parameters $C_1,\ C_2,\ C_3$ can be obtained by standard interpolation techniques by using (measured or Monte Carlo) data that takes into account the scattering. The equation (9) is, hence, replaced by

$$\tilde{q}(a_i, b_i)(u_1) = \Psi_i(u_1),\ u \in U_i$$

where

$$\tilde{q}(a_i, b_i)(u_1) = \Psi_0 \int_0^T \tilde{H}(a_i(t) - u_1)\tilde{H}(u_1 - b_i(t))dt. \tag{13}$$

In the following we correct the model due to the scattering from the leaf sides (and due to the "groove and tongue effect" which is not considered here). Let $s = s(u_2)$ be the "portion of the scattered radiation"

$$s = \tilde{H} - H. \tag{14}$$

Denote

$$\begin{aligned} s_1(a_i, b_i)(u) &= \Psi_0 s(u_2 - u_{2,i}) \int_0^T [H(u_1 - a_{i+1}(t))H(a_i(t) - u_1) \\ &+ H(b_{i+1}(t) - u_1)H(u_1 - b_i(t))]dt,\ i = 1, ..., N-1 \end{aligned}$$

$$\begin{aligned} s_2(a_i, b_i)(u) &= \Psi_0 s(u_{2,i-1} - u_2) \int_0^T [H(a_i(t) - u_1)H(u_1 - a_{i-1}(t)) \\ &+ H(u_1 - b_i(t))H(b_{i-1}(t) - u_1)]dt,\ i = 2, ..., N \end{aligned}$$

$$s_3(a_1, b_1)(u) = \Psi_0 s(u_{2,0} - u_2) \int_0^T H(a_1(t) - u_1)H(u_1 - b_1(t))dt,$$

$$s_4(a_N, b_N)(u) = \Psi_0 s(u_2 - u_{2,N}) \int_0^T H(a_N(t) - u_1)H(u_1 - b_N(t))dt.$$

Let $s(a_i, b_i)(u)$ be a function

$$s(a_i, b_i)(u) = \begin{cases} s_1(a_1, b_1)(u) + s_3(a_1, b_1)(u), & u \in U_1 \\ s_1(a_i, b_i)(u) + s_2(a_i, b_i)(u), & u \in U_i,\ i = 2, ..., N-1\ . \\ s_2(a_N, b_N)(u) + s_4(a_N, b_N)(u), & u \in U_N \end{cases}$$

Then in the corrected model we replace (9) by the equality

$$\tilde{q}(a_i, b_i)(u_1) + s(a_i, b_i)(u) = \Psi_i(u_1),\ \in u \in U_i,\ i = 1, ..., N. \tag{15}$$

Remark 2 *In the above formulas of $s_k(a_i,b_i)$, $k=1,2,3,4$ we can (in practise) replace the pure Heavyside function H by the approximation*

$$H(x) = \mathrm{erf}_\epsilon(x) \tag{16}$$

where ϵ is small.

The above model is valid only, when the leaves are not too near to each other, or when the leaves are closed. Modelling of leaf tops causes problems when the leaves are very near to each other. This limitation can be removed, but we do not consider the correction here. Besides we consider an additional constraint

$$a_i(t) - b_i(t) \geq \overline{\gamma} \text{ or } a_i(t) - b_i(t) = 0 \tag{17}$$

where $\overline{\gamma}$ is a positive number (between $0.5 - 1$ cm). Since $a_i(t) - b_i(t) \geq 0$ the constraint (17) is equivalent to

$$(a_i(t) - b_i(t))(a_i(t) - b_i(t) - \overline{\gamma}) \geq 0. \tag{18}$$

3 An optimal solution for the leaf control problem

3.1 Calculation of intensity

We shall assume that the leaf trajectories are given by the linear combinations

$$a_i(t) = \sum_{k=1}^{n} a_{ik}\phi_k(t), \tag{19}$$

$$b_i(t) = \sum_{k=1}^{n} b_{ik}\phi_k(t) \tag{20}$$

where $\{\phi_1, ..., \phi_n\}$ is an appropriate basis system of piecewise continuous functions.

In the following, for simplicity we shall neglect the correction term $s(a_i,b_i)(u)$. Instead, we shall give some results also for the corrected model. Substituting the expressions (19-20) in the integral (13) we obtain

$$\begin{aligned} \tilde{q}(a_i,b_i)(u_1) &= \Psi_0 \int_0^T \tilde{H}\left(\sum_{k=1}^{n} a_{ik}\phi_k(t) - u_1\right) \tilde{H}\left(u_1 - \sum_{k=1}^{n} b_{ik}\phi_k(t)\right) dt \\ &= \int_0^T Q_i(u_1,t)dt \end{aligned} \tag{21}$$

where we denote for $u \in U_i$

$$Q_i(u_1,t) = \Psi_0 \tilde{H}\left(\sum_{k=1}^{n} a_{ik}\phi_k(t) - u_1\right) \tilde{H}\left(u_1 - \sum_{k=1}^{n} b_{ik}\phi_k(t)\right). \tag{22}$$

Denote

$$\overline{a}_i = (a_{i1}, ..., a_{in}), \ \overline{b}_i = (b_{i1}, ..., b_{in}).$$

and

$$q(\overline{a}_i, \overline{b}_i)(u_1) = \int_0^T Q_i(u_1,t)dt. \tag{23}$$

Then, by (21), we have

$$\Psi_i(u_1) = q(\overline{a}_i, \overline{b}_i)(u_1). \tag{24}$$

3.2 Multiple static collimation

Multiple static collimation means that corresponding to each field $S_l,\ l = 1, ..., L$ the treatment time interval $[0, T_l]$ is divided into n_l subintervals

$$[t_{l0}, t_{l1}], ..., [t_{l(n_l-1)}, t_{ln_l}].$$

During each subinterval the leaf configuration is fixed. So the whole treatment time will be greater than $T_1 + ... + T_l$ since the change of the leaf configuration corresponding to the subinterval $[t_{l(k-1)}, t_{lk}]$ to the leaf configuration corresponding to the next subinterval $[t_{lk}, t_{l(k+1)}]$ takes time. Also the change of field configurations will take time. The leaf configurations which correspond to the subintervals $[t_{l(k-1)}, t_{lk}],\ k = 1, ..., n_l$ are called *subfields* of the field S_l.

As mentioned above it suffices to consider only one individual field S. In the multiple static treatment technique the basis functions ϕ_k can be chosen to be step functions. Let $\{t_0, ..., t_n\}$ be a partition of the interval $[0, T]$ and let χ_k be the characteristic function of the subinterval $[t_{k-1}, t_k],\ k = 1, ..., n$, that is

$$\chi_k(t) = \begin{cases} 1, & t \in [t_{k-1}, t_k] \\ 0, & \text{otherwise} \end{cases}.$$

We choose $\phi_k = \chi_k$.

Since $a_{ik}(t) = a_{ik},\ b_{ik}(t) = b_{ik}$ for $t \in [t_{k-1}, t_k]$ we find that

$$\begin{aligned} q(\overline{a}_i, \overline{b}_i)(u_1) &= \Psi_0 \int_0^T \tilde{H}\,(a_i(t) - u_1)\,\tilde{H}\,(u_1 - b_i(t))\,dt \\ &= \Psi_0 \sum_{k=1}^{n} \int_{t_{k-1}}^{t_k} \tilde{H}\,(a_i(t) - u_1)\,\tilde{H}\,(u_1 - b_i(t))\,dt \\ &= \Psi_0 \sum_{k=1}^{n} \tilde{H}(a_{ik} - u_1)\tilde{H}(u_1 - b_{ik})(t_k - t_{k-1}). \end{aligned} \quad (25)$$

Remark 3 *The practical interpretation of parameters $a_{ik},\ b_{ik}$ is that the tops of the i^{th} leaf pair (B_i, A_i) corresponding to the k^{th} subfield of the field S are at points a_{ik} and b_{ik}.*

The above observation shows that in multiple static collimation the lengths $\delta t_k := t_k - t_{k-1}$ of the subintervals $[t_{k-1}, t_k]$ can also be chosen as variables in the optimization processes. From a practical point of view this possibility is very desirable because this degree of freedom will decrease the number of subfields and hence the total treatment time. Thus we replace the quantity $q(\overline{a}_i, \overline{b}_i)(u_1)$ by

$$q(\overline{a}_i, \overline{b}_i, \delta t)(u_1) := \Psi_0 \sum_{k=1}^{n} \tilde{H}(a_{ik} - u_1)\tilde{H}(u_1 - b_{ik})\delta t_k \quad (26)$$

where $\delta t := (\delta t_1, ..., \delta t_n) \in \mathbf{R}^n$. The intensity Ψ_i can be computed from

$$\Psi_i(u_1) = q(\overline{a}_i, \overline{b}_i, \delta t)(u_1),\ u \in U_i. \quad (27)$$

For the corrected model one obtains

$$\Psi_i(u_1) = q(\overline{a}_i, \overline{b}_i, \delta t)(u_1) + s(\overline{a}_i, \overline{b}_i, \delta t)(u),\ u \in U_i \quad (28)$$

where $s(\overline{a}_i, \overline{b}_i, \delta t)(u)$ is given by

$$s(\overline{a}_i, \overline{b}_i, \delta t)(u) = \begin{cases} s_1(\overline{a}_1, \overline{b}_1, \delta t)(u) + s_3(\overline{a}_1, \overline{b}_1, \delta t)(u), & u \in U_1 \\ s_1(\overline{a}_i, \overline{b}_i, \delta t)(u) + s_2(\overline{a}_i, \overline{b}_i, \delta t)(u), & u \in U_i,\ i = 2, ..., N-1 \\ s_2(\overline{a}_N, \overline{b}_N, \delta t)(u) + s_4(\overline{a}_N, \overline{b}_N, \delta t)(u), & u \in U_N \end{cases}. \quad (29)$$

In (29)

$$s_1(\overline{a}_i, \overline{b}_i, \delta t)(u) = \Psi_0 s(u_2 - u_{2,i}) \sum_{k=1}^{n} [H(u_1 - a_{(i+1)k}) H(a_{ik} - u_1)\delta t_k + H(b_{(i+1)k} - u_1) H(u_1 - b_{ik})\delta t_k],$$

$$s_2(\overline{a}_i, \overline{b}_i, \delta t)(u) = \Psi_0 s(u_{2,i} - u_2) \sum_{k=1}^{n} [H(a_{ik} - u_1) H(u_1 - a_{(i-1)k})\delta t_k + H(u_1 - b_{ik}) H(b_{(i-1)k} - u_1)\delta t_k],$$

$$s_3(\overline{a}_1, \overline{b}_1, \delta t)(u) = \Psi_0 s(u_{2,0} - u_2) \sum_{k=1}^{n} H(a_{1k} - u_1) H(u_1 - b_{1k})\delta t_k,$$

$$s_4(\overline{a}_N, \overline{b}_N, \delta t)(u) = \Psi_0 s(u_2 - u_{2,N}) \sum_{k=1}^{n} H(a_{Nk} - u_1) H(u_1 - b_{Nk})\delta t_k.$$

3.3 The optimization problem for multiple static collimation

From (27) we are able to compute approximately the intensity Ψ_i when $\tilde{H}(x)$ is suitably chosen. The optimization is based on the minimization of an error (objective) function

$$\sum_{i=1}^{N} ||q(\overline{a}_i, \overline{b}_i, \delta t)(\cdot) - \Psi_i||^2 \tag{30}$$

with respect to $(\overline{a}_i, \overline{b}_i, \delta t) \in \mathbf{R}^{3n}$. Here the norm may be e.g. the $L_2([-a, a])$-norm or some corresponding discrete norm. Denote

$$(\mathbf{a}, \mathbf{b}, \delta t) = (\overline{a}_1, ..., \overline{a}_N, \overline{b}_1, ..., \overline{b}_N, \delta t) \in \mathbf{R}^{2nN+n}.$$

The objective function $f : \mathbf{R}^{2nN+n} \mapsto \mathbf{R}$ used in the optimization is given by

$$f(\mathbf{a}, \mathbf{b}, \delta t) = \sum_{i=1}^{N} ||q(\overline{a}_i, \overline{b}_i, \delta t)(\cdot) - \Psi_i||^2. \tag{31}$$

The constraints of Problem B can be computed. Since $a_{ik}(t) = a_{ik},\ b_{ik}(t) = b_{ik}$ for $t \in [t_{k-1}, t_k]$ and 0 otherwise the constraints of Problem B are equivalent to the following conditions

$$b_{ik} \le a_{ik},\ i = 1, ..., N,\ k = 1, ..., n \tag{32}$$

$$a_{ik} \le a,\ b_{ik} \ge -a,\ i = 1, ..., N,\ k = 1, ..., n \tag{33}$$

In practice one sets some additional conditions such as

$$a_i(t) \ge -\kappa \text{ and } b_i(t) \le \kappa,\ i = 1, ..., N$$

for all $t \in [0, T]$. Here κ is a given positive number. This limitation brings in the following constraints for the leaf parameters

$$a_{ik} \ge -\kappa \text{ and } b_{ik} \le \kappa,\ i = 1, ..., N,\ k = 1, ..., n \tag{34}$$

In addition a natural requirement is

$$0 \le \delta t_k \le T \tag{35}$$

In practice it is sensible instead of (35) to prescribe

$$c_0 \le \delta t_k \le T \text{ or } \delta t_k = 0$$

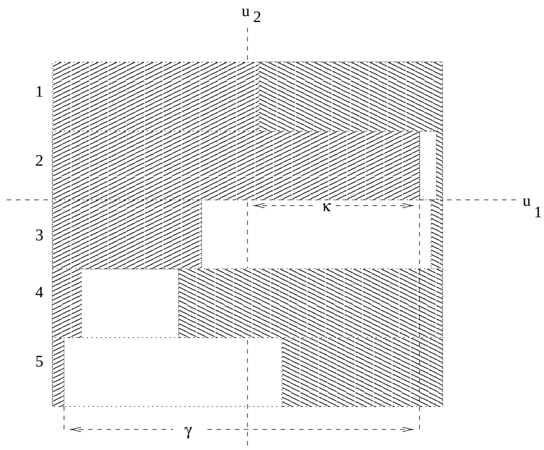

Figure 3: A schematic figure of some of the leaf constraints. Leaf pair 1 shows the leaf overlapping condition, the left leaf of pair 2 shows restricted movement over field central axis (κ), pairs 3 and 4 (also pairs 1 and 2) show the first interleaf condition and pairs 5 and 2 show the second interleaf condition (γ).

where c_0 is a positive number. By this we avoid too short subfields. This constraint is equivalent to

$$0 \leq \delta t_k \leq T, \;\; \delta t_k(\delta t_k - c_0) \geq 0. \tag{36}$$

From (18) we obtain the constraint

$$(a_i(t) - b_i(t))(a_i(t) - b_i(t) - \overline{\gamma}) \geq 0$$

which means in multiple static collimation the restriction

$$(a_{ik} - b_{ik})(a_{ik} - b_{ik} - \overline{\gamma}) \geq 0. \tag{37}$$

Applying certain treatment units we shall require some interleaf conditions such as

$$a_i(t) - a_j(t) \leq \gamma \;\text{ and } b_i(t) - b_j(t) \leq \gamma, \; i,j = 1, ..., N \tag{38}$$

and

$$b_i(t) \leq a_{i+1}(t), \;\; b_{i+1}(t) \leq a_i(t), \; i = 1, ..., N-1 \tag{39}$$

for all $t \in [0, T]$ where γ is a positive number. These conditions lead to the restrictions

$$a_{ik} - a_{jk} \leq \gamma \;\text{ and } b_{ik} - b_{jk} \leq \gamma, \; i,j = 1, ..., N, \; k = 1, ..., n \tag{40}$$

and

$$b_{ik} \leq a_{(i+1)k}, \;\; b_{(i+1)k} \leq a_{ik}, \; i = 1, ..., N-1, \; k = 1, ..., n. \tag{41}$$

The constraint (39) is used to diminish the so called "groove and tongue" effect.

In some delivery techniques one demands the uni-directionality of the leaves. For example, if the leaves may move only from left to right we must set the constraint

$$a_{ik} \leq a_{i(k+1)}, \;\; b_{ik} \leq b_{i(k+1)}, \; i = 1, ..., N, \; k = 1, ..., n-1. \tag{42}$$

In the following formulations we take into account only the conditions (32-37). Then the number of constraints is $6Nn + 2n$.

Applying the above concepts we are able to formulate different kinds of optimal solutions. As an example we consider the following possibility.

Define an objective function

$$f(\mathbf{a},\mathbf{b},\delta t)=\sum_{i=1}^{N}||q(\overline{a}_i,\overline{b}_i,\delta t)(\cdot)-\Psi_i||^2_{L_2([-a,a])} \tag{43}$$

Find the global minimum

$$\min_{(\mathbf{a},\mathbf{b},\delta t)\in\mathbf{R}^{2nN+n}} f(\mathbf{a},\mathbf{b},\delta t) \tag{44}$$

under the constraints (32-37), that is

$$b_{ik}\le a_{ik},\ i=1,...,N,\ k=1,...,n \tag{45}$$

$$a_{ik}\le a,\ b_{ik}\ge -a,\ i=1,...,N,\ k=1,...,n \tag{46}$$

$$a_{ik}\ge -\kappa,\ b_{ik}\le \kappa\ i=1,...,N,\ k=1,...,n \tag{47}$$

$$(a_{ik}-b_{ik})(a_{ik}-b_{ik}-\overline{\gamma})\ge 0,\ i=1,...,N,\ k=1,...,n \tag{48}$$

$$0\le \delta t_k\le T, \tag{49}$$

$$\delta t_k(\delta t_k-c_0)\ge 0,\ k=1,...,n \tag{50}$$

.

In the corrected model the objective function must be replaced by

$$\begin{aligned} f(\mathbf{a},\mathbf{b},\delta t) &= ||q(\overline{a}_1,\overline{b}_1,\delta t)+s_1(\overline{a}_1,\overline{b}_1,\delta t)+s_3(\overline{a}_1,\overline{b}_1,\delta t)-\Psi_1||^2_{L_2(U_1)} \\ &+ \sum_{i=2}^{N-1}||q(\overline{a}_i,\overline{b}_i,\delta t)+s_1(\overline{a}_i,\overline{b}_i,\delta t)+s_2(\overline{a}_i,\overline{b}_i,\delta t)-\Psi_i||^2_{L_2(U_i)} \\ &+ ||q(\overline{a}_N,\overline{b}_N,\delta t)+s_2(\overline{a}_N,\overline{b}_N,\delta t)+s_4(\overline{a}_N,\overline{b}_N,\delta t)-\Psi_N||^2_{L_2(U_N)} \end{aligned} \tag{51}$$

The norm may be, as in (51) the $||\ ||_{L_2(U_i)}$-norm or some corresponding discrete norm in U_i.

3.4 Change of decision variables

In the optimization it is useful to introduce new decision variables d_{ik} and c_{ik} by

$$d_{ik}=a+b_{ik},\ c_{ik}=a_{ik}-b_{ik}.$$

Then we have

$$b_{ik}=d_{ik}-a,\ a_{ik}=c_{ik}+b_{ik}=c_{ik}+d_{ik}-a$$

and so the objective function (43) is replaced by

$$F(\mathbf{c},\mathbf{d},\delta t)=f(\mathbf{c}+\mathbf{d}-\hat{a},\mathbf{d}-\hat{a},\delta t)$$

where

$$\mathbf{c}=(\overline{c}_1,...,\overline{c}_N),\ \overline{c}_i=(c_{i1},...,c_{in})$$
$$\mathbf{d}=(\overline{d}_1,...,\overline{d}_N),\ \overline{d}_i=(d_{i1},...,d_{in})$$
$$\hat{a}=(a,...,a)\in\mathbf{R}^{2nN}.$$

The constraints (45-50) are replaced by the following inequalities

$$0\le c_{ik}\le 2a \tag{52}$$

$$0\le d_{ik}\le 2a \tag{53}$$

$$c_{ik}+d_{ik}\le 2a \tag{54}$$

$$a - \kappa \le c_{ik} + d_{ik} \le 2a \tag{55}$$

$$0 \le d_{ik} \le a + \kappa \tag{56}$$

$$c_{ik}(c_{ik} - \overline{\gamma}) \ge 0 \tag{57}$$

$$0 \le \delta t_k \le T, \tag{58}$$

$$\delta t_k(\delta t_k - c_0) \ge 0. \tag{59}$$

Also the other above expressed constraints can be easily given with the help new decision variables. Here (52, 53, 56, 58) are box constraints. The remaining constraints (54, 55, 57, 59) are handled correspondingly by the following penalty terms

$$\sum_{i=1}^{N}\sum_{k=1}^{n}(\max(0, c_{ik} + d_{ik} - 2a))^p \tag{60}$$

$$\sum_{i=1}^{N}\sum_{k=1}^{n}(\max(0, a - \kappa - (c_{ik} + d_{ik})))^p,\ \sum_{i=1}^{N}\sum_{k=1}^{n}(\max(0, c_{ik} + d_{ik} - 2a))^p \tag{61}$$

$$\sum_{i=1}^{N}\sum_{k=1}^{n}(\max(0, -c_{ik}(c_{ik} - \overline{\gamma})))^p \tag{62}$$

$$\sum_{k=1}^{n}(\max(0, -\delta t_k(\delta t_k - c_0)))^p \tag{63}$$

where p is a positive number (e.g. $p = 1$ or $p = 2$). The penalty functions (60-62) have been added to the objective function F. Similarly we can handle the constraints for the original decision variables in Section 3.3.

4 Optimization algorithm

Nowadays most of the treatment units allow use of 40 MLC leaf pairs but in practice, the number N of leaf pairs is typically $20 - 25$. Assuming that the number n of subfields, is between $5 - 15$ we find that the number of optimization parameters is between $2nN + n = 205 - 765$. The number $6Nn + 2n$ of constraints is between $610 - 2280$. Some additional constraints are often imposed which will increase the number of constraints. Hence the optimization problem is a large scale global optimization problem. The constraints are mainly simple linear inequality constraints (the exceptions are (48), (50)). The objective function f is defined in a subset of $\mathbf{R}^{2Nn+n}$ and it is nonlinear.

For the determination of the global minimum of the objective function, the LGO program ([20, 21, 22]) was used. LGO is an integrated software package including both global and local search strategies. It is primarily developed for solving Lipschitz-continuous global optimization problems. In the user interface of the program, the objective function and the explicit constraints can be defined in a Fortran 90 coded user function file. Ranges for the variables and some termination criteria for the searches can also be set by the user. In the global phase, two search strategies, branch and bound and adaptive random search, are available. The branch and bound search is more structured and has a built-in deterministic strategy. However, both strategies use random search elements. In the local search phase, either unconstrained or constrained local search solvers are available.

A deterministic local optimizer was also applied. The algorithm was Hooke-Jeeves direct search method [17]. A local optimizer needs a good initial solution if global optimum is desired. An *ad hoc* method for setting the initial point was applied (Figure 4).

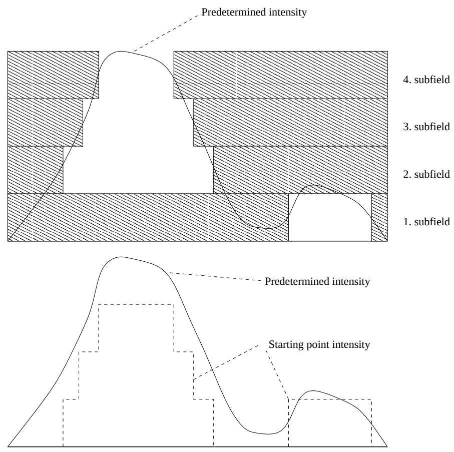

Figure 4: Illustration of the method to find an initial point for local optimizer for one leaf pair.

5 Numerical experiments

In this study, we use the noncorrected model for the experiments. The objective function can have various explicit forms like

$$f(\mathbf{a}, \mathbf{b}, \delta t) = \sum_{i=1}^{N} \int_{-a}^{a} \left| \Psi_0 \sum_{k=1}^{n} \mathrm{erf}_\tau(a_{ik} - u_1)\mathrm{erf}_\tau(u_1 - b_{ik})\delta t_k - \Psi_i(u_1) \right|^2 du_1, \tag{64}$$

$$f(\mathbf{a}, \mathbf{b}, \delta t) = \sum_{i=1}^{N} \int_{-a}^{a} \left| \Psi_0 \sum_{k=1}^{n} (\mathrm{erf}_\tau(a_{ik} - u_1) - \mathrm{erf}_\tau(b_{ik} - u_1))\delta t_k - \Psi_i(u_1) \right|^2 du_1 \tag{65}$$

or

$$f(\mathbf{a}, \mathbf{b}, \delta t) = \sum_{i=1}^{N} \int_{-a}^{a} |\Psi_0 \sum_{k=1}^{n} [C_1 + C_2 \overline{\mathrm{arc}} \tan(C_3(a_{ik} - u_1))] \tag{66}$$

$$\cdot \quad [C_1 + C_2 \overline{\mathrm{arc}} \tan(C_3(u_1 - b_{ik}))]\delta t_k - \Psi_i(u_1)|^2 du_1. \tag{67}$$

or

$$f(\mathbf{a}, \mathbf{b}, \delta t) = \sum_{i=1}^{N} \int_{-a}^{a} |\Psi_0 \sum_{k=1}^{n} [C_1 + \frac{C_2}{2}(1 - \tanh(C_3(a_{ik} - u_1))] \tag{68}$$

$$\cdot \quad [C_1 + \frac{C_2}{2}(1 - \tanh(C_3(u_1 - b_{ik}))]\delta t_k - \Psi_i(u_1)|^2 du_1. \tag{69}$$

In our experiments, we have used the discrete counterpart of the latest form of the objective function.The leaf side scattering was neglected.

The problem used in the experiments was a 35-variable 45-constraint test problem. In the problem, there are three leaf pairs and five subfields. The leaf collision constraint (45) and edges of the field (46) were explicitly determined as constraints in the problem. Also the constraints (47 - 50) were explicitly determined. We made runs both with original decision variables and with the new decision variables given in Section 3.4. The predetermined intensity distributions were a simple example where the field was divided to area of zero intensity and to a rectangular area of uniform intensity of value 9. This intensity distribution corresponds to a conventional open field and is called an open field like distribution. This distribution was used to confirm that our method basically works, since the optimal solution of MLC

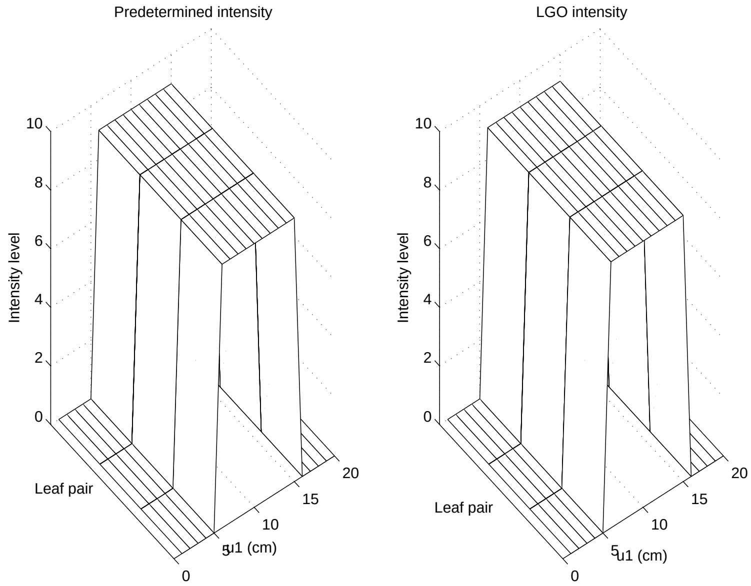

Figure 5: The predetermined (left) and the optimized (right) intensity distribution corresponding to open field like distribution.

trajectories for this intensity distribution is trivial. Also a more difficult distribution having two separate intensity peaks with low intensity between them was used. The two peak intensity distribution is an arbitrary, but more realistic distribution in intensity modulated radiation therapy. In this study it was used to simulate a real situation in optimization. The distributions are presented in figures 5 and 6 as references.

The optimization of MLC parameters to match the open field distribution was successful. The results varied a little between the experiments, but the best solution very accurately corresponded to the predetermined distribution (Table 1). The mean intensity difference was 0.042 units, when the intensity ranged between 0 and 9.0. The results of the experiment are presented in Figure 5.

In the optimization problem using two peak intensity distribution, finding of the MLC parameters corresponding to the desired distribution more difficult. Figure 6 indicates the results of this experiment. The optimization program is capable to find a solution, where both peaks exist, but the resulting distribution only coarsely follows the predetermined.The mean intensity difference is 0.595 in the intensity range of 0 – 9.628, but the difference between resulting and predetermined intensies ranges from -3.310 to 1.677. Concerning the two peak intensity distribution we made also some other simulations which showed the uselfulness of the global search.

For the latter problem the Hooke-Jeeves local optimizing strategy was also applied using four subfields. The mean intensity difference is 0.430 in the intensity range of 0 – 9.628, but the difference between resulting and predetermined intensies ranges from -1.623 to 1.123 (Figure 6).

6 Discussion

In this study a new approach was introduced for optimization of the multileaf parameters during intensity modulated radiation therapy. The method is basically a multipurpose algorithm, which can be applied to different intensity modulation techniques.In this study, the method was applied for optimization of multileaf parameters of two predetermined intensity distributions using multiple static collimation technique. For the optimization, LGO ([20, 21, 22]) was used. The optimization program finds MLC parameters corresponding to a dose distribution of open field very accurately. For intensity distribution with two

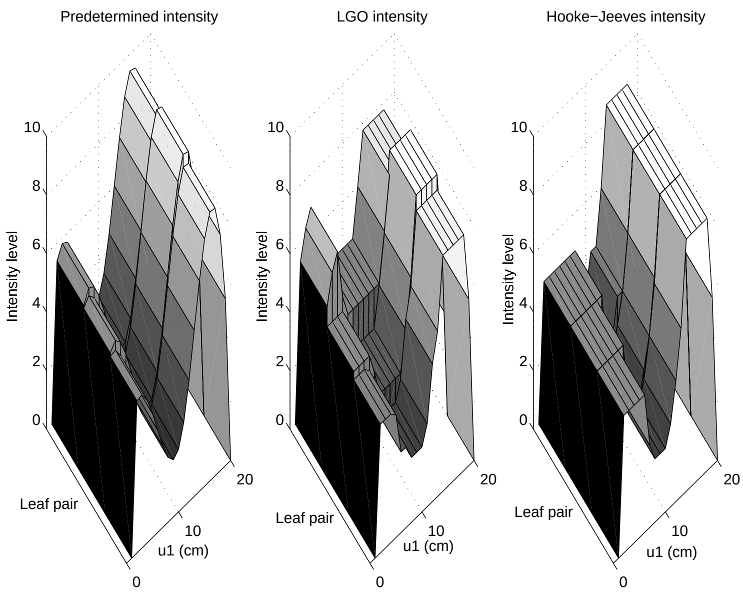

Figure 6: The predetermined (left), LGO optimized (middle) and Hooke-Jeeves optimized (right) intensity distributions corresponding to the two peak distribution.

maximums, finding suitable solutions is apparently more difficult.

For the inverse treatment planning, different algorithms have been developed. One of the simplest approach is to optimize weights for the prescribed fields to get the best available dose distribution to the target, simultaneously keeping the normal tissue dose below a tolerance level ([29]). In the more complicated problems, in treatment delivery of intensity modulated radiation therapy, the problem is usually divided into two parts, finding optimal intensity distribution for each field to obtain the desired dose distribution in the patient and determining the multileaf trajectories based on the intensity distribution. In this study, our approach was introduced in the latter purpose, the multileaf parameters were optimized for two predetermined intensity distributions. However, our approach can be extended towards *the direct optimization of multileaf parameters in order to match a desired dose distribution in the patient domain, without optimizing at first the intensity distribution.*

We have used multiple static collimation, where leaves are moved only in discrete steps between the subfields and the radiation is interrupted during the motion. One of the advantages to use this technique is the easier control of leaves, since the limited velocity and acceleration of the leaves need not to be accounted. On the other hand, disadvantage is that it may prolong the total treatment time. Our method is, however, applicable also for the dynamic collimation, where leaves are moved during the dose delivery continuously corresponding to each individual field. In the implementation of the dynamic collimation, different techniques are used. Practical implementation of dynamic collimation to our method will produce additional restrictions, such as maximal acceleration and velocity or possible unidirectionality of the leaves, which have to be added to the constraints.

Optimization of a dose distribution in a patient is normally based either on physical or on radiobiological criteria. ([10, 24, 29, 5, 6]). Regardless of the criteria used, the problems are normally large dimensional problems with multiple local minima ([10]), similarly to our problem in which MLC parameters were optimized for a predetermined intensity distribution. Therefore, algorithms capable for global optimization are strongly recommended. Nowadays there are effective special tools such as stochastic global optimization, deterministic branch and bound techniques and different kinds of regularization methods to solve reliably this kind of problems. We have used LGO ([20, 21, 22]) for the optimization. LGO integrates a suite of robust, derivative-free global and local optimization strategies.

Numerical results in 35-variable 45-constraint problem are excellent in a very simple open field like distribution. The resulting intensity distribution follows very accurately the predetermined distribution. This problem is a rough simplification of the optimization needed in the intensity modulated radiation therapy. However, it shows that the method developed in this study basically works. When the method is applied to more complicated dose distribution, *e.g.* the two peak distribution, the resulting intensity distribution only coarsely follows the predetermined intensity distribution. This may, naturally, follow from the difficulties of the optimization program to find the real global minimum of the objective function. According to our experiences, after the formulation of the new decision variables (Section 3.4) the optimization results were better. It may be that improving the formulation of the problem will still lead to better results. Another question is, whether five subfields are enough to fulfil such a difficult dose distribution. The optimal number of the subfields is a matter of future research, too (not necessarily the smallest number, cf. [28]). Finally, our present model neglects the so called 'tongue-and-groove problem' ([30]). In future this effect will be added to the model.

With the Hooke-Jeeves local optimization method a slightly better solution was obtained in the two-peak experiment (Figure 6). The problem is, as always with local optimizers, the determination for the initial point. Although our scheme seems to be working in this case, further development of strategies to determine the best initial point is necessitated.

In conclusion, this study introduces a new algorithm for the optimization of the MLC parameters in intensity modulated radiation therapy treatment. The simple test problem optimization shows the applicability of the algorithm, but in optimization of the more complicated problem difficulties exist. It indicates that more research is needed in the field of optimization methods and problem dimension determination, especially in finding the "best suitable" number of the subfields. We conclude that this approach is worth development for wider use in the field of intensity modulated radiation therapy.

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