Optimal control model for radiation therapy inverse planning applying the Boltzmann transport equation

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Received 31 July 2006; accepted 4 March 2007
Available online 24 March 2007
Submitted by Y. Censor

Abstract

We consider an inverse problem related to external radiation therapy treatment planning. The dose calculation (the forward problem) is based on the Boltzmann Transport Equation (BTE) which models exactly the transport of charged particles in tissue. The inverse planning (the inverse problem) is formulated as an optimal boundary control problem. The optimal control variable is the incoming (external) flux and the output is the dose distribution in patient domain. Both physical and biological cost functions are defined but here we concentrate on the physically based optimization. The discretization is done by finite element approximations for which the BTE is expressed in its variational form. In the optimization process of the discrete model we apply so called parametrization (which may essentially diminish the decision variables in optimization) of the matrix equations. Parametrization is based on certain linear algebraic decompositions of matrices. One simulation is presented which show the functionality of the developed methods.

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Keywords: Boltzmann transport equation; Radiotherapy; Optimal control; Parametrization; Global optimization

1. Introduction

In the field of radiation therapy much research has been done to obtain new innovative techniques for treating cancer patients with radiation. New equipments and new computational approaches have been developed but there still is a lack of automatic treatment planning system. Treatment planning is an inverse problem in nature. In solving the inverse problem one always

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needs a dose calculation model, that is, a physical “dose law” which determines the dose in the patient based on the knowledge of the radiation flux incident on the surface of the patient domain. In the mathematical terminology, this means the solution of the forward problem.

For solving the forward problem one has developed and applied various dose calculation models. Widely used models are variants of so-called pencil beam models which require the application of a dose deposition kernel. The most accurate, physically rigorous and robust models are based on the Boltzmann transport equation (BTE) \([1,6,8,9,12,15]\). Transport equation based dose calculation models are valid in inhomogeneous material and they also take rigorously into account the scattering effects. Mainly due to computational problems, BTE based models are not yet extensively used in solving the forward problem.

In oncological society the solution of the inverse problem, i.e., the concept of “the best plan” seems not to be absolutely unique. In some cases it may be difficult to measure the optimality criteria. However, the principles of the optimal plan can be founded either on the physical criteria or on the biological criteria. Nowadays in practice the criteria are mainly based on physical ones.

In the case of physical criteria one tries to create a prescribed dose distribution in the target (tumor) such that the dose in the healthy tissue is under certain prescribed value. In addition, one takes special care of critical organs by demanding that the dose in vulnerable regions is under certain prescribed level. Some additional constraints (e.g. dose volume constraints) may be included. Using physical criteria the objective functions are relatively easy to construct and a lot of various alternatives can be found in literature (e.g. \([23,24]\) and the references therein). Another possibility in the optimization applying physical criteria is to seek only feasible (nearly optimal) solutions \([5,16]\). Recently we have developed optimization algorithms which use directly the multileaf collimator (MLC) system parameters in optimization \([16–19]\). The corresponding delivery quality (objective) functions are usually highly nonlinear and multiextremal. The model constraints are mainly linear inequalities and so relatively simple.

In the optimization which is based on biological criteria one utilizes statistical data collected from clinical trials. In the case of biological criteria, two different probabilities, namely the tumor control probability (TCP) and the normal tissue complication probability (NTCP) are employed in the treatment planning \([3,4,24]\). The aim is to provide as high TCP as possible and at the same time maintain the NTCP at an acceptable level in certain organs of the patient. The biological objective functions are more difficult to construct and as a rule one can say that the biological objective functions are mathematically more complex to handle than the physical objective functions.

Recently we have developed an optimal control approach for solving the optimization problem \([20]\). In this approach the BTE has been utilized and the optimization problem is solved by the boundary control optimization theory. In this paper we introduce a radiation treatment planning approach that is based on the Boltzmann transport equation and optimal control. A novel linear algebraic parametrization approach is utilized for the discretized model in order to reduce the number of optimized parameters in the optimization procedure. Solving effectively large dimensional linear systems and the calculation of the singular value decompositions for them are difficulties in our approach. The control parameters in this study are the intensities of the applied radiation fields, though it would be fairly straightforward to formulate the problem also for the case of MLC. In that case, however, the objective functions become highly nonlinear and the number of decision parameters increases. Numerical results for two-dimensional patient body are shown in the paper. In numerical considerations we have concentrated on the use of physical optimization criteria but the optimization scheme applying the biological optimization criteria is also defined in the paper. The optimization problems for realistic (3-dimensional patient body) cases are very large dimensional and they are still computationally too expensive.
2. Calculation of dose

2.1. Boltzmann transport equation model

Physically the Boltzmann transport equation is based on the particle equilibrium in infinitesimal small voxels of tissue. The modeling requires the knowledge of the differential and total cross sections which depend on the nature of interactions of particles. The total dose is obtained as a superposition of different fields as will be described in detail below (Section 2.3).

We consider only the stationary transport of particles. Assume that 
\[ \psi_j = \psi_j(x, E, \omega), \ j = 1, 2, 3 \]
are the phase space densities for photons, electrons and positrons, respectively. 
\[ x = (x_1, x_2, x_3) \]
is the point in the patient domain \( V \subset \mathbb{R}^3 \). \( \omega \) is a point on the unit sphere \( S \) of \( \mathbb{R}^3 \).

In the case where elastic collision, inelastic collision and bremsstrahlung are taken into account the model consists of the following coupled system of partial differential–integral equations

\[
\begin{align*}
\Omega \cdot \nabla \psi_1 + K_1(\psi_1, \psi_2, \psi_3) &= Q_1(x, E, \omega), \\
\Omega \cdot \nabla \psi_2 + K_2(\psi_1, \psi_2, \psi_3) &= Q_2(x, E, \omega), \\
\Omega \cdot \nabla \psi_3 + K_3(\psi_1, \psi_2, \psi_3) &= Q_3(x, E, \omega).
\end{align*}
\] (2.1)

The model (2.1) is linear. It neglects some nonlinear interactions which are not essential in dose calculation. The functions \( K_j(\psi_1, \psi_2, \psi_3), \ j = 1, 2, 3 \) are collision terms resulting from different kind of interactions (mentioned above). \( K_1, K_2, K_3 \) are linear functions of 
\[ \psi := (\psi_1, \psi_2, \psi_3). \]
The interactions can be described by the integrals

\[
K_j \psi = \sum_{k=1}^{3} \int_{I} \int_{S} \sigma_{k,j}(x, E', E, \omega', \omega) \psi_k(x', E', \omega') \, d\omega' \, dE' - \sum_{k=1}^{3} \Sigma_{k,j}(x, E) \psi_k.
\]

Above \( \sigma_{k,j}(x, E', E, \omega', \omega) \) are differential cross sections and \( \Sigma_{k,j}(x, E) \) are total cross sections. If the interaction from particle \( j \) to particle \( k \) is not possible, \( \sigma_{k,j} = 0 \). For total cross sections

\[
\Sigma_{k,j}(x, E) = 0, \quad j \neq k.
\] (2.2)

Finally, \( Q_j(x, E, \omega) \) are the source terms. These may describe sources in tissue (interior therapy).

The integral \( \int_{S} f(\omega) \, d\omega \) denotes the standard surface integral. We denote by \( I \) the energy interval, say \([E_1, E_2]\). The solution \( \psi \) is defined in the 6-dimensional state space \( G := V \times I \times S \).

In the following we denote the system (2.1) more simply by

\[
(\Omega \cdot \nabla + K) \psi = Q,
\] (2.3)

where

\[
\Omega \cdot \nabla \psi = (\Omega \cdot \nabla \psi_1, \Omega \cdot \nabla \psi_2, \Omega \cdot \nabla \psi_3)
\]
and \( K \psi = (K_1 \psi, K_2 \psi, K_3 \psi), \ Q = (Q_1, Q_2, Q_3) \). We consider exterior radiation therapy. Hence we have \( Q = 0 \) and the boundary condition is used to model the extrageneous particle fluxes.

2.2. Photon inflow. The boundary condition

We consider the photon inflow in the stationary case. This corresponds the exterior photon radiation. Other modalities are similarly considered. We assume that the boundary \( \partial V \) is a Lipschitz-boundary. Then the outward normal \( \nu(x) \) exists and is it continuous on \( \partial V \) in spite of possibly a set with surface measure zero.
To take into account the incoming extrageneous flux we must put some (boundary) conditions for the solution. In the exterior therapy the typical condition for the solution $\psi$ is of the form

$$\psi_2(x, E, \Omega) = \psi_3(x, E, \Omega) = 0 \text{ for } (x, E, \Omega) \in \partial V \times I \times S$$

such that $\Omega \cdot v(x) < 0$,

$$\psi_1(x, E, \Omega) = u(x, E, \Omega) \text{ for } (x, E, \Omega) \in \partial V \times I \times S$$

such that $\Omega \cdot v(x) < 0$. \hfill (2.4)

$u$ is the photon flux density incident on $\partial V$. We assume that $u \in L^2(\partial V \times I \times S)$. The condition $\psi_1 = u$ for $\Omega \cdot v(x) < 0, x \in \partial V$ means that the beam (the flux $u$) is inwardly on the patch $\partial V$ and the condition $\psi_j = 0, j = 2, 3$ for $\Omega \cdot v(x) < 0$ means that no other particles generate inward fluxes.

**Remark 1.** For the exterior electron radiation the roles of $\psi_1$ and $\psi_2$ are changed in the boundary condition. Otherwise the boundary condition is same as in (2.4).

### 2.3. The definition of dose

In practical situations the total dose distribution is computed as follows. Let the incoming (initial) flux density of the $l$th field $S_l$ be $u_l$. We assume that $u_l \in L^2(\Gamma_l \times I \times S)$, where $\Gamma_l$ is a patch of $\partial V$ through which the radiation is entering into domain $V$. Let $\psi^l = (\psi^l_1, \psi^l_2, \psi^l_3)$ be the flux density corresponding to the field $S_l$, that is $\psi^l$ is the solution of the equation

$$(\Omega \cdot \nabla + K)\psi^l = 0$$

\hfill (2.5)

with the boundary condition

$$\psi^l_2(x, E, \Omega) = \psi^l_3(x, E, \Omega) = 0 \text{ for } (x, E, \Omega) \in \partial V \times I \times S$$

such that $\Omega \cdot v(x) < 0$,

$$\psi^l_1(x, E, \Omega) = 0, \text{ for } (x, E, \Omega) \in (\partial V \setminus \Gamma_l) \times I \times S$$

such that $\Omega \cdot v(x) < 0$, \hfill (2.6)

$$\psi^l_1(x, E, \Omega) = u_l(x, E, \Omega) \text{ for } (x, E, \Omega) \in \Gamma_l \times I \times S$$

such that $\Omega \cdot v(x) < 0$.

Above

$$\Omega \cdot \nabla \psi^l := (\Omega \cdot \nabla \psi^l_1, \Omega \cdot \nabla \psi^l_2, \Omega \cdot \nabla \psi^l_3), \quad K \psi^l := (K_1 \psi^l, K_2 \psi^l, K_3 \psi^l).$$

The dose contribution $D_l(x)$ from the field $S_l$ at a point $x$ of the patient domain $V$ is obtained from the (measurement) integral

$$D_l(x) = \sum_{j=1}^3 \int_S \int_I \kappa_j(x, E) \psi^l_j(x, E, \Omega) \, dE \, d\Omega,$$ \hfill (2.7)

where $\kappa_j(x, E)$ are known (stopping power) factors ($\kappa_1(x, E) = 0$). The total dose is obtained from
\[ D(x) = \sum_{l=1}^{L} D_l(x) = \sum_{l=1}^{L} \sum_{j=1}^{3} \int_{S} \int_{I} \kappa_j(x, E) \psi_j^l(x, E, \Omega) \, dE \, d\Omega. \tag{2.8} \]

The computation of total dose can also be formulated as follows. Define \( u \in L_2(\partial V \times I \times S) \) such that

\[ u = \sum_{l=1}^{L} u_l \chi_l, \tag{2.9} \]

where \( \chi_l : \partial V \times I \times S \to \mathbb{R} \) are the characteristic functions of \( \Gamma_l \times I \times S \). Let \( \psi = (\psi_1, \psi_2, \psi_3) \) be the solution of the problem

\[ (\Omega \cdot \nabla + K) \psi = 0 \tag{2.10} \]

with the boundary condition

\[ \psi_2(x, E, \Omega) = \psi_3(x, E, \Omega) = 0 \quad \text{for} \quad (x, E, \Omega) \in \partial V \times I \times S \]

such that \( \Omega \cdot \nu(x) < 0 \),

\[ \psi_1(x, E, \Omega) = u, \quad \text{for} \quad (x, E, \Omega) \in \partial V \times I \times S \]

such that \( \Omega \cdot \nu(x) < 0 \), \( \tag{2.11} \)

where \( u \) is defined by (2.9).

The solution of the problem (2.10)–(2.11) is

\[ \psi = \left( \sum_{l=1}^{L} \psi_1^l, \sum_{l=1}^{L} \psi_2^l, \sum_{l=1}^{L} \psi_3^l \right), \tag{2.12} \]

where \( \psi^l (l = 1, \ldots, L) \) are the solutions of (2.5)–(2.6). The proof follows from the uniqueness of solutions (2.3)–(2.4) which we will formulate in Section 2.4. Now the total dose is

\[ D(x) = \sum_{j=1}^{3} \int_{S} \int_{I} \kappa_j(x, E) \psi_j(x, E, \Omega) \, dE \, d\Omega, \tag{2.13} \]

where \( \psi \) is the solution of (2.10)–(2.11). We find that (2.10)–(2.11) is exactly the problem (2.3)–(2.4) with \( u \in L_2(\partial V \times I \times S) \) given by (2.9).

**Remark 2.** The energy deposition in a patient is due to the charged particles. Hence in practice we can assume that \( \kappa_1(x, E) = 0 \). More generally the factors \( \kappa_j \) may depend also on \( \Omega \).

### 2.4. Variational form of equations

Let \( G \) be as above and let \( L_2(G) \) be the Lebesgue space of (real valued) square integrable functions on \( G \) with the usual inner product. Furthermore, let

\[ L_2(\partial V \times I \times S, |\Omega \cdot \nu| \, d\sigma \, dE \, d\Omega) := \left\{ g : \partial V \times I \times S \to \mathbb{R} | g \text{ is measurable and} \right. \]

\[ \left. \int_{S} \int_{I} \int_{\partial V} |\Omega \cdot \nu| g^2 \, d\sigma \, dE \, d\Omega < \infty \right\}. \]
where \( \sigma \) is the surface measure on \( \partial V \). Then \( L_2(\partial V \times I \times S, |\Omega \cdot v| \, d\sigma \, dE \, d\Omega) \) is a Hilbert space equipped with the inner product

\[
\langle g_1, g_2 \rangle_{L_2(\partial V \times I \times S, |\Omega \cdot v| \, d\sigma \, dE \, d\Omega)} := \int_S \int_I \int_{\partial V} |\Omega \cdot v| g_1 g_2 \, d\sigma \, dE \, d\Omega.
\]

Denote

\[
\mathcal{D}(\nabla \times I \times S) := \{ f |_{\nabla \times I \times S} | f \in C^\infty(\mathbb{R}^3 \times \mathbb{R} \times S) \}.
\]

Let \( H_1 \) be the completion of \( \mathcal{D}(\nabla \times I \times S) \) with respect to the inner product

\[
\langle f_1, f_2 \rangle_{H_1} := \langle f_1, f_2 \rangle_{L_2(\partial V)} + \langle f_1, f_2 \rangle_{L_2(\partial V \times I \times S, |\Omega \cdot v| \, d\sigma \, dE \, d\Omega)}.
\]

Furthermore, let \( H_2 \) be the completion of \( \mathcal{D}(\nabla \times I \times S) \) with respect to the inner product

\[
\langle f_1, f_2 \rangle_{H_2} = \langle f_1, f_2 \rangle_{L_2(\partial V)} + \langle \Omega \cdot \nabla f_1, \Omega \cdot \nabla f_2 \rangle_{L_2(G)}.
\]

Finally, let \( H := H_1 \cap H_2 \) is equipped with the standard Hilbert space inner product

\[
\langle f_1, f_2 \rangle_H = \langle f_1, f_2 \rangle_{H_1} + \langle f_1, f_2 \rangle_{H_2}.
\]

For any \( f \in H_1 \) the trace \( f |_{\partial V \times I \times S} \) is well defined in the sense that there exists a sequence \( \{ f_n \} \subset \mathcal{D}(\nabla \times I \times S) \) such that

\[
f_n \to f |_{\partial V \times I \times S} \quad \text{in} \quad L_2(\partial V \times I \times S, |\Omega \cdot v| \, d\sigma \, dE \, d\Omega).
\]

One knows that for each \( f \in H_2 \) the restriction \( f |_{\partial V \times I \times S} \in L_2(K) \) where \( K \) is a compact subset of

\[
\{(x, E, \Omega) \in \partial V \times I \times S ||\Omega \cdot v(x)| > 0\}
\]

but \( f |_{\partial V \times I \times S} \) is not necessarily in \( L_2(\partial V \times I \times S, |\Omega \cdot v| \, d\sigma \, dE \, d\Omega) \) [8, pp. 220–221]. For \( \psi, v \in H \) the Green’s formula

\[
\langle \psi, \Omega \cdot \nabla v \rangle_{L^2(G)} + \langle \Omega \cdot \nabla \psi, v \rangle_{L^2(G)} = \int_S \int_I \int_{\partial V} (\Omega \cdot v) \psi v \, d\sigma \, dE \, d\Omega
\]

is valid [8, p. 225].

In the product spaces \( H_i^3, i = 1, 2 \) we use the usual inner products

\[
\langle f, h \rangle_{H_i^3} = \sum_{j=1}^3 \langle f_j, h_j \rangle_{H_i}
\]

for \( f = (f_1, f_2, f_3), h = (h_1, h_2, h_3) \in H_i^3 \). In the similar way we define the inner product in \( H^3 \).

In the following the subscript “−” refers to the negative part of a function and the subscript “+” refers to the positive part of a function. The variational formulation of the problem (2.3)–(2.4) is given by [21].

**Theorem 1.** Assume that

1. \( \Sigma_{k,j} \in L_\infty(V \times I), \) \hspace{1cm} \( (2.15) \)
2. \( \sigma_{k,j} \in C(\nabla \times I^2 \times S^2), \) \hspace{1cm} \( (2.16) \)
3. \( Q_j \in L_2(G), u \in L_2(\partial V \times I \times S). \) \hspace{1cm} \( (2.17) \)
Then the variational form of the equation (2.10) with the stated boundary condition (2.11) is given by

\[ B(\psi, v) = F(v), \quad v \in H^3, \]  

(2.18)

where \( B(\cdot, \cdot) : H^3 \times H^3 \rightarrow \mathbb{R} \) is the bilinear form

\[ B(\psi, v) = -\langle \psi, \Omega \cdot \nabla v \rangle_{L^2(G)^3} + \sum_{j=1}^{3} \int_{S} \int_{I} \int_{\partial V} (\Omega \cdot v)_+ \psi_j v_j \, d\sigma \, dE \, d\Omega + \langle K\psi, v \rangle_{L^2(G)^3} \]  

(2.19)

and

\[ F(v) = (Q, v)_{L^2(G)^3} + \int_{S} \int_{I} \int_{\partial V} (\Omega \cdot v)_- u v_1 \, d\sigma \, dE \, d\Omega. \]  

(2.20)

We formulate the following lemma [21]:

**Lemma 1.** Assume that

1. \( \Sigma_{k,j} \in L_\infty(V \times I), \)  

(2.21)

2. \( \sigma_{k,j} \in \mathcal{C}(V \times I^2 \times S^2). \)  

(2.22)

3. There exists \( \kappa > 0 \) such that for \( \psi \in H^3 \)

\[ \langle K\psi, \psi \rangle_{L^2(G)^3} \geq \kappa \| \psi \|^2_{L^2(G)^3}. \]  

(2.23)

Then the bilinear form \( B(\psi, v) \) satisfies

\[ B(\psi, v) \leq C \| \psi \|_{H^1} \| v \|_{H^3} \]  

(boundedness)  

(2.24)

for \( \psi, v \in H^3 \) and

\[ B(\psi, \psi) \geq c \| \psi \|^2_{H^1} \]  

(\( H^3 \) - coercivity)  

(2.25)

for \( \psi \in H^3 \).

In addition, \( F \in (H^3)'^* \) (here the superscript “\( * \)” refers to the adjoint space) and there exists \( C > 0 \) such that

\[ \| \psi \|_{H^1} \leq C \| F \|, \]  

(2.26)

where

\[ \| F \| := \| Q \|_{L^2(G)^3} + \sqrt{\int_{S} \int_{I} \int_{\partial V} |(\Omega \cdot v)_- u|^2 \, d\sigma \, dE \, d\Omega}. \]

In [2,21] we have proved the following sufficient algebraic criterion for the coercitivity assumption (2.23)
Lemma 2. Suppose that $\Sigma_{j,j} \in L_\infty(V \times I)$ and $\sigma_{k,j} \in C(V \times I^2 \times S^2)$. Furthermore, suppose that (2.2) is valid and that there exists $\alpha > 0$ such that almost everywhere $(x, E, \Omega) \in G$

$$\Sigma_{j,j}(x, E, \Omega) - \int_{S} \int_{I} \sum_{k=1}^{3} \sigma_{k,j}(x, E', E, \Omega', \Omega) \, dE' \, d\Omega' \geq \alpha \tag{2.27}$$

and

$$\Sigma_{j,j}(x, E, \Omega) - \int_{S} \int_{I} \sum_{k=1}^{3} \sigma_{j,k}(x, E, E', \Omega, \Omega') \, dE' \, d\Omega' \geq \alpha \tag{2.28}$$

for $j = 1, 2, 3$. Then the assumption

$$\langle K\psi, \psi \rangle_{L_2(G)^3} \geq \alpha \|\psi\|_{L_2(G)^3}^{2} \tag{2.29}$$

is valid.

A physical background can be easily found for the condition (2.27), where the integrations over energy and angular domains basically describe the total scattering cross sections. The condition (2.27) states that the sum of these scattering cross sections cannot be larger than the total cross section itself. This is always true, because the total cross section is the sum of scattering and absorption cross sections. The physical meaning of the second condition (2.28) is not so clear. It states that those integrated ‘inverse’ scattering cross sections, which change particles from $j$ to $k$ cannot be larger than the total cross section of the particle $j$. However, it seems that this second condition (2.28) is also physically relevant.

By the boundedness (2.24) the bilinear form $B(\cdot, \cdot)$ can be extended on $H_1^3 \times H^3$ (here we denote the extension again by $B(\cdot, \cdot)$). The extension satisfies the estimates

$$|B(\psi, v)| \leq C\|\psi\|_{H_1^3}\|v\|_{H^3}, \quad \psi \in H_1^3, \quad v \in H^3 \tag{2.30}$$

and

$$B(\psi, \psi) \geq c\|\psi\|_{H_1^3}^{2}, \quad \psi \in H_1^3. \tag{2.31}$$

We formulate the following existence result of solutions:

Theorem 2. Suppose that the assumptions of Theorem 1 are valid and that (2.2) and (2.27)–(2.28) hold. Then the variational equation

$$B(\psi, v) = F(v), \quad v \in H^3 \tag{2.32}$$

has one and only one solution $\psi \in H^3$.

In addition, $F \in (H_1^3)^*$ and

$$\|\psi\|_{H_1^3} \leq \frac{1}{c}\|F\|, \tag{2.33}$$

where

$$\|F\| \leq \|Q\|_{L_2(G)^3} + \sqrt{\int_{S} \int_{I} \int_{\partial V} |(\Omega \cdot v) - u^2| \, d\sigma \, dE \, d\Omega}. \tag{2.34}$$

Proof. The proof follows from estimates (2.30), (2.31) and the generalized Lax–Milgram Theorem [22, p. 403]. We omit the details here. □
Theorem 2 gives the existence of weak solutions for the problem (2.10)–(2.11).

3. Optimal control problem in radiation therapy

3.1. Inverse problem based on physical objectives

The patient domain \( V \subset \mathbb{R}^3 \) contains tumor’s (target’s) region \( T \), critical organs’ region \( C \) and normal tissue’s region \( N \) and so we have the union \( V = T \cup C \cup N \). Let us assume that we have \( L \) fields \( S_l, l = 1, \ldots, L \). This means that gantry, couch and collimator angles are determined and the whole treatment contains \( L \) different angle settings.

Above we have found that the dose can be obtained from the functional

\[
D(x) = \sum_{j=1}^{3} \int_{S} \int_{I} \kappa_j(x, E) \psi_j(x, E, \omega) \, dE \, d\omega, \tag{3.1}
\]

where \( \psi \) is the solution of (2.10)–(2.11). In (3.1) \( \kappa_j(x, E) \) are known factors (so-called stopping powers). We assume that \( \kappa_j \in L_\infty(V \times I) \). Considering the external therapy we have no internal sources. So \( Q_l = 0 \) for each field \( S_l \). Applying the above concepts, the inverse radiation treatment planning problem states:

Suppose that \( D_0 \) is the prescribed (uniform) dose in tumor \( T \) and that \( D_C \) and \( D_N \) are the upper bounds of dose in the critical organ \( C \) and in the normal tissue \( N \), respectively. Furthermore, suppose that the number \( L \) and the gantry, couch and collimator angles \( \alpha_l, \beta_l \) and \( \theta_l \) of fields \( S_l \) are given.

Determine the incoming flux \( u \in L_2(\partial V \times I \times S) \) such that

\[
D(x) = D_0, \quad x \in T, \\
D(x) \leq D_C, \quad x \in C, \\
D(x) \leq D_N, \quad x \in N. \tag{3.2}
\]

and that

\[
u \geq 0.\tag{3.3}
\]

Tumor, critical organ and normal tissue may be divided into many separate parts and dose limits may be different in these parts.

Besides the requirements (3.2) one often demands that so called dose volume constraints [3,23] are fulfilled. Dose volume constraints may be necessary for certain structures, for example for critical organs. We describe this requirement shortly for critical organ \( C \). Let \( v(D) \) be the volume fraction of \( C \) that receives a dose greater than \( D \). We demand that

\[
\mu(\{x \in C | D(x) \geq d_C\}) \leq \mu(C) \tag{3.4}
\]

where \( v_0 \) is a given volume fraction and \( d_C \) is a given dose. Since the function \( v = v(D) \) is a decreasing function of \( D \) the condition (3.4) is equivalent to

\[
v(d_C) \leq v_0. \tag{3.5}
\]

The condition (3.5) means that

\[
\frac{\mu(\{x \in C | D(x) \geq d_C\})}{\mu(C)} \leq v_0. \tag{3.6}
\]
where $\mu$ is the Lebesgue measure. Let $H : \mathbb{R} \to \mathbb{R}$ be the Heaviside function $H(x) = \begin{cases} 1, & x \geq 0 \\ 0, & x < 0 \end{cases}$.

Then the dose volume constraint (3.6) can be expressed as

$$\frac{1}{\mu(C)} \int_C H(D(x) - d_C) \, dx \leq v_0.$$  

(3.7)

In computer programs the Heaviside function $H$ can be accurately replaced by the error function $\text{erf}_\epsilon(x) = \frac{1}{\sqrt{\pi\epsilon}} \int_{-\infty}^{x} e^{-s^2/\epsilon^2} \, ds$. Furthermore, the requirement (3.6) can be approximated accurately by the requirement

$$\frac{1}{|I_C|} \sum_{p \in I_C} \text{erf}_\epsilon(D(x_p) - d_C) \leq v_0,$$

(3.8)

where $I_C$ is a selected finite set of $C$ (for example, the set of nodes in finite element computations).

When the dose volume constraints are taken into account requirements like (3.7) (or 3.8) are added to the requirements (3.2).

### 3.2. Optimal control problem

To clarify the $u$-dependence of variables we denote $\psi = \psi(u)$, if needed. Let $F : L_2(\partial V \times I \times S) \to (H^3)^*$ be the operator defined by

$$(Fu)(v) = \int_S \int_I \int_{\partial V} (\Omega \cdot \nu) - u v_1 \, d\sigma \, dE \, d\Omega.$$  

Note that $F(v) = (Fu)(v)$ (or $F = Fu$). Using these notations $\psi = \psi(u)$ satisfies the variational equation

$$B(\psi(u), v) = (Fu)(v), \quad v \in H^3.$$  

(3.9)

Let $L : L_2(G)^3 \to L_2(V)$ be the functional

$$(L\psi)(x) = \sum_{j=1}^3 \int_S \int_I \kappa_j(x, E) \psi_j(x, E, \Omega) \, dE \, d\Omega.$$  

(3.10)

Then we have for the dose

$$D = L\psi = L\psi(u).$$  

(3.11)

For later needs we notice that the adjoint $L^* : L_2(V) \to L_2(G)^3$ of $L$ is given by

$$L^* v = (\kappa_1 v, \kappa_2 v, \kappa_3 v), \quad v \in L_2(V).$$  

(3.12)

The dose $D(x)$ must be as near as possible to the described dose $D_0$ in the tumor and the upperbounds of dose in critical organs and normal tissue may not be violated. Hence we try to optimize the incoming flux $u$ so that this holds. The concrete implementation of this leads to the following kind of optimization problems, for example.

Define a cost functional by

$$J(u) = c_1 ||D_0 - L\psi(u)||^2_{L_2(T)} + c_2 ||(D_C - L\psi(u))||^2_{L_2(C)} + c_3 ||(D_N - L\psi(u))||^2_{L_2(N)} + c_4 ||(u)||^2_{L_2(\partial V \times I \times S)} + c_5 ||u||^2_{L_2(\partial V \times I \times S)},$$  

(3.13)
where \(c_j, j = 1, \ldots, 5\) are positive weights and the subscript “-” refers as above to the negative part of a function. The first term penalizes the violation of the requirement \(D_0 = D(x), x \in T\). The minimization of the second and the third terms tries to maintain the requirements \(D(x) \leq D_C, x \in C\) and \(D(x) \leq D_N, x \in N\). To keep the admissible control set as the whole space \(L_2(\partial V \times I \times S)\), we added a penalty term

\[
c_4 \| u - \|^2_{L_2(\partial V \times I \times S)},
\]

which hinders the violation of the constraint \(u \geq 0\). The last (convex) term regularizes the schemes and helps the optimization process in theory and in numerical considerations. To diminish the incoming flux \(u\) may also have practical importance.

If the dose volume constraint is used, say in critical organ, one adds a penalty term

\[
c_6 \left( \left( v_0 - \frac{1}{\mu(C)} \int_C H(L\psi(u) - d_C) \, dx \right) \right)^2,
\]

where the Heaviside function can be replaced by an error function \(\text{erf}\) (as suggested above). The penalty term for the dose volume constraint can also be replaced by its discrete counterpart

\[
c_6 \left( \left( v_0 - \frac{1}{|I_C|} \sum_{p \in I_C} \text{erf}(L\psi(u)(x_p) - d_C) \right) \right)^2.
\]

Remark 3. To smoothen the dose in the target one may add the term

\[
c_7 \| \nabla_x L\psi(u) \|^2_{L_2(T)}
\]

in the cost function. We leave this consideration here.

As a conclusion we find that the corresponding optimization problem states:

Find the global minimum

\[
\min_{u \in L_2(\partial V \times I \times S)} J(u)
\]

such that

\[
B(\psi(u), v) = (Fu)(v), \quad v \in H^3.
\]

3.3. Optimization based on biological objectives

In the following we suggest an inverse treatment planning based on the biological response. Let \(k\) denote the probability of the death of a single clonogen at \(x \in T\). The probability \(k\) depends on the dose \(D(x)\) and so \(k = k(D(x))\). Typically the graph of \(k\) is a sigmoidal. The function \(k\) is based on the oncological data and its continuous expression can be obtained using appropriate basis system and data fitting. Denoting the number density of clonogens by \(\rho = \rho(x)\) the tumor control probability \(TCP\) can be expressed as follows [3]:

\[
TCP(D) = e^{\int_T \rho(x) \ln(k(D(x))) \, dx}.
\]

For the normal tissue complication probability \(NTCP\) we apply the model based on [11]. For the organ at risk we get [3]

\[
NTCP_C(D) = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^0 e^{-t^2/2} dt,
\]

For the normal tissue complication probability \(NTCP\) we apply the model based on [11]. For the organ at risk we get [3]
where
\[ \langle D \rangle_{L^p} = \frac{1}{\mu(C)^{1/p}} \left\| D \right\|_{L^p(C)} = \frac{1}{\mu(C)^{1/p}} \left( \int_C |D(x)|^p \, dx \right)^{1/p}. \]
Here \( \mu(C) \) is the measure (volume) of \( C \). Parameters \( D_{C,50}, p \) and \( \sigma_C \) are statistical values based on the oncological data.

Similarly we obtain for the normal tissue
\[ NTCP_N(D) = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{\langle D \rangle_{L^q} - D_{N,50}/\sigma_N} e^{-t^2/2} \, dt, \quad (3.20) \]
where
\[ \langle D \rangle_{L^q} = \frac{1}{\mu(N)^{1/q}} \left( \int_N |D(x)|^q \, dx \right)^{1/q}. \]
Here \( \mu(N) \) is the measure (volume) of \( N \). Parameters \( D_{N,50}, q \) and \( \sigma_N \) are statistical values based on the oncological data.

Putting \( D = L\psi(u) \) we obtain the probabilities as functions of the incoming flux \( u \)
\[ TCP(u) = e^{\int r \rho(x) \ln(k((L\psi(u))(x))) \, dx}, \quad (3.21) \]
\[ NTCP_C(u) = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{\langle L\psi(u) \rangle_{L^p} - D_{C,50}/\sigma_C} e^{-t^2/2} \, dt, \]
\[ NTCP_N(u) = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{\langle L\psi(u) \rangle_{L^q} - D_{N,50}/\sigma_N} e^{-t^2/2} \, dt. \]

**Remark 4.** A. For the \( NTCP \) there exists also alternative models [3] and these can be similarly implemented to our algorithms.

B. The organ at risk \( C \) can be divided into several disjoint parts \( C = C_1 \cup \cdots \cup C_n \). For individual \( C_i \) the above parameters may be different. For simplicity we assume one organ at risk.

Let \( p_C \) and \( p_N \in [0, 1] \) be the prescribed probability values (acceptable safes). Using the above definitions the inverse problem can be stated as follows:

**Suppose that** \( p_C \) and \( p_N \in [0, 1] \) **are given. Suppose that the number \( L \) of fields \( S_1 \), gantry, couch and collimator angles \( \alpha_1, \beta_1, \theta_1 \) of the fields \( S_1 \) are given.**

**Determine the incoming flux \( u \in L_2(\mathbb{R} \times I \times S) \) such that** \( TCP(u) \) **is maximal and that**
\[ NTCP_C(u) \leq p_C, \quad (3.22) \]
\[ NTCP_N(u) \leq p_N \quad (3.23) \]
**and**
\[ u \geq 0. \quad (3.24) \]

We are able to formulate different kinds of optimal and/or feasible problems. We proceed as follows. Define a cost function
\[ J(u) = c_1 \left( \frac{1}{TCP(u) + 1} \right) + c_2((p_C - NTCP_C(u))_-)^2 + c_3((p_N - NTCP_N(u))_-)^2 + c_4\|u\|^2_{L_2(\mathbb{R} \times I \times S)} + c_5\|u\|^2_{L_2(\mathbb{R} \times I \times S)}, \quad (3.25) \]
where \( c_j, j = 1, \ldots, 5 \) are positive weights.
The corresponding optimization problem states:

Find the global minimum

$$\min_{u \in L_2(\partial V \times I \times S)} J(u)$$

such that

$$B(\psi(u), v) = (Fu)(v), \quad v \in H^3.$$  \hspace{1cm} (3.27)

In the following we apply the physical cost function. Optimization results applying biological objective function will be addressed in future work. The initial solution for the optimization can be obtained as in the case of physical cost function given below.

4. Discretized model applying FEM

For computer needs we must discretize the above models. We apply here the finite element method which has some advantages for this problem. For example, the inflow boundary condition is quite easy to handle (via variational formulations). In addition, the convergence can be proven (not proven here), if the boundedness and coercitivity estimates given in Section 2 hold.

4.1. Finite element method for the control system

Let $X_h$ be a finite dimensional subspace of $H^3$ and let $Y_h$ be a finite dimensional subspace of $L_2(\partial V \times I \times S)$. Denote a basis of $X_h$ by $\{v_1, \ldots, v_N\}$ and denote a basis of $Y_h$ by $\{w_1, \ldots, w_M\}$. Let

$$\psi_h = \sum_{n=1}^{N} \alpha_n v_n, \quad u_h = \sum_{m=1}^{M} \beta_m w_m.$$  \hspace{1cm} (4.1)

Then the FEM approximation of the variational equation (3.9) is defined as

$$B(\psi_h, v) = (F u_h)(v), \quad v \in X_h.$$  \hspace{1cm} (4.2)

This requirement leads to the matrix equation

$$A\alpha = B\beta,$$

where $A \in M(N \times N), B \in M(N \times M)$ such that

$$A(k, n) = B(v_n, v_k), \quad B(k, m) = (F w_m)(v_k), \quad \alpha = \begin{pmatrix} \alpha_1 \\ \vdots \\ \alpha_N \end{pmatrix}, \quad \beta = \begin{pmatrix} \beta_1 \\ \vdots \\ \beta_M \end{pmatrix}.$$  \hspace{1cm} (4.4)

Eq. (4.3) can be put into the form

$$\begin{pmatrix} A & -B \end{pmatrix} \begin{pmatrix} \alpha \\ \beta \end{pmatrix} = 0,$$

which is the control system (3.27) in its discrete form.

4.2. Optimal control system for the discrete model

Denote

$$D(x) = \begin{pmatrix} Lv_1(x) & \cdots & Lv_n(x) \end{pmatrix}.$$
Then we find that
\[(L\psi_h)(x) = L \left( \sum_{n=1}^{N} \alpha_n v_n \right)(x) = D(x)\alpha. \tag{4.6} \]

To emphasize the dependence of \(\alpha\) on \(\beta\) we denote \(\alpha = \alpha(\beta)\). Applying the above approximations we are able to formulate the optimal control problem as follows. Define a cost functional by
\[
J(\beta) = c_1 \|D_0 - D\alpha(\beta)\|_{L^2(T)}^2 + c_2 \|(D_C - D\alpha(\beta))_+\|_{L^2(C)}^2 + c_3 \|(D_N - D\alpha(\beta))_+\|_{L^2(N)}^2
+ c_4 \left\| \sum_{m=1}^{M} \beta_m w_m \right\|_{L^2(\partial V \times I \times S)}^2 + c_5 \left\| \sum_{m=1}^{M} \beta_m w_m \right\|_{L^2(\partial V \times I \times S)}^2. \tag{4.7} \]

We can add the penalty term for the dose volume constraint
\[
c_6 \left( \left( v_0 - \frac{1}{\mu(C)} \int_C H(D\alpha(\beta) - d_C) \, dx \right) \right)^2,
\]
which can be replaced by its discrete counterpart
\[
c_6 \left( \left( v_0 - \frac{1}{|I_C|} \sum_{p \in I_C} \text{erf}_\epsilon(D\alpha(\beta)(x_p) - d_C) \right) \right)^2.
\]
One may also add the term to smoothen the dose in the target (when \(\kappa_j\) and \(v_n\) are sufficiently smooth)
\[
c_7 \left\| \sum_{n=1}^{N} \alpha_n \nabla_x L v_n \right\|_{L^2(T)}^2 \tag{4.8}
\]
in the cost function.

As a conclusion we find that the discretized optimal control problem states:
Find the global minimum
\[
\min_{\beta \in \mathbb{R}^M} J(\beta) \tag{4.9}
\]
such that
\[
(A - B) \begin{pmatrix} \alpha \\ \beta \end{pmatrix} = 0. \tag{4.10}
\]

The functional \(J(\beta)\) is not generally differentiable. One can however show that the cost function \(J : \mathbb{R}^M \to \mathbb{R}\) is locally Lipschitz continuous.

For many commonly used basis \(\{w_1, \ldots, w_M\}\) it is reasonable to assume that the coefficients \(\beta_m\) are bounded
\[
|\beta_m| \leq C, \quad m = 1, \ldots, M. \tag{4.11}
\]
Hence the global minimum of the above problem exists.

4.3. Parametrization of discrete system

In [20] we gave some simulations using the variational equations for the optimal control (Section 4.2). Here we concentrate on the numerical results obtained by the parametrization.
We say that the (control) system (4.10) is parametrized by a matrix \( S \in M(N + M, p) \) if
\[
(A - B) \begin{pmatrix} \alpha \\ \beta \end{pmatrix} = 0 \iff \begin{pmatrix} \alpha \\ \beta \end{pmatrix} = S \gamma, \quad \gamma \in \mathbb{R}^p.
\] (4.12)

Let \( p_1, p_2 \) be the canonical projections
\[
p_1 : \mathbb{R}^{N+M} \to \mathbb{R}^N, \quad p_2 : \mathbb{R}^{N+M} \to \mathbb{R}^M.
\]

Denote \( S_j \gamma = p_j(S \gamma), j = 1, 2 \). Then \( \alpha = S_1 \gamma, \beta = S_2 \gamma \). Hence
\[
\psi \approx \psi_h = \sum_{n=1}^N \alpha_n v_n = \sum_{n=1}^N (S_1 \gamma)_n v_n, \quad \gamma \in \mathbb{R}^p
\] (4.13)

and
\[
u \approx u_h = \sum_{m=1}^M \beta_m w_m = \sum_{m=1}^M (S_2 \gamma)_m w_m, \quad \gamma \in \mathbb{R}^p.
\] (4.14)

Denote
\[
S_1 \gamma = \sum_{n=1}^N (S_1 \gamma)_n v_n, \quad S_2 \gamma = \sum_{m=1}^M (S_2 \gamma)_m w_m.
\]

We have verified

**Theorem 3.** The FEM approximation \( u_{h,0} \) for the optimal control \( u_0 \) of the problem (4.2) is
\[
u_{h,0} = \sum_{m=1}^M (S_2 \gamma_0)_m w_m,
\] (4.15)

where \( \gamma_0 \in \mathbb{R}^p \) is the global minimum of the unconstrained problem
\[
\min_{\gamma \in \mathbb{R}^p} J(\gamma),
\] (4.16)

where
\[
J(\gamma) = c_1 \|D_0 - L(S_1 \gamma)\|_{L^2(\Gamma)}^2 + c_2 \|D_C - L(S_1 \gamma)\|_{L^2(\mathbb{C})}^2 + c_3 \|D_N - L(S_1 \gamma)\|_{L^2(\mathbb{N})}^2 + c_4 \|S_2 \gamma\|_{L^2(\mathbb{V} \times I \times S)}^2 + c_5 \|S_2 \gamma\|_{L^2(\mathbb{V} \times I \times S)}^2.
\] (4.17)

Here the penalty term for the dose volume constraint is
\[
c_6 \left( \frac{1}{\mu(C)} \int_C H(L(S_1 \gamma) - d_{C}) \, dx \right)_-^2.
\]

Note that
\[
L(S_1 \gamma) = DS_{1 \gamma}, \quad L(S_2 \gamma) = DS_{2 \gamma},
\]

where \( D \) is as above and \( D'(x) = (w_1(x), \ldots, w_M(x)) \).
A good initial point for the optimization is the solution of the quadratic problem

$$\min_{\gamma \in \mathbb{R}^p} J(\gamma),$$

(4.18)

where

$$J(\gamma) = c_1 \| D_0 - L(S_1 \gamma) \|_{L_2(T)}^2 + c_5 \| S_2 \gamma \|_{L_2(\partial V \times I \times S)}^2.$$  

(4.19)

Denote the elements of matrices $S_j$ by $S_1(n, l)$ and $S_2(m, l)$. We have

**Theorem 4.** The minimum $\gamma$ of the problem (4.18) satisfies the linear equations

$$c_1 \sum_{n=1}^{N} S_1(n, l) \langle L^*(e_T LS_1 \gamma), v_n \rangle_{L_2(G)^3} - c_5 \sum_{m=1}^{M} S_2(m, l) \langle S_2 \gamma, w_m \rangle_{L_2(\partial V \times I \times S)}$$

$$= c_1 \sum_{n=1}^{N} S_1(n, l) \langle L^*(e_T D_0), v_n \rangle_{L_2(G)^3}, \quad l = 1, \ldots, p,$$

(4.20)

where $e_T$ is the “extension by zero operator” from the set $T$ on $V$.

**Proof.** The minimum point satisfies $J'(\gamma) = 0$. We find that

$$J'(\gamma)y = 2c_1 \langle D_0 - LS_1 \gamma, LS_1 y \rangle_{L_2(T)} + 2c_5 \langle S_2 \gamma, S_2 y \rangle_{L_2(\partial V \times I \times S)}$$

$$= 2c_1 \langle L^*(e_T D_0 - LS_1 \gamma), S_1 y \rangle_{L_2(G)^3} + 2c_5 \langle S_2 \gamma, S_2 y \rangle_{L_2(\partial V \times I \times S)}.$$  

(4.21)

For any $v \in L_2(G)^3$ we have

$$\langle v, S_1 y \rangle_{L_2(G)^3} = \left( v, \sum_{n=1}^{N} (S_1 y)_n v_n \right)_{L_2(G)^3}$$

$$= \left( v, \sum_{n=1}^{N} \sum_{l=1}^{p} S_1(n, l) v_n \right)_{L_2(G)^3} = \sum_{l=1}^{p} \sum_{n=1}^{N} S_1(n, l) \langle v, v_n \rangle_{L_2(G)^3} y_l$$

and similarly for any $w \in L_2(\partial V \times I \times S)$

$$\langle w, S_2 y \rangle_{L_2(\partial V \times I \times S)} = \sum_{l=1}^{p} \sum_{m=1}^{M} S_2(m, l) \langle w, w_m \rangle_{L_2(\partial V \times I \times S)} y_l.$$

Hence the assertion follows from (4.21).  \qed

Since

$$L^*(e_T (LS_1 \gamma)) = \sum_{q=1}^{N} (S_1 \gamma)_q L^*(e_T (L v_q)) = \sum_{j=1}^{p} \sum_{q=1}^{N} S_1(q, j) L^*(e_T (L v_q)) \gamma_j$$  

(4.22)

and

$$S_2 \gamma = \sum_{j=1}^{p} \sum_{r=1}^{M} S_2(r, j) w_r \gamma_j,$$

(4.23)

$\gamma$ can be immediately solved from (4.20).
4.4. Compatibility operator for the discrete system

Let \( F \in M(m, n) \) be a matrix. We consider the parametrization of the equation \( FX = 0 \) that is, we consider the existence of a matrix \( S \in M(n, p) \) such that

\[
FX = 0 \iff X = SY. \quad (4.24)
\]

We recall the following well-known theorem (Singular Value Decomposition).

**Theorem 5.** Suppose that the matrix \( F \in M(m, n) \) has rank \( r \). Then there exist orthogonal matrices \( U \in M(m, m) \) and \( V \in M(n, n) \) such that

\[
U^* F V = \begin{pmatrix} D_r & 0 \\ 0 & 0 \end{pmatrix} =: D \in M(m, n), \quad (4.25)
\]

where \( D_r \in M(r, r) \) is a nonsingular diagonal matrix.

**Proof.** See e.g. [10]. \( \square \)

In (4.25) the diagonal elements of \( D_r \) are \( \sqrt{\mu_j}, j = 1, \ldots, r \) where \( \mu_j \) are the nonzero eigenvalues of the positive semidefinite symmetric matrix \( F^* F \in M(n, n) \) (in decreasing order). From Theorem 5 it follows:

**Corollary 1.** For any matrix \( F \in M(m, n) \) the parametrization can be given by \( S = VP \in M(m, n - r) \), where \( P = \begin{pmatrix} 0 \\ I_{n-r} \end{pmatrix} \).

From Corollary 1 we find that the system \( (A - B)(\begin{pmatrix} \alpha \\ \beta \end{pmatrix}) \) has a parametrization. This parametrization is useful for us since applying it the optimization contains only \( n - \text{rank}(A - B) \) free parameters.

5. Numerical results and discussion

To simulate the use of parametrization in the optimal control, the FEM is used for one scalar (non coupled) BTE in 2D spatial domain. Then the angular domain is flattened to be \( \theta \in [0, 2\pi] \), \( \Omega = (\sin \theta, \cos \theta) \). This neglects the scattering out of the 2D plane. As mentioned in the introduction real spatially 3D simulations are still computationally too expensive. Our aim here is that the optimal control model works in general. The phantom and incoming particles are artificial. All the computations are made using MATLAB\textsuperscript{\textregistered} in a normal PC (2 GHz Pentium IV with 2 GB of total memory).

The spatial domain \([0, 20] \times [-10, 10] \text{ cm}^2\) is divided into 100 rectangular elements having 121 node points. The angular domain \([0, 2\pi]\) is divided into 8 evenly distributed intervals with 8 node points and energy interval \([0.1, 1] \text{ MeV}\) consisted of 3 evenly distributed intervals with 4 node points. Thirty-six spatial boundary nodes are used as source nodes. The source nodes and spatial geometry is shown in Fig. 1.

The energy of the incoming radiation is restricted such that only maximum energy is allowed and the intensities of the directions of the source nodes are optimized. Thus, \( N = 121 \cdot 8 \cdot 4 = 3872 \) and \( M = 36 \cdot 3 = 108 \), in which only those three inward angular node points for which \( \Omega \cdot \nu < 0 \) are included at each spatial node. For the finite element discretization we refer to [2], in which we have solved the BTE forward problem. The matrix \( S \) is computed using SVD, which
Fig. 1. On the left are the optimized directions of boundary flux intensities. On the right is the optimized dose distribution with isodose curves, in which 100% corresponds 10 Gy. Also the spatial grid and source nodes are shown. The dark gray area defines the tumor and the light gray area defines the critical organ.

took approximately three hours. The initial point is achieved from the solution of the quadratic problem (4.18), in which $c_1 = 1$, $c_5 = 10^{-6}$ and $D_0 = 10$ Gy. Simulated annealing [7] is used in the global optimization of the unconstrained problem (4.16), in which $c_1 = 1$, $c_2 = 1.5$, $c_3 = 0.5$, $c_4 = 1$, $c_5 = 0$, $D_0 = 10$ Gy, $D_N = 5$ Gy and $D_C = 2$ Gy. The computation of the initial point took a few seconds and the global optimization took approximately one hour. The optimized intensities of different directions and the dose distribution with isodose curves are shown in Fig. 1.

It can be seen from Fig. 1 that the optimization works in general. 90% isodose curve conforms quite well to the tumor area while the critical organ receives relatively low dose, i.e., less than 40% of the prescribed dose for the tumor. Small areas of high dose are present at the normal tissue, which might be removed by adding more weight to the normal tissue criterion. However, this may pose violation in other dose requirements. With parametrization the number of unknown variables is decreased from $N + M = 3980$ to $M = 108$ and the global optimization is much easier to accomplish. Here the idea was to demonstrate the use of some kind of tomotherapy approach, in which the directions of the small fields with preset energies are optimized. In the case where we apply conventional treatment planning we must choose the admissible space of control variables as described below in Conclusions. We shall not give any simulation for that case here. These will be issued in subsequent works. In Fig. 1 it can be seen that some of the optimized directions are zero or they are very small. These could be neglected and the ‘treatment’ could be done using only those meaningful directions. Near the corners there are intensities at directions which are wrong. These errors occur because the FEM causes some instability to the solution of the forward problem at the corner nodes.

6. Conclusion

Optimal dosing of radiation on tumors while avoiding the healthy parts of the body within the tolerance is a necessity in successful radiation therapy treatment planning. Here the planning is
based on the Boltzmann Transport Equation and optimal boundary control model. Our approach contains various subfields such as

1. The solution of the forward problem. We have applied here the BTE which is most relevant from a physical point of view. This modeling needs correct cross sections and their study is one part of the research.

2. Discretization for computer needs. We used FEM approach which seems to be well-suited for this problem. Our selection of element basis system may not be optimal. E.g. the adaptivity of the grid and wavelet based basis system certainly improves the computations. Also the so called multi group methods (for energy variable) have benefits and we are aiming to study them in near future. Other potential possibility for the discretization is to apply (wavelet based) collocation method. In any case the BTE in its discrete form is large dimensional linear system of equations.

3. The optimal solution of the inverse problem. This needs the selection of the cost function. We used physically based criteria for the cost but we also formulated how the optimization can be founded on biological cost functions. In both cases the cost functions are multiextremal and global optimizations or good initializations are needed. To diminish the complexity of the optimization we applied novel approach, so called parametrization, to handle the large dimensional linear system mentioned in item 2.

Multileaf collimator (MLC), have provided new facilities in dose delivery for a patient [23,24]. The MLC provides use of intensity modulated treatment techniques allowing construction of three-dimensional and conformal dose distributions with sharp dose gradients. The determination of MLC parameters, that is, locations and time lengths of subfields (in the multiple static delivery technique) or velocities of leaf trajectories (in the dynamical delivery technique) such that the incoming intensity distribution, produces the desired dose distribution is the practical aim in modern inverse radiotherapy treatment planning. Nowadays, in practice one first optimizes the incoming flux (such as in this contribution) and afterward uses some optimization algorithm (“leaf sequencer”) to set the MLC parameters optimally. In our approach it is also possible to use MLC parameters as optimal control variable. We omit these formulations here. The key idea is that we are able to express the incoming flux $u$ as a function of MLC trajectories (see [14,17,19]). The “direct MLC optimization” has obvious benefits. One of its shortcomings is that it leads to more severe nonlinearities and so the present global optimization algorithms and computer researches are still not sufficient to solve these problems in reasonable time.

Monodirectionality (for each field) is nowadays in general a practical requirement but in future it is possible to use multidirectional incoming fluxes applying, e.g. robotics. In the monodirectional case or more generally cases where the direction or energy of the incoming flux is constraint, we simply choose

$$L_2(\Gamma_1 \times I_{ad,1} \times S_{ad,1}) \times \cdots \times L_2(\Gamma_L \times I_{ad,L} \times S_{ad,L})$$

for the control space where $I_{ad,l}$ and $S_{ad,l}$ are the admissible energies and directions for the incoming flux, respectively. In strictly monodirectional and monoenergetic case we choose

$$ (Fu)(v) = \sum_{l=1}^{L} \int_{\Gamma_l} (\Omega_{0,l} \cdot v) \cdot u_l(x) v_1(x, E_{0,l}, \Omega_{0,l}) \, d\sigma, \quad (6.1) $$

where $u_l = u_l(x)$. 


We conclude that the parametrization can be used in solving the BTE based control problem in radiotherapy purposes. Further studies needs to be done in making the parametrization easier to compute. We applied SVD in parametrization, but more sophisticated linear algebraic methods certainly exist. Also the possibility to use approximations for the parametrization has to be studied as well. Furthermore, with better global optimizers (see e.g. [14]) the global optimization would be more powerful. These issues will be considered in future work.

Acknowledgments

This work was supported by Varian Medical Systems Finland, Espoo, Finland and by the Academy of Finland (decision number 78001) which is greatly acknowledged. We thank the referees for their suggestions and corrections.

References