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Abstract

Patient motion during treatment is one of the future challenges in the field of external beam radiotherapy. In this paper, we address this problem by considering a time–dependent Boltzmann transport model for dose calculation and by deriving closed-loop control laws for the treatment planning problem. We formulate an optimal control problem for the desired dose using boundary and distributed control and derive optimality conditions. For the construction of the closed-loop control laws we use an inexact variant of model predictive control called instantaneous control. We compare numerical results obtained with instantaneous control to those obtained by optimal open-loop control, and present numerical simulations in one and two spatial dimensions.

Key words. Radiative transfer; optimal control; first-order optimality; radiotherapy

1 Introduction

Mathematical methods play an increasing role in medicine, especially in radiation therapy. Several special journal issues have been devoted to cancer modeling and treatment, cf. [2, 3, 4, 11] among others. While until recently, treatment planning was done by an experienced physician "by hand", computer-aided treatment planning systems based on optimization algorithms currently enter into clinical practice, cf. [22] and references therein.

The use of ionizing radiation is one of the main tools in the therapy of cancer. The aim of radiation treatment is to deposit enough energy in cancer cells so that they are destroyed. On the other hand, healthy tissue around the cancer

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cells should be harmed as little as possible. Furthermore, some regions at risk, like the spinal chord, should receive almost no radiation at all. Patient motion during treatment is one of the future challenges in the field of external beam radiotherapy. For instance, tumors near the lung move due to breathing and it is hard to ensure that enough does is deposited within the tumor, while at the same time harming the healthy tissue around the tumor as little as possible. Techniques addressing this problem have become known as 4D radiotherapy [7], meaning that time, the fourth dimension, also has to be taken into account. A further technique, named Image-Guided Radiotherapy (IGRT) is currently being developed. In this method, the radiation is used to create patient images during treatment. The mathematical methods developed in this paper are based on the hypothesis that momentary patient images from IGRT can be used to adapt the external radiation and thus to improve the dose distribution.

Most dose calculation algorithms in clinical use rely on the Fermi–Eyges theory of radiation which is insufficient at inhomogenities, e.g. void-like spaces like the lung. We start with a Boltzmann transport model for the radiation which accurately describes all physical interactions, and based on this model we develop a direct optimization approach based on adjoint equations.

Until recently, dose calculation using a Boltzmann transport equation has not attracted much attention in the medical physics community. This access is based on deterministic transport equations of radiative transfer. Similar to Monte Carlo simulations it relies on a rigorous model of the physical interactions in human tissue that can in principle be solved exactly. Monte Carlo simulations are widely used, but it has been argued that a grid-based Boltzmann solution should have the same computational complexity [5]. Electron and combined photon and electron radiation were studied in the context of inverse therapy planning cf. [28, 27] and most recently [29]. A consistent model of combined photon and electron radiation was developed [17] that includes the most important physical interactions. Furthermore, several neutral particle codes have been applied to the dose calculation problem, see [16] for a review.

Guided by the hypothesis that momentary patient images from IGRT can be used to adapt the external radiation we develop an instantneous closed-loop control concept for external beam radiotherapy which also allows patient motion during treatment. Instantaneous control is a closed loop control concept similar to model predictive control [15] and receding horizon control [25], developed by mechanical engineers and applied mathematicians in the context of suboptimal flow control, see [10, 8, 23, 24, 20, 9]. In [18] instantaneous control for the Navier-Stokes system is interpreted as a time-discrete version of a nonlinear closed loop controler associated to the Navier-Stokes system. A rigorous stability analysis for instantaneous control for the Burgers equation is provided in [21], and for the Navier-Stokes system in [19]. All mentioned contributions do not consider contraints on the controls. In the present work we adapt the concept of instantaneous control to external beam radiotherapy, also allowing for hard constraints on the controls.

2 Modeling of Dose Distribution for Radiotherapy

2.1 Transport Equation

Consider a part of the patient's body which contains the region of the cancer cells. We assume that this part of the body can be described as a convex, open, bounded domain Ω in $\mathbb{R}^3$. Furthermore, we assume that Ω has a smooth boundary with outward normal vector n. The direction, into which the electron is moving is given by $\omega \in S^2$, where S^2 is the unit sphere in three dimensions. Moreover, let

$$\partial\Omega^- := \{(x,\omega) \in \Omega \times S^2 : n(x)\cdot\omega < 0\}$$
$$\partial\Omega^+ := \{(x,\omega) \in \Omega \times S^2 : n(x)\cdot\omega > 0\}.$$

We consider particle transport modeled by the time–dependent Boltzmann equation for the particle density $\psi(x,t,\omega)$ as

$$\begin{aligned}\frac{1}{c}\partial_t\psi(x,t,\omega) + \omega\cdot\nabla_x\psi(x,t,\omega) + \sigma_t(x,t)\psi(x,t,\omega)\\ = \sigma_s(x,t)\int_{S^2} s(x,t,\omega\cdot\omega')\psi(x,t,\omega')d\omega' + q_1(x,t,w)\end{aligned} \tag{1}$$

with

$$\psi(x,t,\omega) = q_2(x,t,\omega) \text{ on } [0,T]\times\partial\Omega^-.$$

For the sake of simplicity, we neglect the energy dependence of ψ. Here, $\psi(x,t,\omega)\cos\theta dAd\omega$ is the number of electrons that pass through an area dA at point x into a solid angle $d\omega$ around ω at time t. The angle θ is the angle between ω and dA. The total cross section $\sigma_t(x,t)$ is the sum of absorption cross section $\sigma_a(x,t)$ and total scattering cross section $\sigma_s(x,t)$. The scattering phase function is normalized,

$$2\pi\int_{-1}^{1} s(x,t,\mu)d\mu = 1. \tag{2}$$

All quantities describing the medium depend on time since we want to model a patient's body in motion. From the physical interpretation, we have that ψ, q, σ_t, σ_s and s are non-negative quantities. The detailed interactions of electrons with atoms give rise to complicated explicit formulas for the scattering coefficient, see e.g. [17]. Because of this, many studies use the simplified Henyey-Greenstein scattering kernel [1],

$$s_{HG}(x,\mu) = \frac{1-g^2}{4\pi(1+g^2-2g\mu)^{3/2}}. \tag{3}$$

The parameter g, which can depend on x, is the average cosine of the scattering angle and is a measure for the anisotropy of the scattering. In the strongly forward peaked range ($g > 0.8$), other scattering kernels have been proposed, which are in better agreement with Mie scattering theory [1].

In the equation above two external controls $q_1(x,t)$ and $q_2(x,t)$ appear and in principle model two types of radiation therapy. In the context of brachytherapy the source term q_1 corresponds to the sealed dose distribution in the patient's body and we have $q_2 \equiv 0$. For external beam radiotherapy, we have no distributed source $q_1 \equiv 0$, but a boundary control q_2. In both applications, we have $q_i \geq 0$.

2.2 Treatment Optimization

A number of functionals and methods have been devised to describe the effect of radiation on biological tissue, cf. the extensive lists of references in the reviews [6] and [26]. It is clear that the amount of destroyed cells in a small volume, be they cancer or healthy cells, is not directly proportional to the dose

$$D(x,t) = \int_{S^2} \psi(x,t,\omega) d\omega \tag{4}$$

deposited in that volume. However, no single accepted type of model has emerged yet. Moreover, current biological models require input parameters which are not known exactly [26]. This is why the authors of [26] opted not to investigate these models but rather to focus on some general mathematical cost functionals. A quadratic objective function together with nonlinear constraints was identified as the most versatile model.

We try to find a source configuration q_1 or boundary values q_2 such that the quadratic deviation from the prescribed dose $\bar{D}$ and a weighting function $\alpha_1 = \alpha_1(x,t)$

$$J_1(D) = \int_0^T \int_\Omega \frac{\alpha_1}{2} (D - \bar{D})^2 dx dt \tag{5}$$

is minimal under the constraint that the transfer equation (1) is fulfilled. We also consider the problem

$$J_2(\psi) = \int_0^T \int_\Omega \int_{S^2} \frac{\alpha_2}{2} (\psi - \bar{\psi})^2 dx t \omega \tag{6}$$

Here, we are interested in the case of a moving patient and the reactions of the control to that motion. Thus the desired dose distribution $\bar{D}$ (which is high in the tumor and low outside), the control q_i and the penalty parameters explicitly depend on time.

Furthermore, we include a penalty term proportional to the applied external source in the minimization process to prevent trivial solutions. In case of distributed control we regularize J_i by

$$J_B := \int_0^T \int_\Omega \alpha q_1^2 dx dt \tag{7}$$

and for boundary control by

$$J_T := \int_0^T \int_{\partial\Omega^-} \alpha(n\cdot\omega) q_2^2 dx dt. \tag{8}$$

2.3 Theoretical Results

For the mathematical analysis we introduce the spaces

$$D(\mathbf{A}) := \{\psi \in L^2(\Omega\times S^2) : \nabla_x\psi \in L^2(\Omega\times S^2)\}, \tag{9a}$$

$$\widetilde{D(\mathbf{A})} := \{\psi \in D(\mathbf{A}) : \psi = 0 \text{ on } \partial\Omega^-\}, \tag{9b}$$

$$\widetilde{D(\mathbf{A})}^* := \{\lambda \in D(\mathbf{A}) : \lambda = 0 \text{ on } \partial\Omega^+\}, \tag{9c}$$

$$L^2_{ad} := \{q \in L^2(\Omega\times S^2) : q \geq 0\},\ L^2 := \{q \in L^2(\Omega\times S^2)\} \tag{9d}$$

and we assume that the scattering and absorption coefficients fulfill

$$s, \sigma_t, \sigma_s \geq 0,\ \sigma_t, \sigma_s \in L^\infty,\ \int_{-1}^1 s(x,t,\mu)d\mu \leq c_0, \tag{10a}$$

$$\sigma_t(x,t) - \sigma_s(x,t)\int_{-1}^1 s(x,t,\mu)d\mu \geq c_1 > 0. \tag{10b}$$

Both conditions are satisfied for physically reasonable media. The assumptions (10) guarantee that the following operators are well–defined, c.f. [12].

$$\begin{array}{ll} \mathbf{A} : D(\mathbf{A}) \to L^2, & \mathbf{A}\psi := -\omega\nabla_x\psi \\ \mathbf{\Sigma} : L^2 \to L^2, & \mathbf{\Sigma}\psi := \sigma_t\psi \\ \mathbf{K} : L^2 \to L^2, & \mathbf{K}\psi := \sigma_s\int_{S^2} s(x,\omega\omega')\psi d\omega' \\ \mathbf{T} : D(\mathbf{A}) \to L^2, & \mathbf{T}\psi := -\mathbf{A}\psi + \mathbf{\Sigma}\psi - \mathbf{K}\psi \end{array} \tag{12}$$

where $q^+ := \max(q,0)$. Furthermore, we recall the following result from ([13]) for the case of distributed control.

Lemma 1 *Under assumption (10) the previously defined operators have the following properties.*

- *The operators $\mathbf{\Sigma}, \mathbf{K}$ are linear and bounded operators on L^2. The operator $\mathbf{T}$ fulfills $(\psi, \mathbf{T}\psi)_{L^2} \geq c_1\|\psi\|^2_{L^2}$. The operator $\mathbf{T}^* := \mathbf{A}+\mathbf{\Sigma}-\mathbf{K} : D(A) \to L^2$ satisfies the estimate $(\psi, \mathbf{T}^*\psi)_{L^2} \geq c_1\|\psi\|^2_{L^2}$.*

- *The operator $\mathbf{E} : L^2_{ad} \to \widetilde{D(A)}$ defined by*

$$\mathbf{E}q_1 = \psi :\Leftrightarrow \mathbf{T}\psi = q_1, \psi = 0 \text{ on } \partial\Omega^-$$

is a well–defined operator. $\mathbf{E}$ as operator from $L^2 \to L^2$ is a linear and bounded operator. There exists an operator $\mathbf{E}^*(r) = \lambda : L^2 \to \widetilde{D(A)}^*$ such that $\mathbf{A}\lambda + \mathbf{\Sigma}\lambda - \mathbf{K}\lambda = r$ and $\lambda = 0$ on $\partial\Omega^+$. $\mathbf{E}^*$ is also a linear and bounded operator on L^2 and $\mathbf{E}^*$ is adjoint to $\mathbf{E}$.

- *For any* $\bar{\psi} \in L^2(\Omega)$, $0 < \alpha, 0 \leq \alpha_1 \in L^\infty(\Omega)$, *the following problem admits a unique solution* $q_1 \in L^2_{ad}(\Omega), q_2 \equiv 0$:

$$\int_\Omega \alpha_1 \left(\int_{S^2} \psi d\omega - \bar{\psi} \right)^2 + \alpha q_1^2 dx \to \min \;\; \textit{sbj. to } \mathbf{T}\psi = q_1, \psi = 0 \textit{ on } \partial\Omega^- \tag{13}$$

satisfying

$$\mathbf{T}\psi = q_1, \; \mathbf{T}^*\lambda = \int_{S^2} \psi d\omega - \bar{\psi}, \; q_1 = (q_1 - \int_{S^2} \lambda d\omega - \alpha q_1)^+, \psi, \lambda = 0 \textit{ on } \partial\Omega^\mp \tag{14}$$

- *For any* $\bar{\psi} \in L^2$, $0 < \alpha, 0 \leq \alpha_1 \in L^\infty(\Omega)$, *the following problem admits a unique solution* $q_1 \in L^2_{ad}, q_2 \equiv 0$:

$$\int_{S^2 \times \Omega} \alpha_1 \left(\psi - \bar{\psi} \right)^2 + \alpha q_1^2 dx d\omega \to \min \;\; \textit{sbj. to } \mathbf{T}\psi = q_1, \psi = 0 \textit{ on } \partial\Omega^- \tag{15}$$

satisfying

$$\mathbf{T}\psi = q_1, \; \mathbf{T}^*\lambda = \alpha_1(\psi - \bar{\psi}), \; q_1 = (q_1 - \lambda - \alpha q_1)^+, \; \psi, \lambda = 0 \textit{ on } \partial\Omega^\mp \tag{16}$$

Clearly, the previous Lemma yields existence of an optimal control in the case of time–independent distributed control. For results on boundary control, we refer to [29]. To the best of our knowledge there are currently no results on time–dependent control problems available.

3 Control Laws

3.1 Distributed Control

Offline computed optimal time-dependent dose distributions do not offer the ideal solution to treatment planing with external radiation due to the motion of the patient's body since this would require a priori knowledge of this motion. This information is typically not available. Therefore, we propose a closed-loop control approach yielding efficiently computable suboptimal controls, see the computational results below.

The outline of this section is as follows. We first derive the control laws for distributed control in the case of functional J_2 and $\bar{\psi} \equiv 0$. Then, we extend the results to a general $\bar{\psi}$ and finally to the cost functional J_1. We then proceed with a control law for boundary control.

The derivation of the control law follows [19]. We –at first– consider the case of distributed control. An implicit semi–discretization of the radiative transfer equation with control $q_1 := Q$ applied at time k and $q_2 \equiv 0$ reads

$$-\Delta t \mathbf{A}\psi^k + \left(\frac{1}{c} + \Delta t \mathbf{\Sigma} \right) \psi^k - \Delta t \mathbf{K}\psi^k = \frac{1}{c}\psi^{k-1} + Q. \tag{17}$$

Model predictive control on the time horizon $[t, t+dt]$ now uses the optimal solution Q^* obtained by minimizing an approprtitate cost functional (see (20)) which is formed using currently available observations of the system. The optimal control then can be expressed in terms the available observations, and thus in terms of the state itself. This yields a closed-loop control law. Here we even proceed in a simpler way by using a suboptimal control obtained by applying only one steepest descent step to the solution of the optimization problem. This resulting closed-loop control scheme is called instantaneous control and is developed in [18, 19]. For its construction in the present setting we define the operators

$$\mathcal{A} := \Delta t\mathbf{A},\ \mathcal{S} := (\frac{1}{c} + \Delta t\mathbf{\Sigma}),\ \mathcal{K} := \Delta t\mathbf{K}, \tag{18}$$

$$\mathcal{T} := -\mathcal{A} + \mathcal{S} - \mathcal{K},\ \mathcal{E}(Q) = \psi \Leftrightarrow \mathcal{T}\psi = Q, \psi = 0 \text{ on } \partial\Omega^- \tag{19}$$

and obtain the following Lemma.

Lemma 2 *Let assumption (10) hold true.*

Then, the operators $\mathcal{S}, \mathcal{K} : L^2 \to L^2$ are linear and bounded operators. The operator $\mathcal{T}$ satisfies $(\psi, \mathcal{T}\psi) \geq (\frac{1}{c} + c_1\Delta t)\|\psi\|^2_{L^2}$. The operator $\mathcal{T}^* := \mathcal{A} + \mathcal{S} - \mathcal{K} : D(A) \to L^2$ satisfies the same estimate. The operator $\mathcal{E} : L^2_{ad} \to \widetilde{D(A)}$ is well-defined. $\mathcal{E}$ is a linear and bounded operator on L^2. There exists an adjoint operator $\mathcal{E}^*$ on L^2 and $\mathcal{E}^*(r) = \lambda : L^2 \to \widetilde{D(A)}^* \subset L^2$ is a well–defined operator, such that for all $\lambda \in \widetilde{D(A)}^* : \mathcal{E}^*\mathcal{T}\lambda = \lambda$. Finally, for any $\bar{\psi}^{k-1}, \psi^{k-1} \in L^2, \alpha > 0$ the optimal control problem

$$\int_{S^2\times\Omega} (\psi^k - \bar{\psi}^{k-1})^2 + \alpha Q^2 dx d\omega \to \min\ \text{sbj. to } \mathcal{T}\psi = \frac{1}{c}\psi^{k-1} + Q,\ \ \psi = 0 \text{ on } \partial\Omega^- \tag{20}$$

admits a unique solution $Q \in L^2$ and $\psi \in \widetilde{D(A)}$ and the necessary first–order optimality system reads

$$\mathcal{T}\psi = \frac{1}{c}\psi^{k-1} + Q,\ \psi = 0 \text{ on } \partial\Omega^- \tag{21a}$$

$$\mathcal{T}^*\lambda = (\psi - \bar{\psi}^{k-1}),\ \psi = 0 \text{ on } \partial\Omega^+ \tag{21b}$$

$$Q = (Q - \lambda - \alpha Q)^+ \tag{21c}$$

If we perform a one–step projected gradient algorithm with step–width ρ we obtain

$$\begin{aligned} Q^{n+1} &= (Q^n - \rho\lambda - \rho\alpha Q^n)^+ \\ &= \big((1-\rho\alpha)Q^n - \rho\mathcal{E}^*(\psi - \bar{\psi}^{k-1})\big)^+ \\ &= \Big((1-\rho\alpha)Q^n - \rho\mathcal{E}^*(\frac{1}{c}\mathcal{E}\psi^{k-1} + \mathcal{E}Q^n - \bar{\psi}^{k-1})\Big)^+ \end{aligned}$$

In order to derive a control law we assume for a moment $\bar{\psi} \equiv 0$. Then, we obtain a control law by setting $Q^n \equiv 0$ and (17) yields for $Q \equiv Q^{n+1}$:

$$-\mathcal{A}\psi^k + \mathcal{S}\psi^k - \mathcal{K}\psi^k = \frac{1}{c}\psi^{k-1} + \left(-\frac{\rho}{c}\mathcal{E}^*\mathcal{E}\psi^{k-1}\right)^+, \tag{22}$$

i.e., a semi–implicit discretization of

$$\frac{1}{c}\partial_t\psi - \mathbf{A}\psi + \mathbf{\Sigma}\psi = \mathbf{K}\psi + \left(-\frac{\rho}{\Delta tc}\mathcal{E}^*\mathcal{E}\psi\right)^+ \tag{23}$$

We emphasize that this discretization is not consistent in time, due to the appearance of the factor Δt in the denomenator of (23). However, we are not interested in consistent approximations but in stabilizing nonlinear control operators. In this sense the operator $\left(-\frac{\rho}{\Delta tc}\mathcal{E}^*\mathcal{E}\psi\right)^+$ has to be understood. The factor $\frac{\rho}{\Delta tc}$ here may be considered as one constant which defines the stabilizing properties of the operator, compare the discussion related to Fig. 1. Let us emphasize that controller is defined through a nonlinear operator.

We prove now the decay of the continuous equation to $\bar{\psi} \equiv 0$ under the assumption

$$\psi \geq 0 \implies \mathcal{E}\psi \geq 0 \text{ and } \mathcal{E}^*\psi \geq 0 \tag{24}$$

Let $D^t_\pm := \{(x,\omega) \in \Omega \times S^2 : \psi(x,\omega,t) \geq (\leq)0\}$ and we assume that $\partial D^t_\pm$ is sufficiently regular.

Fix $t > 0$ and test (23) by ψ. Integrating on $D^t_\pm$ yields under the assumption (24):

$$\frac{1}{2}\partial_t\|\psi\|^2_{L^2} + (\psi, \mathbf{T}\psi)_{L^2} = -\frac{\rho}{\Delta tc}\int_{D^t_-}\psi\mathcal{E}^*\mathcal{E}\psi dx d\omega.$$

If $D^t_\pm$ is sufficiently regular for all t, we have $\int_{D^t_-}\psi\mathcal{E}^*\mathcal{E}\psi dx d\omega = \int_{D^t_-}\mathcal{E}\psi\mathcal{E}\psi dx d\omega$ since $\psi = 0$ on ∂D^t_-. Hence, for all $t > 0$:

$$\frac{1}{2}\partial_t\|\psi\|^2_{L^2} \leq -\left(c_1\|\psi\|^2_{L^2} + \frac{\rho}{\Delta tc}\|\mathcal{E}\psi\|^2_{L^2(D^t_-)}\right)$$

If additionally $\mathcal{E}$ is a coercive operator with constant c_2 we obtain the exponential decay

$$\|\psi(t)\|^2_{L^2} \leq \|\psi(0)\|^2_{L^2}\exp\left(-2c_1 t - 2c_2\frac{\rho}{\Delta tc}t\right). \tag{25}$$

If $\mathcal{E}$ is not coercive, then let

$$c_2 := \min_{\phi:\|\phi\|_{L^2=1}}\|\mathcal{E}\phi\|^2_{L^2(D^t_-)}, \tag{26}$$

and we obtain again (25). Note that in case of $D^t_- = \emptyset$ or $c_2 \equiv 0$ we still obtain decay at rate c_1. This is the uncontrolled case. We summarize the previous calculations.

Lemma 3 *Let $\bar{\psi} \equiv 0$. Under assumption (10) and (24) and if the set $D^t_\pm$ is sufficiently regular, any solution $\psi(t)$ to the controlled time–dependent radiative transfer equation (22) exponentially decays to $\bar{\psi}$ for $t \to \infty$ at rate $2c_1 + 2c_2 \frac{\rho}{\Delta tc}$ where c_2 is given by (26).*

The result extends to the case of a general $\bar{\psi} \in C^1(\mathbb{R}^+, D(A))$ as follows. The control law (22) is replaced by

$$\frac{1}{c}\partial_t \psi + \mathbf{T}\psi = \left(-\frac{\rho}{\Delta tc}\mathcal{E}^*\mathcal{E}(\psi - \bar{\psi})\right)^+ + \frac{1}{c}\partial_t\bar{\psi} + \mathbf{T}\bar{\psi},\ \psi = 0 \text{ on } \partial\Omega^-, \tag{27}$$

and we recover the previous results by setting $\tilde{\psi} := \psi - \bar{\psi}$. The decay is given by

$$\|\psi(t) - \bar{\psi}(t)\|^2_{L^2} \leq \|\psi(0) - \bar{\psi}(0)\|^2_{L^2} \exp(-2c_1 t - 2c_2 \frac{\rho}{\Delta tc} t). \tag{28}$$

This yields the exponential decay also in the case $\bar{\psi} \neq 0$. The result offers the following interpretation: If $\psi > \bar{\psi}$, then the only control is $\frac{1}{c}\partial_t + \mathbf{T}$ yielding a decay towards $\bar{\psi}$. If $\psi < \bar{\psi}$, then the additional feedback $-\frac{\rho}{\Delta tc}\mathcal{E}^*\mathcal{E}(\psi - \bar{\psi}) > 0$ is active.

The previous calculations can also be applied for the cost functional J_1 given by (5). In this case the problem at time–step k is given by

$$\min \int_\Omega \left(\int_{S^2} \psi d\omega'\right)^2 - \bar{\psi}^2 dx + \alpha Q^2 dx \text{ subject to } \mathbf{T}\psi = Q$$

and similarly as before we obtain the control law

$$\frac{1}{c}\partial_t \psi + \mathbf{T}\psi = \left(\frac{-\rho}{c\Delta t}\int_{S^2} \mathcal{E}^* \left(\int_{S^2} \mathcal{E}(\psi - \bar{\psi}) d\omega'\right) d\omega''\right)^+ + \frac{1}{c}\partial_t\bar{\psi} + \mathbf{T}\bar{\psi} \tag{29}$$

We note that equations (27) and (29) are of mainly theoretical value. They require to apply a source term which is anisotropic. Typically, this is out of scope for brachytherapy applications.

3.2 Boundary Control

Finally, we consider the case of teletherapy, where anisotropic boundary values can be prescribed. The procedure is similar to the previous calculations. We start with the semi–implicit discretization of (1) with $q_1 \equiv 0$ given by

$$-\Delta t\mathbf{A}\psi^k + \left(\frac{1}{c} + \Delta t\mathbf{\Sigma}\right)\psi^k - \Delta t\mathbf{K}\psi^k = \frac{1}{c}\psi^{k-1}, \psi^k = Q \text{ on } \partial\Omega^- \tag{30}$$

We denote its solution operator by $\mathcal{E}(Q, \psi^{k-1}) = \psi^k$ defined by $\mathcal{T}(\psi^k) = \frac{1}{c}\psi^{k-1}, \psi^k = Q$. The instantaneous problem reads then

$$\min \frac{1}{2}\int_\Omega \left(\int_{S^2} \psi^k - \bar{\psi}^{k-1} d\omega\right)^2 dx + \frac{\alpha}{2}\int_{\partial\Omega} \left(\int_{\Gamma_x{}^-} Qn(x)\omega d\omega\right)^2 dS_x. \tag{31}$$

¿From the optimality system

$$\mathcal{T}(\psi^k) = \frac{1}{c}\psi^{k-1}, \psi^k = Q \text{ on } \partial\Omega^- \tag{32a}$$

$$\mathcal{T}^*(\lambda) = \int \psi^k - \bar{\psi}^{k-1} d\omega, \lambda = 0 \text{ on } \partial\Omega^+ \tag{32b}$$

$$Q = \left(Q + \lambda - \alpha \int_{\Omega^-} n(x)\omega Q d\omega \right)^+ \quad \text{on } \partial\Omega^- \tag{32c}$$

with the operators $\mathcal{T}^* := \Delta t\mathbf{A} + \frac{1}{c} + \Delta t\mathbf{\Sigma} - \Delta t\mathbf{K}$ and the solution operator $\mathcal{E}^*(\int \psi^k - \bar{\psi}^{k-1}) = \lambda$ and $\lambda = 0$ on $\partial\Omega^+$, we obtain by a single gradient step with step–length $\rho > 0$, the control Q as

$$Q = \rho\mathcal{R} \left(\mathcal{E}^* \int_{S^2} \mathcal{E}\left(0, \psi^{k-1}/c\right) - \bar{\psi}^{k-1} d\omega \right)^+ \tag{33}$$

where $\mathcal{R}$ is the restriction to the boundary $\partial\Omega^-$. This yields analogously as before the following control law for the boundary control of time–dependent radiative therapy

$$\frac{1}{c}\partial_t\psi + \mathcal{T}(\psi) = 0,\ \psi = \rho\mathcal{R}\left(\mathcal{E}^* \left(\int_{S^2} \mathcal{E}(0, \psi/c) - \bar{\psi} d\omega \right) \right)^+ \quad \text{on } \partial\Omega^- \tag{34}$$

4 Numerical Results

All numerical results are computed on an AMD 64x machine using MATLAB.

4.1 Distributed Control

The purpose of this example is to illustrate the theoretically found exponential decay. The results are for one–space dimension. The equations of the optimality system are solved using the P_N-discretization, cf. [13] for a detailed derivation. The P_N approximation assumes a decomposition of the intensity ψ into a finite number of Fourier modes $\psi_{(l)}$, $l = 0, \ldots, N$

$$\psi(x, t, \mu) = \sum_{l=0}^{N} \psi_{(l)}(x, t) \frac{2l + 1}{2} P_l(\mu). \tag{35}$$

We apply the P_N approximation to the variables ψ and λ for the time–dependent optimization problem and cost functional (6) and (7). The optimality system is obtained for $l = 0, \ldots, N$ as

$$\frac{1}{c}\partial_t \psi_{(l)} + \partial_x \left(\frac{l+1}{2l+1}\psi_{(l)} + \frac{l}{2l+1}\psi_{(l)} \right) + (\sigma_t - \sigma_s)\psi_{(l)} = 2q_1^{(l)}\delta_{l0} \tag{36}$$

$$\frac{1}{c}\partial_t \lambda_{(l)} - \partial_x \left(\frac{l+1}{2l+1}\lambda_{(l)} + \frac{l}{2l+1}\lambda_{(l)} \right) + (\sigma_t - \sigma_s)\lambda_{(l)} = 2\alpha_1 \psi_{(0)}\delta_{l0} \tag{37}$$

$$q_1^{(l)} = \left(q_1^{(l)} - \lambda_{(0)} - \alpha_2 q_1^{(l)} \right)^+ \tag{38}$$

with $\psi_{(-1)} = \lambda_{(-1)} = \psi_{(N+1)} = \lambda_{(N+1)} = 0$. Similarly to the continuous approach we define the operators $\mathcal{E}_{PN} = \mathcal{E}_{PN}{}^+$ and $\mathcal{E}_{PN}* = \mathcal{E}_{PN}{}^-$ where $\mathcal{E}_{PN}{}^\pm$ is given by

$$\mathcal{E}_{PN}{}^\pm(\psi_{(l)}^{k-1}) = \psi_{(l)}^k \Leftrightarrow \frac{1}{c\Delta t}\psi_{(l)}^k \pm \partial_x \left(\frac{l+1}{2l+1}\psi_{(l)}^k + \frac{l}{2l+1}\psi_{(l)}^k \right) + (\sigma_t - \sigma_s)\psi_{(l)}^k = 2\psi_{(l)}^{k-1}\delta_{l0}$$

The P_N approximation to the control law for a desired state $\overline{\psi_{(l)}}$, a stepwidth ρ and a time–grid Δt, is hence given by

$$\frac{1}{c}\partial_t \psi_{(l)} + \partial_x \left(\frac{l+1}{2l+1}\psi_{(l)} + \frac{l}{2l+1}\psi_{(l)} \right) + (\sigma_t - \sigma_s)\psi_{(l)} =$$
$$2\left(\left(-\frac{\rho}{\Delta t c}\mathcal{E}_{PN}{}^*\mathcal{E}_{PN}(\psi_{(l)} - \overline{\psi_{(l)}}) \right)^+ \delta_{l0} + \frac{1}{c}\partial_t \overline{\psi_{(l)}} + \mathbf{T}\overline{\psi_{(l)}} \right).$$

First we consider an academic example in order to illustrate the assertions of Lemma 3. We compute a desired state $\bar{\psi}(x,t) := \left(\bar{\psi}^{(l)}(x,t) \right)$ as solution to

$$\mathbf{T}\bar{\psi} = \begin{cases} 100, & |x - t| \leq 5\ dx + \frac{1}{5} \\ 0, & \text{otherwise.} \end{cases}$$

using the P_N-approximation on a space–time grid of $(x,t) \in [0,1] \times [0,1]$. The grid size is $dx = \frac{1}{M+1}$, $dt = \frac{1}{N+1}$. We prescribe zero boundary values. We set $\sigma_t = 13$ and $\sigma_s \int_{-1}^{1} s d\mu = 2$. We then compute $\psi^{(l)}(x,t)$ as obtained from the control law starting with $\psi^0 \equiv 0$. The number of variables is $(M+1) \times (N+1)$. We compute the L_2 and the L_∞ norm of $\psi - \bar{\psi}$ for each fixed time t. We expect an exponential decay over time of the L_2-norm of this difference. We give results on the rate of decay for the uncontrolled case $\rho/\Delta t = 0$ and the controlled case $\rho/\Delta t > 0$. We give results for varying parameters $\rho/\Delta t$ in figure 1 and study the dependence of the rate of decay on the discretization in space dx in figure 2 and angular variable N in figure 3. We observe in all cases the expected exponential decay and as expected we note that the controlled cases are superior to the uncontrolled case. Moreover, we observe that the finer the discretization is taken with respect to the angular and spatial variables, the better the controller performs.

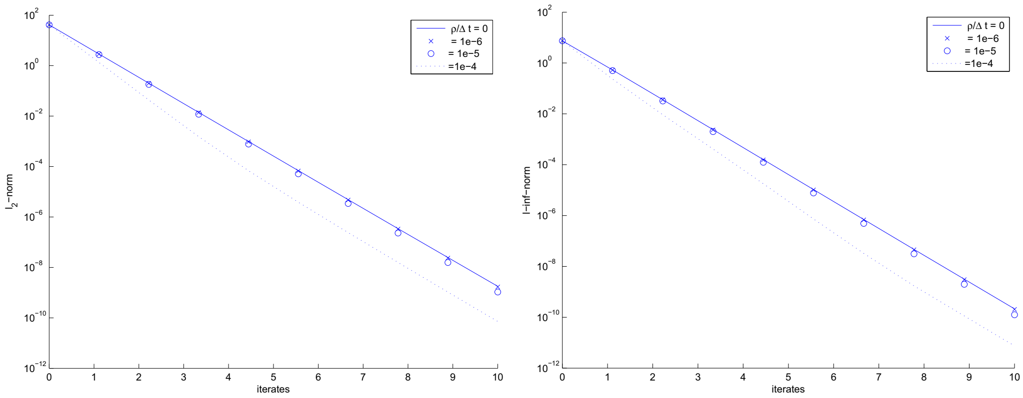

Figure 1: L_2norm and L_∞-norm decay over time for varying $\rho/\Delta t$ in a log–plot. Dependence on $\rho/\Delta t$ for $c\Delta t = 1$, $dx = 10^{-2}$ and $P_N, N = 5$.

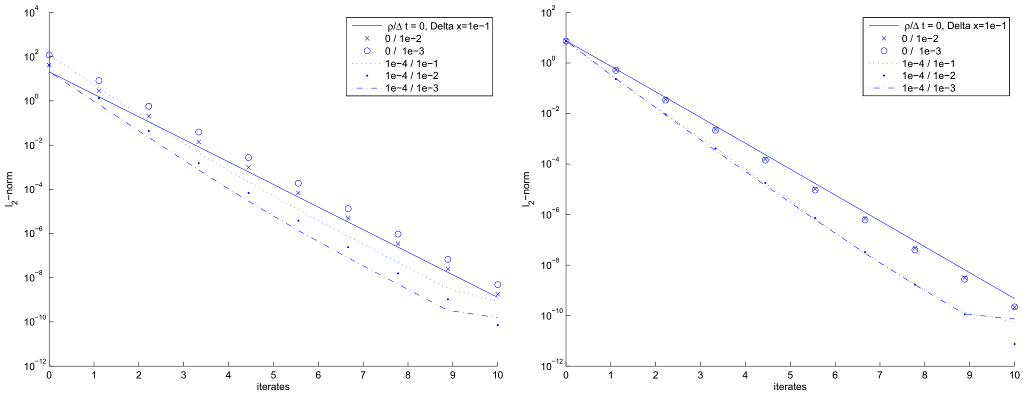

Figure 2: L_2 and $L_\infty-$norm decay for varying discretization of the spatial interval dx in a log-plot. Dependence on the spatial discretization $dx \in \{10^{-1}, 10^{-2}, 10^{-3}\}$ for $P_N, N = 5$, $c\Delta t = 1$ and $\rho/\Delta t \in \{0, 10^{-4}\}$.

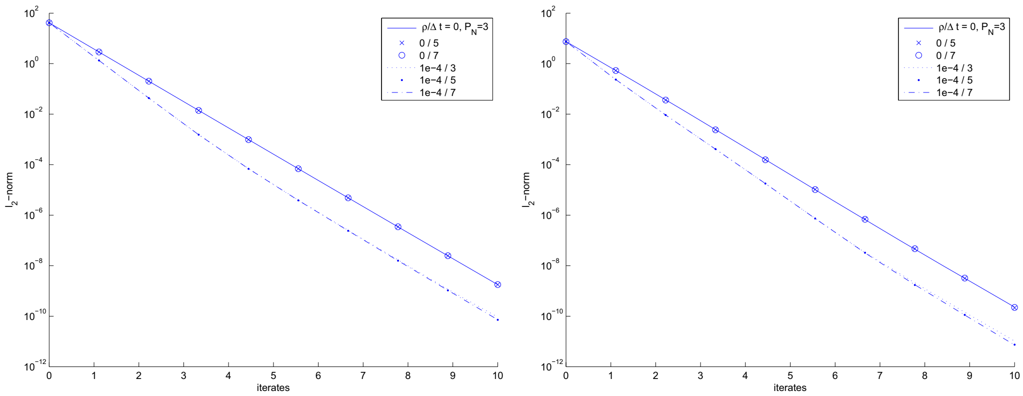

Figure 3: L_2 and $L_\infty-$norm decay for varying discretization of the sphere P_N for $N \in \{3, 5, 7\}$ in a log-plot. Results given for $dx = 10^{-2}$, $c\Delta t = 1$ and $\rho/\Delta t \in \{0, 10^{-4}\}$.

4.2 Boundary Control

We apply the optimize–then–discretize approach to the control law. In our 2D simulations, we use the time-dependent Simplified P_1 (SP_1) or diffusion approximation. The unknown is the energy

$$\psi_{(0)} = \int_{S^2} \psi d\omega. \tag{39}$$

The SP_1 approximation for the time–dependent radiative transfer equation [14] reads for isotropic scattering

$$\frac{1}{c}\partial_t \psi_{(0)} - \nabla \frac{1}{3\sigma_t} \nabla \psi_{(0)} + (\sigma_t - \sigma_s)\psi_{(0)} = 0. \tag{40}$$

The boundary conditions are

$$n \cdot \nabla \psi_{(0)} = \frac{3}{2}\sigma_t \left(l_1(q_2) - \psi_{(0)} \right), \tag{41}$$

where

$$l_1(q_2) = -4 \int_{\partial\Omega^-} n\omega q_2 d\omega.$$

Appropriate initial conditions have to be prescribed. From the time–dependent SP_1–approximation and the cost functional (5) and (8), we obtain the optimality system using SP_1 asymptotic as

$$\frac{1}{c}\partial_t \lambda_{(0)} + \nabla \frac{1}{3\sigma_t} \nabla \lambda_{(0)} - (\sigma_t - \sigma_s)\lambda_{(0)} = -4\pi\alpha(\psi_{(0)} - \bar{\psi}_{(0)}) \tag{42}$$

with boundary condition

$$n \cdot \nabla \lambda_{(0)} = -\frac{3}{2}\sigma_t \lambda_{(0)} \quad \text{on} \quad \partial\Omega^+, \tag{43}$$

terminal condition $\lambda_{(0)} = 0$ at time $t = T$ and gradient equation

$$\lambda_{(0)} - \frac{2}{3\sigma_t} n \cdot \nabla \lambda_{(0)} = -2\pi\alpha_1 l_1(q_2). \tag{44}$$

To state the control law for the SP_1 approximation we introduce the operators $\mathcal{E}_{SP}$ and $\mathcal{E}_{SP}{}^*$ as

$$\begin{aligned} \mathcal{E}_{SP}(q_2, \psi_{(0)}^{k-1}) = \psi_{(0)}^k \Leftrightarrow \\ -\nabla \frac{1}{3\sigma_t} \nabla \psi_{(0)}^k + \left(\frac{1}{c\Delta t} + \sigma_t - \sigma_s \right) \psi_{(0)}^k = \psi_{(0)}^{k-1}, \\ n \nabla \psi_{(0)} = \frac{3}{2}\sigma_t \left(l_1(q_2) - \psi_{(0)} \right) \text{ on } \partial\Omega^- \end{aligned}$$

and similarly

$$
\begin{aligned}
{\mathcal{E}_{SP}}^*(\psi_{(0)}^{k-1}) = \lambda_{(0)}^k \Leftrightarrow \\
-\nabla \frac{1}{3\sigma_t} \nabla \lambda_{(0)}^k + (\frac{1}{c\Delta t} + \sigma_t - \sigma_s)\lambda_{(0)}^k = 4\pi \psi_{(0)}^{k-1}, \\
n\lambda_{(0)}^k + \frac{3}{2}\sigma_t \lambda_{(0)}^k = 0 \text{ on } \partial\Omega^+.
\end{aligned}
$$

For a stepwidth ρ, a time–grid of width Δt and a desired dose of $\bar{\psi_{(0)}}$ we then obtain the SP_1-approximation to the control law as

$$
\begin{aligned}
\frac{1}{c}\partial_t \psi_{(0)} - \nabla \frac{1}{3\sigma_t} \nabla \psi_{(0)} + (\sigma_t - \sigma_s)\psi_{(0)} = 0, \\
n \cdot \nabla \psi_{(0)} = \frac{3}{2}\sigma_t \left(l_1(Q) - \psi_{(0)} \right), \\
Q = \rho \mathcal{R} \left({\mathcal{E}_{SP}}^* \left(\int_{S^2} \mathcal{E}_{SP} \left(0, \frac{\psi_{(0)}}{c\Delta t} \right) - \bar{\psi_{(0)}} d\omega \right) \right)
\end{aligned}
$$

We consider the example of a moving tumor. We compare the solution to the full time–dependent optimal control problem and the predictions of the control law. We consider the more realistic functional given by (5) and (8). When solving the optimal control problem we set $\alpha_2 = 0$ (no regularization for the boundary control) and $\alpha_1 = 1$ and hence the optimal control problem reads

$$
\min_{q_2, \psi} J_1 (\int_{S^2} \psi d\omega) \text{ subject to } (1), \psi(x, t, \omega) = q_2
$$

Its solution (q_2^*, ψ^*) is then compared over time with the solution ψ^{**} to (34) and $q^{**} := \rho \mathcal{R} \left(\mathcal{E}^* \left(\int_{S^2} \mathcal{E}(0, \psi^{**}/c) - \bar{\psi}^{**} d\omega \right) \right)^+$. When solving for the control law we set $\rho \equiv 1$. All computations are done on a 50×50 grid in the domain $[0, 1]^2$ and with 100 time–steps. The realistic parameters [1] $\sigma_s = 0.05$ and $\sigma_t = 0.5$ are used. Time is scaled such that $c = 1$.

In the first example we move the desired state along the boundary of the domain, i.e., $\bar{\psi}(x, y, t) = \delta(\frac{t}{T} - x)\, \delta(y - \frac{1}{10})$ A reasonable control then acts. This case is used to verify that the control law also yields a control moving in time along the same boundary as the desired state. This is observed for both the solution to the optimal control problem (see figure 5) as well as in the solution to the control law (see figure 4). As expected both controls and the corresponding states show the same qualitative behavior.

In the second example we move the desired state along the diagonal $x = y$ in the domain and solve again the optimal control problem and the control law. We have $\bar{\psi}(x, y, t) = \delta(x - t/T)\delta(y - t/T)$. In both cases the optimal control acts on both corners of the domain for a certain time. Their corresponding states are given in figure 6.

In both examples one clearly sees that instantaneous control yields much more localised dose distributions than open-loop optimal control. From a practical point of view this is a clear indication to apply the developed close-loop control concept instead of optimal open loop control.

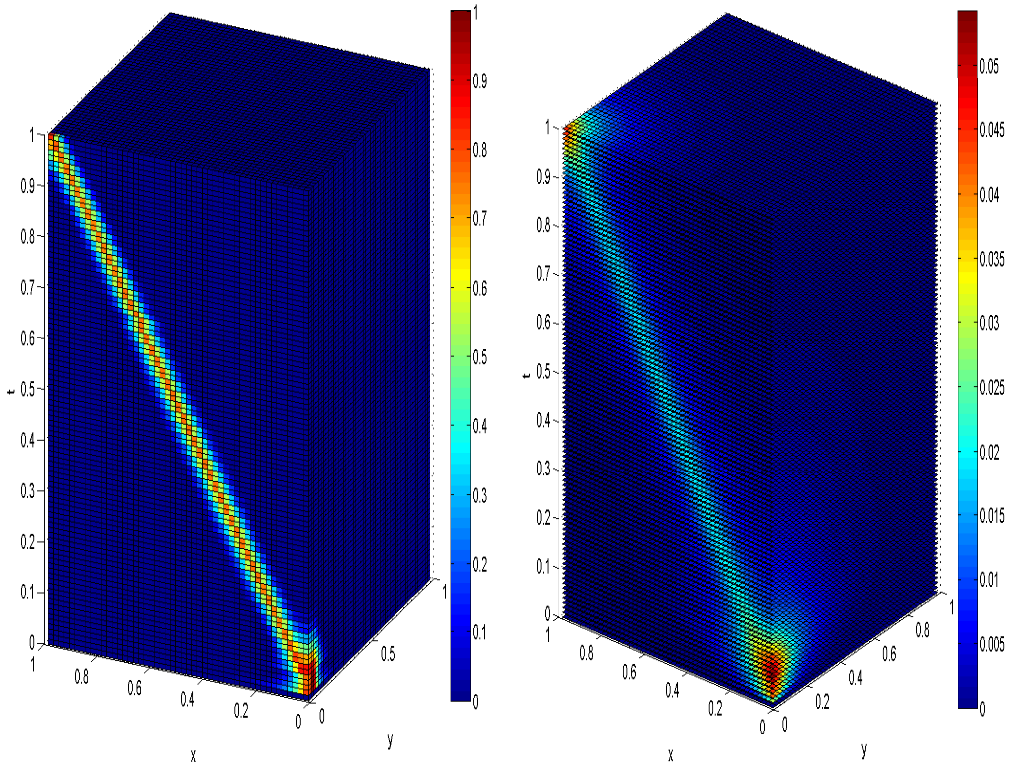

Figure 4: Control Law. The obtained control follows the desired state as its moves along the boundary of the domain. The corresponding dose distribution is depicted to the right.

5 Summary

We study a time–dependent optimal treatment planning problem. We use instantaneous control to derive closed-loop control laws for the control of the dose distribution which allow patient movement during treatment, without using a priori information of the movement of the patient. We consider distributed control as well as the more realistic setting of boundary control with control constraints. We present closed-loop control laws based on P_N- and SP_1- approximations for numerical treatment and present results including the case of a $2D-$ boundary control. We compare the performance of the closed-loop control laws with that of an optimal open loop control law. As a result we conclude that closed-loop control allows movement during treatment, and yields much more localised dose distributions than obtained with the optimal open loop control procedure.

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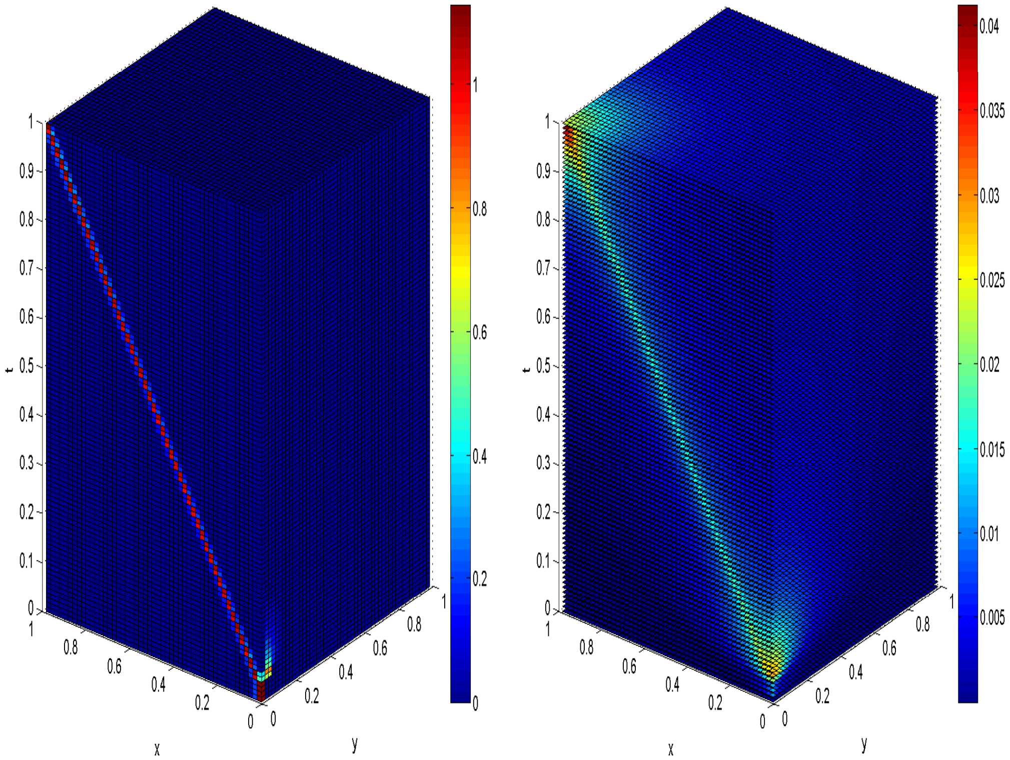

Figure 5: Optimal control problem. The obtained control follows the desired state as its moves along the boundary of the domain. The corresponding dose distribution is depicted to the right.

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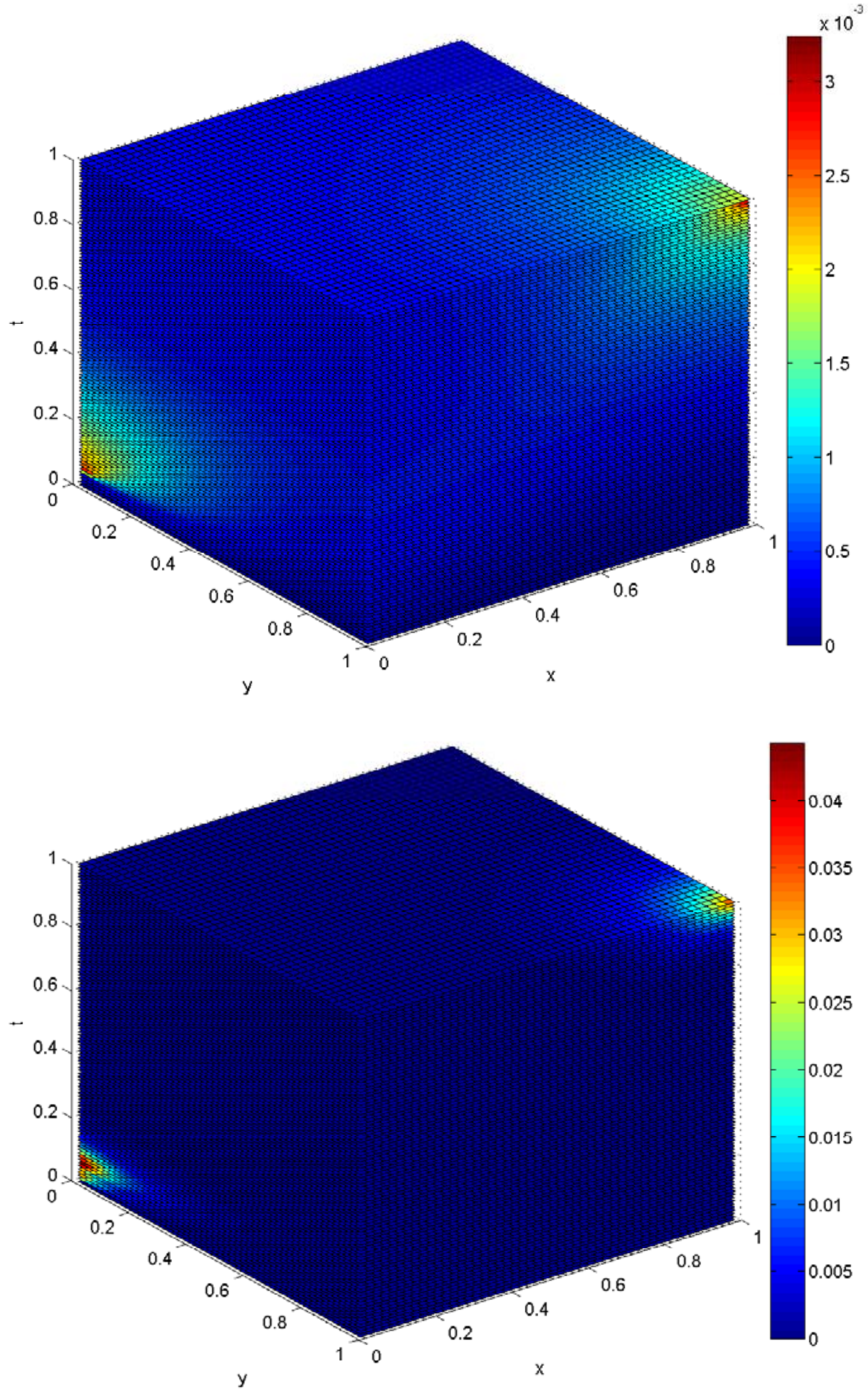

Figure 6: Dose distribution corresponding to the optimal control (top) and to the control law.

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