Konrad-Zuse-Zentrum
für Informationstechnik Berlin

Takustraße 7
D-14195 Berlin-Dahlem
Germany

MARTIN WEISER

Optimization and Identification in Regional Hyperthermia

ZIB-Report 08-40 (October 2008)

Optimization and Identification in Regional Hyperthermia *

Martin Weiser

October 13, 2008

Abstract

Regional hyperthermia is a cancer therapy aiming at heating tumors using phased array applicators. This article provides an overview over current mathematical challenges of delivering individually optimal treatments. The focus is on therapy planning and identification of technical as well as physiological quantities from MR thermometry measurements.
AMS MSC 2000: 92C50, 65M32

Keywords: hyperthermia treatment planning, identification, MR thermometry, interior point methods

1 Introduction

Hyperthermia is a cancer therapy aiming at heating tumors in order to either destroy cancer cells directly or to make them more susceptible to an accompanying radio- or chemotherapy. Several different mechanisms are responsible for the cytotoxic effect of hyperthermia [7, 9]. Different technological means are used to deliver heat to the tumor. Heating techniques applied mostly to smaller or more superficial tumors are RF ablation [1], highly focused ultrasound [11], or magnetic nanoparticles [10].

*Supported by the DFG Research Center MATHEON "Mathematics for key technologies" in Berlin.

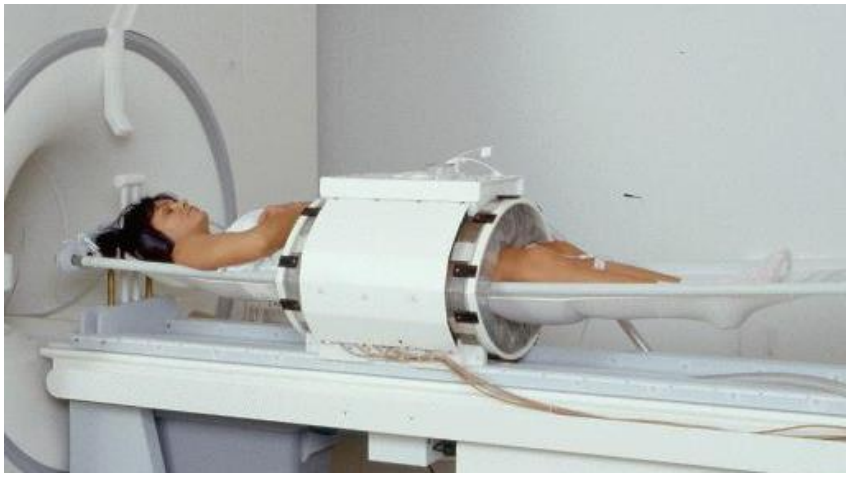

Figure 1: Hybrid MR-hyperthermia treatment system in Berlin (Charité).

For large, deeply seated, and inoperable tumors, regional hyperthermia is used [25]. Here, a time-harmonic electrical interference field is generated by a phased array of antennas which can be controlled individually by amplitude and phase. During a treatment session of up to two hours, the patients's tissue absorbs energy from the electrical field. The heat is distributed inside the body, resulting in a leveraged temperature distribution. By now, several clinical studies have demonstrated the beneficial effect of regional hyperthermia.

In order to deliver an optimal therapy, the phased array applicator needs to be controlled in such a way that the tumor is maximally heated without damaging healthy tissue by excessive temperatures. Due to individually varying tumor location and patient geometry, individual therapy planning is necessary. The physical processes of field interference and heat distribution inside the very heterogeneous human body is too complex to be optimized manually. Thus, optimization algorithms are required for therapy planning, which is considered in Section 2.

The reliability of the mathematical optimization depends on the accuracy of the models describing the physical situation. As is quite common in biomedical settings, in particular the physiological parameters are individually varying to a significant amount, such that a priori models are subject to significant modeling errors. Online parameter identification based on magnetic resonance imaging (MRI) may be a remedy. This is considered in Section 3.

Due to both, the technical complexity of the HF power generation and distribution and the irregular geometry, modeling errors for computing the electrical field are virtually unavoidable. Thus, even accurate solution of Maxwell's

equations will not provide the actual electrical field. Again, MRI can be used for identification of the applicator parameters, which is considered in Section 4.

2 Therapy Planning with Interior Point Methods

The distribution of heat in the patient's body is a dynamic process. However, the transient heating phase takes about 15 minutes, while the duration of a single treatment session is about two hours. For this reason, usually only the steady state of the temperature distribution is optimized, which results in a significantly simpler optimization task.

Objective. The ultimate goal of hyperthermia is the destruction of the tumor. The thermal damage inflicted on cancer cells follows the Arrhenius law [3], with a rate constant

$$k(T) = Ae^{-\frac{\Delta E}{RT}}.$$

Frequency factor A and activation energy ΔE depend on the tissue type, and R is the universal gas constant. Now an estimate s of the fraction of surviving cells is given by $\dot{s}(t,T) = -k(T)s(t,T)$ with $s(0,T) = 1$ and hence $s(\tau,T) = \exp(-k(T)\tau)$. The cost functional to be minimized is then the total number of surviving cancer cells:

$$\min \int_{\text{tumor}} \exp\left(A\tau e^{-\frac{\Delta E}{RT}}\right) dx \tag{1}$$

The thermal isoeffect dose is an established quantity for assessing the therapeutic benefit of a treatment [3, 18]. Treatment planning based on the tumor cell survival has been proposed for thermoseed placement [21], but up to now rather ad hoc cost functionals based on the temperature distribution [1, 15] or on the absorption rate density [16] have been used for regional hyperthermia.

Constraints. The state equation is given by the bio-heat transfer equation (BHTE) describing the distribution of heat in the human body. The most simple variant dates back to [17]:

$$\operatorname{div}(\kappa\nabla T) + c_b w(T_a - T) + \frac{\sigma}{2}|E|^2 = 0 \quad \text{in } \Omega \tag{2}$$

$$\kappa\partial_n T = h(T_{\text{out}} - T) \quad \text{on } \partial\Omega \tag{3}$$

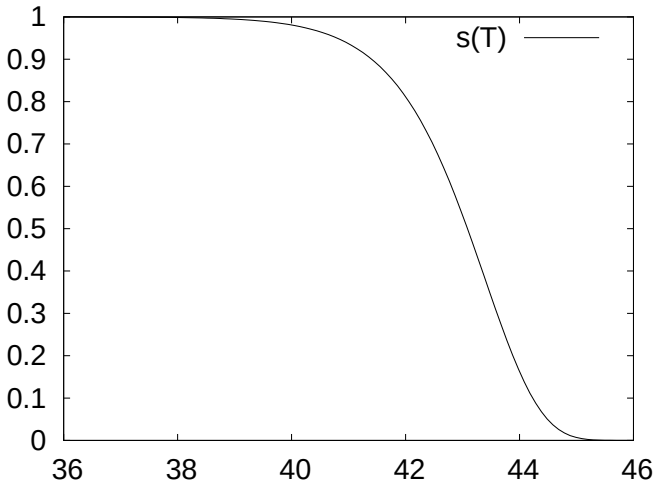

Figure 2: Arrhenius model of fraction of surviving cancer cells versus temperature.

Here, κ is the tissue's heat conductivity, c_b heat capacity of blood, w the perfusion, and σ the electric conductivity. The domain Ω covers the part of the patient's body that is relevant for therapy planning.

The electrical field E satisfies the time-harmonic Maxwell's equation

$$\mathrm{curl}\frac{1}{\mu}\mathrm{curl}E - \omega^2 E = i\omega \sum_{k=1}^{n} u_k J_k \quad \text{in } \Omega_E, \tag{4}$$

where the n antenna currents $u_k J_k$ are determined by the applicator control $u \in \mathbb{C}^n$. The computational domain Ω_E for (4) includes Ω as well as the water bolus, the applicator antennas, and a region of air around the applicator. On the boundary $\partial\Omega_E$, approximately transparent boundary conditions are prescribed to avoid artificial reflections.

Since (4) is linear and its solution is expensive, inside the optimization algorithm the electric field $E = Vu$ is computed as a superposition of antenna profiles V_k satisfying (4) with $u_i = \delta_{ik}$. Thus, equation (4) needs to be solved only n times.

Of course, healthy tissue should not be damaged by too high temperatures. Therefore, an upper bound is imposed on the temperature:

$$T \leq T_{\mathrm{lim}} \tag{5}$$

Typical values for T_{lim} are 44°C for muscle, fat, and bone tissues, and 42°C for more sensitive organs such as bladder or intestine.