An Optimal Control Approach for High Intensity Focused Ultrasound Self-Scanning Treatment Planning

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Abstract. In noninvasive abdominal tumor treatment, research has focused on canceling organ motion either by gating, breath holding or tracking of the target. This paper is based on the novel self-scanning method which combines the advantages of the gated and the tracking method. This approach leverages the respiratory organ motion by holding the focal spot of the high intensity focused ultrasound (HIFU) device static for a given time, while it passively scans the tumor due to respiratory motion. This enables to use a lower-cost HIFU device. We present a planning method for such a system that is based on optimal control theory which optimizes the scanning path and the sonication intensities simultaneously. The method minimizes treatment time and ensures complete tumor ablation according to the thermal dose under free-breathing. To verify our method, we simulated a tumor in two dimensions. The achieved treatment time performs on par to the gold-standard tracking method. Moreover, we measured the temperature profile of the HIFU device in a tissue-mimicking phantom to verify our temperature model.

Keywords: Self-scanning · Treatment planning · HIFU

1 Introduction

High intensity focused ultrasound (HIFU) is a well-known non-invasive thermal ablation modality for tumor treatment which is widely accepted for decades [3,4]. For image guidance during HIFU sonication, magnetic resonance imaging (MRI) is often used, which not only provides images of the tumor, but is also used for temperature mapping [5,11]. The challenge arising in HIFU treatment of abdominal organs, such as kidney and liver, is respiratory motion and organ drift [13]. So far, research has focused on minimizing organ motion either by gating, breath holding or tracking of the target. However, the disadvantage of gating is the prolonged treatment time, and for tracking, the beam of the HIFU device has to be steered, which causes an intensity decay at the focal spot [2].

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In this paper, we use a novel method which takes advantage of the perpetual respiratory motion to passively scan the tumor. In other words, we are placing the static focal point of the HIFU into the tumor [8]. The motion caused by breathing shifts the tumor through this focal point. For tracking of the tumor, a respiratory motion model can be used, for example the one described in [6]. With the motion model we anticipate at which time point tumor tissue is located under the focal spot and thus modulate the HIFU intensity based on this information. Once the tumor has been ablated along the self-scanned trajectory, the focal spot is relocated to a different but static position within the body. With the proposed method, we combine the advantages of the gated and the tracking method: a lower-priced HIFU device can be used and a high duty cycle is achieved. Moreover, the complexity of the beam forming is reduced by not steering the focal spot. However, this comes at the cost of an increased complexity of the planning stage.

We present an optimal control approach to determine optimal sonication plans for such a system ensuring complete tumor ablation. Optimal control approaches have been used before to find treatment plans using HIFU in static tissue [1,7,14]. However, in these approaches the target is still and not moving as in our case. The novelty of our method compared to the self-scanning approach in [8] is that we modeled a realistic temperature elevation and included the thermal dose, whereas they used a simplified temperature and dose model. Our approach optimizes the scanning path and the sonication intensities simultaneously. In a first step an optimal scanning path is found. In a second step, we optimize the thermal dose by adjusting the intensities. We simulated a 2D tumor and showed the feasibility of our method. Moreover, we experimentally evaluated our temperature model by sonicating a tissue-mimicking phantom with a HIFU device and measuring the temperature with MR-Thermometry. We found good correspondence between our model and the measured data.

2 Method

The task of planning a treatment is to find appropriate tumor points which are sonicated by the HIFU device. The focal spot will stay static for a given time to achieve a precalculated temperature rise. During this phase, different tissue will pass through the focal spot due to respiratory motion. The points and the corresponding intensities have to be chosen such that the whole target is ablated. To avoid overtreatment, the energy has to be distributed mainly on the target and healthy tissue should be treated the least possible. Under these conditions, the treatment time is minimized, which consists of beam- and changing time. The beam time is the overall time where the HIFU device is focused on one point. The HIFU system used for the self-scanning approach is able to electrically steer the focal spot rapidly in depth along the acoustic axis. For the other directions, slower mechanical displacement is used, called changing time.

Temperature Model. The temperature inside the body is described by Pennes bioheat equation [10], for which a closed-form solution can be derived [14]. To calculate the temperature induced by a moving heat source, we discretized over time and write it as sum of static heat sources. For a temperature with moving heat source, we can write the temperature rise at point p and time t as

$$T(p,t) = \sum_i T_{\text{off}}(\gamma(p), i\Delta t, I_i), \tag{1}$$

where T_{off} is a closed-form solution for a static heat source similar to [14], γ is the respiratory motion function, I_i denotes the intensity at the time interval i, and each time interval has a duration of Δt seconds.

Thermal Dose. The most accepted model to determine how tissue is affected by temperature is described by the thermal dose model [12], which estimates the cumulative equivalent minutes at a temperature of 43°C (CEM_{43}).

Optimal Control. Our aim is to find an optimal treatment plan u that minimizes the treatment time and overtreatment while ensuring that the whole target is ablated. A treatment plan $u = (u^{\text{p}}(t), u^{\text{I}}(t))$ consists of points that are sonicated $u^{\text{p}}(t)$ (one per breathing cycle) and sonication intensities $u^{\text{I}}(t)$ (m per breathing cycle) for each time point $t \in [0, t_{\text{e}}]$, were $[0, t_{\text{e}}]$ is the treatment time interval. The treatment plan u induces a temperature rise T_u inside the domain, which is calculated by Eq. (1). As we want to prevent tissue from boiling, we claim that a given maximal temperature rise can not be exceeded. From the temperature rise T_u, the thermal dose D_u can be derived to obtain how the tissue is affected [12]. A treatment plan u is admissible, denoted by $u \in U_{\text{ad}}$, if the induced temperature rise T_u does not exceed a given maximal allowed temperature rise. Further, the target has to be ablated, which means that the thermal dose D_u inside the target has to reach to the lethal thermal dose. If T_u and D_u satisfy the mentioned constraints, we say that T_u and D_u are feasible. Moreover, the sonication points $u^{\text{p}}(t)$ have to be inside the domain Ω and the sonication intensities $u^{\text{I}}(t)$ can not exceed the maximal intensity $I_{\max}$.

$$U_{\text{ad}} = \{u = (u^{\text{p}}(t), u^{\text{I}}(t)) \,|\, u^{\text{p}}(t) \in \Omega,\ u^{\text{I}}(t) \in [0, I_{\max}], T_u \text{ and } D_u \text{ feasible}\}.$$

To get the optimal treatment plan, we find u^* which satisfies

$$u^* = \arg\min_{u \in U_{\text{ad}}} G(u) + \|w(D_u - D_{\text{opt}})\|, \tag{2}$$

where G is a functional that measures the treatment time, D_{opt} denotes the desired optimal thermal dose distribution and w is a weighting function that gives less weight to the target border. Note that the target can have any shape and a target zone around the tumor can be defined by adaption of D_{opt}. As it is difficult to not treat the healthy tissue at the border of the target, the weighting

ensures that this sort of overtreatment is less penalized. We define the treatment time measurement function G as

$$G(u) = \underbrace{\sum_i t_i(1 - \delta_0(u^{\mathrm{I}}(t_i)))}_{\star} + \underbrace{\eta \sum_i t_i \max(\nabla u^{\mathrm{I}}(t_i), 0)}_{\bullet},$$

where $\delta_0(x)$ is the Dirac delta at 0 and η is a weighting parameter to ensure that both sums are penalizing equally. The first sum ($\star$) penalizes nonzero intensities, i.e. times where the HIFU beam is on, where the multiplication with time t_i ensures that the longer the sonication, the more it costs. The second sum ($\bullet$) penalizes breaks of the sonication by preventing to turn the beam on again after it was turned off. This ensures that the beam is only turned off at the end of the treatment.

As the problem described in (2) is nonconvex and ill-posed, a good initial value for u is important for the success of the optimization process. To get such an initial value, we first solve the following optimal control problem.

$$u_{\mathrm{start}} = \arg\min_{u \in U_{\mathrm{ad}}} G(u) + \left\| w \left(\max_t T_u - T_{\mathrm{opt}} \right) \right\| + f(u), \quad \text{s.t. } T_{\mathrm{opt}} \leq \max_t T_u,$$

where the function f is defined as $f(u) = \sum_i \|(P_{\mathrm{ac}}(u^{\mathrm{p}}(t_{i+1}) - u^{\mathrm{p}}(t_i)))\|$, and penalizes the changing time. Here, P_{ac} the orthogonal projection along the acoustic axis and T_{opt} is the optimal temperature to be reached. With the constraint we impose that inside the target a minimal temperature has to be attained during the treatment. Note that if one chooses an appropriate optimal temperature T_{opt}, one can predict with a high certainty that the target tissue will be ablated.

Now, we hold the sonication path defined by $u^{\mathrm{p}}_{\mathrm{start}}(t)$ fixed, introduce the sonication gaps resulting from changing the position of the HIFU device, and optimize the intensities according to the optimization framework in Eq. (2) to get the optimal treatment plan u^*. Note that after introducing the sonication gaps, u respects the changing time, which means that when two consecutive sonication points are not lying in the acoustic axis, the beam has to be turned off such that the focal spot can be changed by mechanical displacement. Hence, an optimal scanning path is found in the first step and in the second step, the number of variables can be reduced by solely optimizing the intensities.

3 Materials and Results

To show how well our model fits the actual temperature, HIFU experiments were performed on a tissue-mimicking phantom. We used an MRI-compatible 256-element phased-array transducer (Imasonic, Besançon, France), which is operating in the frequency range of 974–1049 kHz with natural focal length $R = 130$ mm and aperture $d = 140$ mm. A bath of degassed water coupled the ultrasound transducer to the phantom. Each sonication was imaged in the coronal and sagittal plane through the focal spot with a resolution of $1 \times 1 \times 3\,\mathrm{mm}^3$.

The imaging was performed on a 3 T clinical MRI-scanner (Prisma Fit, Siemens AG, Healthcare Sector, Erlangen, Germany). A gradient-recalled echo planar imaging (GRE-EPI) sequence was used to provide PRFS-sensitive images. The imaging parameters were: FOV $= 128 \times 128\,\mathrm{mm}^2$, TR $= 21.7\,\mathrm{ms}$, TE $= 10\,\mathrm{ms}$, flip angle $= 8°$, bandwidth $= 550\,\mathrm{Hz}$, EPI factor $= 7$, 11 cm loop coil. The thermal maps were calculated using the time-referenced single baseline 2D PRFS method, corrected for the background phase drift using three unheated ROIs for each time frame [9]. The sonications were performed at a displacement of $0\,\mathrm{mm}, \pm 5\,\mathrm{mm}$ and $\pm 10\,\mathrm{mm}$ in the radial direction during $3\,\mathrm{s}, 5\,\mathrm{s}$ and $10\,\mathrm{s}$.

We fitted the MRI measurements of the temperature with a least square approach. To test the temperature model given by Eq. (1), we discretized over time with $\Delta t = 0.4\,\mathrm{s}$ and wrote the static heat source as sum of heat sources to get T. For Fig. 1, we compared each MR-Thermometry measurement to the prediction of the temperature model T and the closed-form solution to Pennes equation T_{off}. The error was determined by calculating the difference between the model prediction and the measured temperature. We achieved correlation coefficients of 0.86 and 0.82 for T_{off} and T, respectively. The mean errors are $-0.12°\mathrm{C}$ and $-0.48°\mathrm{C}$, the variances $0.87°\mathrm{C}$ and $1.14°\mathrm{C}$, for T_{off} and T respectively. The fitted lines for the correlation plots have a slope of 1.03 and 1.35 for T_{off} and T, respectively. When comparing the MR-Thermometry measurements to our model, we observe that we are slightly underestimating the temperature. This can be seen by the slope of the fitted line to the correlation plot and as the mean error is negative. The error variance is bigger when calculated with T than with T_{off}. The reason is that T_{off} is an approximation to Pennes equation. If T_{off} was precise, the discretization T would converge to T_{off} for $\Delta t \to 0$. However, by the approximation, this property is not exactly fulfilled. In Fig. 2, this effect is visualized. At the focal spot during the heating time, the temperature T converges to T_{off} for $\Delta t \to 0$, which shows that in this case the model is correct. However, during the decay time as well as for points not equal to the focal spot, the discretization model T underestimates the temperature T_{off}.

Now that we have calibrated our physical HIFU system to our optimization framework, we apply the proposed self-scanning idea on a realistic scenario. As

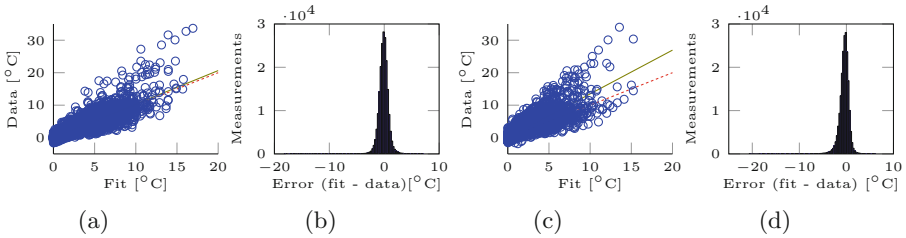

Fig. 1. (a) Correlation and (b) error between T_{off} and the MR-Thermometry data, (c) correlation and (d) error between T and the data. For T, we set $\Delta t = 0.4\,\mathrm{s}$. The solid lines in (a) and (c) are the fitted lines, the dotted are the identity lines.

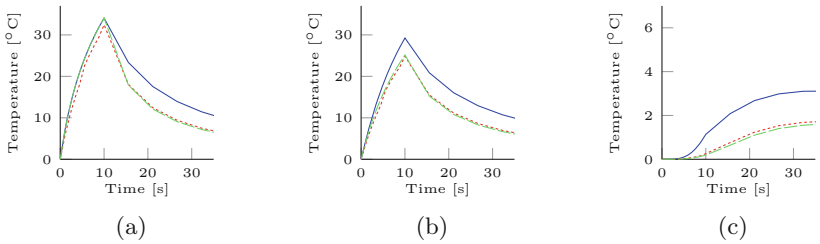

Fig. 2. Comparison of T_{off} and T, where the solid line represents T_{off}, the dashed lines represent T, with red $\Delta t = 0.5\,\text{s}$ and green $0.001\,\text{s}$, (a) temperature rise at the focal spot $(r, z) = (0\,\text{mm}, 0\,\text{mm})$, (b) at position $(r, z) = (1\,\text{mm}, 1\,\text{mm})$, (c) at position $(r, z) = (3\,\text{mm}, 3\,\text{mm})$.

an example, we set the domain $\Omega = 15\,\text{mm} \times 24\,\text{mm}$ to be a two dimensional plane, and the target to a circle with radius $r = 5\,\text{mm}$. The approximate duration of a breathing cycle is around 4 s and the motion in anterior-posterior during one breathing cycle is around 12 mm [13]. Hence, for simplicity, we set the respiratory motion to a sine curve with an amplitude of 6 mm and a period of 4 s. To define the temperature, we used the results of the temperature fit. The focal spot sizes of our HIFU system are $\sigma_r = 1\,\text{mm}$, $\sigma_z = 5\,\text{mm}$, and the diffusivity is $0.0013\,\text{cm}^2$. For the time discretization we use a step of $\Delta t = 0.4\,\text{s}$, and the number of intensity values $u^{\text{I}}(t)$ per breathing cycle was for the first stage $m = 1$, and for the second $m = 10$. Further, the lethal thermal dose was set to $60\,\text{CEM}_{43}$. The minimal temperature rise to reach inside the target during the first step is 20°C, the maximal allowed temperature rise is 50°C. The maximal intensity $I_{\max}$ is normalized such that an intensity of $1\,\text{W/mm}^2$ during 10 s induces a temperature rise of 34°C at the focal spot without motion, and we set $I_{\max} = 1\,\text{W/mm}^2$. We

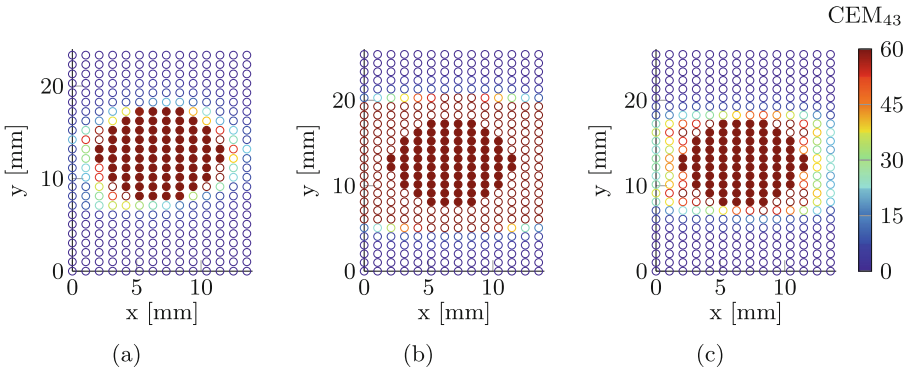

Fig. 3. Thermal dose, the filled dots are target tissue, the acoustic axis is along x-axis and the respiratory motion along y-axis, (a) thermal dose of u^* using the tracking approach, (b) thermal dose of u_{start}, and (c) u^* using the proposed self-scanning approach.

compared the our method to the classical tracking approach, where the focal spot is moved to compensate respiratory motion. We set the intensity decay due to steering to be a Gaussian in radial direction with variance $\sigma = 12\,\text{mm}$.

In Fig. 3, the thermal dose indication for each point in Ω is shown for both stages of the optimization for the self-scanning and the second stage for the tracking approach. In both cases, the whole target is ablated, i.e. the lethal thermal dose of $60\,\text{CEM}_{43}$ is reached inside the whole target. The treatment time found for the self-scanning approach is 268 s, where in this time period 2 changes of the HIFU position have to be made. We set the changing time to last for 4 s, which means that 8 s are used to change the position of the device. The tracking approach on the other hand needs 272 s to ablate the target.

4 Discussion

In the first step of the optimization when solely the temperature is optimized, both the target and also some surrounding tissue is ablated. The reason is that the number of intensities $u^{\text{I}}(t)$ per breathing cycle in the first step is $m = 1$, which means that the intensity can not be changed when the focal spot of the HIFU device is moving outside the target due to respiratory motion. In the second step, $m = 10$, and therefore, the intensity can be turned off when the focal spot is outside the target and overtreatment is successfully reduced. When comparing the results of the self-scanning approach to tracking of the target, we observe that the amount of overtreatment is slightly higher and the treatment times are almost the same. We showed that our optimization framework provides good results in two dimensions with a sine-shaped respiratory motion. Note that the motion can be easily adapted to any kind of motion by adjustment of the motion function γ. However, our method uses still some simplifications, like for example the breathing pattern is not allowed to change during treatment, and can thus not yet be used in clinics. We are currently working on generalizing our method to a more realistic scenario.

When looking at the correlation and the error distribution of the temperature fit, we observe that we are underestimating the temperature rise. However, as we want to guarantee that our treatment plans ablate the whole target, we are on the safe side. The drawback is that there might be more overtreatment of healthy tissue than foreseen and this may cause treatment elongation, as tissue is assumed to heat less than it actually does. However, HIFU treatment devices could be made simpler as only beam steering along the acoustical axis is required.

5 Conclusion

We showed that our optimization framework can be used to calculate feasible treatment plans for a self-scanning HIFU approach in moving tissue. Only few healthy tissue is treated and the treatment time performs on par to the tracking approach. However, the reduced complexity on the beam forming as well as the lower-cost HIFU device renders the idea of self-scanning attractive. In this paper,

we showed on artificial data that our proposed method for calculating optimal treatment plans for a self-scanning HIFU approach in moving tissue works and gives feasible solutions. Further, we showed by HIFU measurements that our temperature model can be fitted to real data. However, it remains to be shown in future studies that our temperature model fits also for moving tissue.

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