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Radiofrequency Ablation Planning Beyond Simulation

Sabrina Haase[1], Torben Pätz[1,2], Hanne Tiesler[1,2], Inga Altrogge[3] and Tobias Preusser[1,2]

***Abstract*— It is a challenging task to plan a radiofrequency (RF) ablation therapy to achieve the best outcome of the treatment and avoid recurrences at the same time. A patient specific simulation in advance that takes the cooling effect of blood vessels into account is a helpful tool for radiologists, but this needs a very high accuracy and thus high computational costs. In this work, we present various methods, which improve and extend the planning of an RF ablation procedure. First, we discuss two extensions of the simulation model to obtain a higher accuracy, including the vaporization of the water in the tissue and identifying the model parameters and to analyze their uncertainty. Furthermore, we discuss an extension of the planning procedure namely the optimization of the probe placement, which optimizes the overlap of the tumor area with the estimated coagulation in order to avoid recurrences. Since the optimization is constrained by the model, we have to take into account the uncertainties in the model parameters for the optimization as well. Finally, applications of our methods to a real RF ablation case are presented.**

I. INTRODUCTION

Due to the increasing clinical importance of image-guidance for thermal ablation therapies such as radiofrequency (RF) ablation, it is an essential task to provide a software tool which focuses on the main difficulties of planning the treatment. To ensure a complete destruction of the tumor, a precise and patient specific treatment planning is necessary. In the case of RF ablation the success of the therapy depends mainly on the cooling effects of the vascular structures in the vicinity of the tumor. In the presence of close vascular structures a proper placement of the probe can only be made by experienced radiologists; in the literature local recurrence rates up to 60% are reported [3]. Due to the cooling effects a simulation in advance and a proposal for an optimal probe placement can be very helpful for the radiologist; such a system can act as a planning tool as well as a training tool for less experienced radiologists. A simulation of the therapy in advance will improve the planning and an optimization would be an additional supplementary benefit for the planning. Both tools together will allow for a smaller recurrence rate and thus a higher quality treatment, in particular in difficult cases. For the simulation as well as for the optimization which is based on the simulation, the patient specific anatomy needs to be incorporated. In the following we will present different aspects which will improve the existing finite element simulation [4] and the planning and optimization of the RF ablation, which is already included in the software planning tool SAFIR [8] (cf. Fig. 1). A review on existing computer assisted planning and intervention of liver tumor ablation can be found in the paper of Schumann et al. [9].

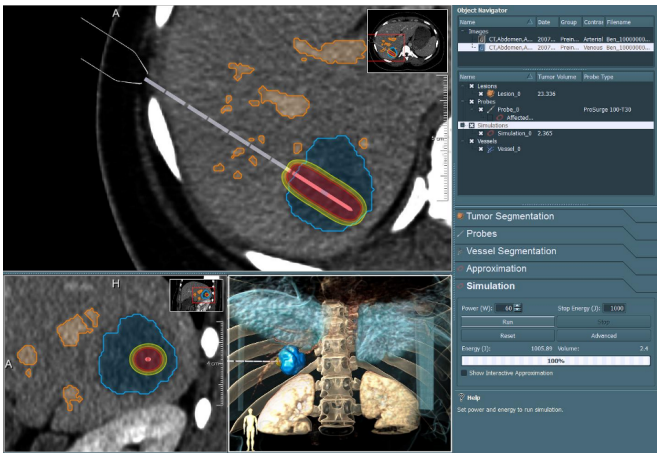

Fig. 1. Screenshot of our software demonstrator SAFIR showing the result of the RF ablation simulation performed on a real clinical dataset. ©Fraunhofer MEVIS

II. MODELING RADIOFREQUENCY ABLATION

An accurate bio-physical model and an efficient numerical implementation are the basis for the advanced topics presented in the following sections. Thus, we review our basic model here.

A. A Time-dependent Model for RF Ablation

We consider RF ablation in the domain D by a probe D_{pr} containing one (monopolar) or two electrodes (bipolar) D_{el} and which is cooled internally. A sketch of the different parts of the computational domain is given in Fig. 2. For the electric potential φ induced by the RF probe we consider the usual electrostatic equation [2]

$$-\nabla\cdot(\sigma\nabla\varphi)=0 \quad \text{in } D\backslash D_{\text{el}} \ , \tag{1}$$

where σ is the electrical conductivity and with suitable boundary conditions. We set $\varphi=\pm 1$ on the positive and negative electrodes boundary respectively, and $\varphi=0$ on the domain boundary, assuming that there is a neutral electrode at the boundary in the monopolar case. For bipolor electrodes a Robin boundary condition is used see e.g. [4]. This arbitrary choice of φ at the electrode boundary Γ_{el} requires a scaling of the electric power as described in [4]. The electric

[1]Fraunhofer MEVIS, Institute for Medical Image Computing, Universitätsallee 29, 28359 Bremen, Germany firstname.surname at mevis.fraunhofer.de
[2]School of Engineering and Science, Jacobs University Bremen, Campus Ring 1, 28759 Bremen, Germany
[3]Center for Complex Systems and Visualization (CeVis), Universitätsallee 29, 28359 Bremen, Germany inga.altrogge at cevis.uni-bremen.de

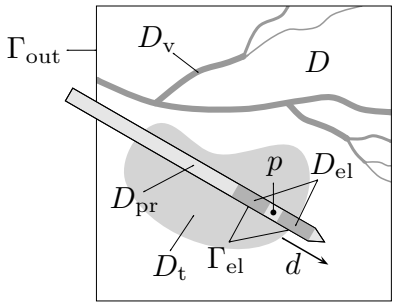

Fig. 2. Sketch of the different parts of the computational domain.©Fraunhofer MEVIS

power acts as right hand side Q_{rf} of the bio-heat transfer equation. Thus, it is given by $Q_{\text{rf}} = s\sigma|\nabla\varphi|^2$.

We obtain the temperature distribution T inside the computational domain from the bio-heat transfer equation

$$\rho c \partial_t T - \nabla \cdot (\lambda \nabla T) = Q_{\text{rf}} + Q_{\text{perf}} \quad \text{in } D \backslash D_{\text{pr}} \ , \qquad (2)$$

where c is the thermal capacity and ρ the density. On the probe boundary we set a Dirichlet boundary condition according to the probes cooling temperature and on the vascular system D_{v} we set a Dirichlet boundary condition according to the body temperature. On the outer domain boundary Γ_{out} we prescribe a homogeneous Neumann boundary condition, assuming that there is no heat flux far away from the probe. The additional term Q_{perf} on the right hand side is due to the perfusion of the tissue. Typically, this perfusion is modeled using Pennes' approach [4]. The material parameters depend nonlinearly on the state of the system, i.e. they depend on the position inside the domain, the temperature and vaporization state (cf. [4]).

The implementation of this model and the presented extensions utilize composite finite elements (CFEs) [7]. CFEs allow to use structured grids even for complicated shaped domain boundaries or material parameter discontinuities inside the domain.

B. Vaporization

The vaporization of the water has a significant influence on the outcome of the ablation. In dry regions, where the water has evaporated, the electrical conductivity σ discontinuously drops down to a value close to zero and thus it is not possible to apply additional electric power. We incorporate the vaporization in the model by tracking the interface between vapor and liquid with a level set approach and by evolving the interface based on the Stefan condition [10]. The difference of the density of liquid vapor and water induces an additional velocity field inside the computational domain that transports mass from the vicinity of the interface into the surrounding tissue. The vapor bubble and the velocity field around the applicator after heating with a maximal power of 40W for 13 minutes are depicted in Fig. 3.

C. Material parameters

To allow for a patient specific modeling the patient's anatomical structures as well as the specific material parameters need to be taken into account. The material parameters constitute a major challenge since they are in general unknown and vary during the treatment due to their temperature dependency. Measurements of these parameters, as e.g. the thermal conductivity λ are found in the literature and there also exist results about the type of temperature dependency [11]. However, most of the parameters can not be directly measured for an individual patient and thus need to be found by different and indirect observations. Here we formulate a parameter identification problem to estimate the unknown properties from temperature measurements during the treatment [12]. During the ablation it is possible to monitor the progress with magnetic resonance (MR) thermometry. These temperature measurements T_{meas} are used to fit the parameters σ and λ to the given data, by minimizing a tracking type functional

$$\min_{\lambda,\sigma} \quad \|T - T_{\text{meas}}\|^2_{H^1(D)} + \text{Regularization}(\lambda, \sigma) \qquad (3)$$

at a certain time point and with additional regularization for the parameters. The norm $H^1(D)$ denotes a norm in the Sobolev space $W^{1,2}(D)$. The whole problem is constrained by the system of partial differential equations (PDEs) (1) and (2). First results on experiments in Agar gel show great promise for an identification of the parameters and therewith an improvement of the whole model, see Fig. 4.

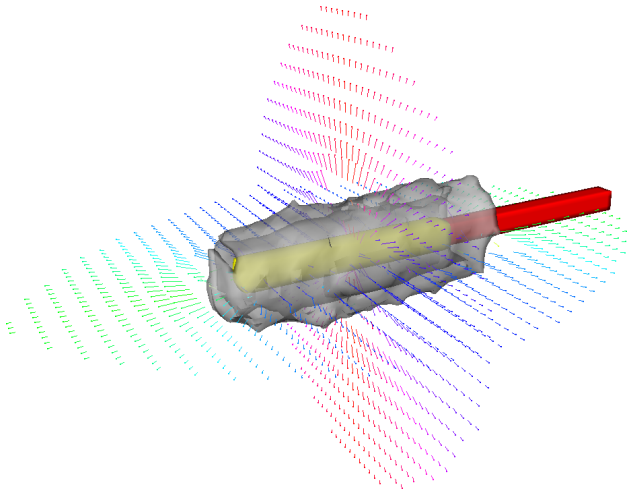

Fig. 3. Vapor extent (transparent-gray) around the electrode (yellow) after 13min at a maximal power of 40W. Due to the different densities of liquid and gaseous water there is a flow field pointing away from the interface. The colored arrows show the flow field in two orthogonal slices. ©Fraunhofer MEVIS

III. OPTIMIZATION OF THE PROBE PLACEMENT

In general, the aim of an RF ablation therapy is to find the best compromise between a complete destruction of the tumorous area including a sufficiently large safety margin (in order to avoid recurrences) and affecting a minimum of native tissue. Thus, for an optimal outcome of the therapy, an accurate probe placement planning is needed. Since we want to optimize the probe location, we first need some information about the "quality" of an RF ablation which can

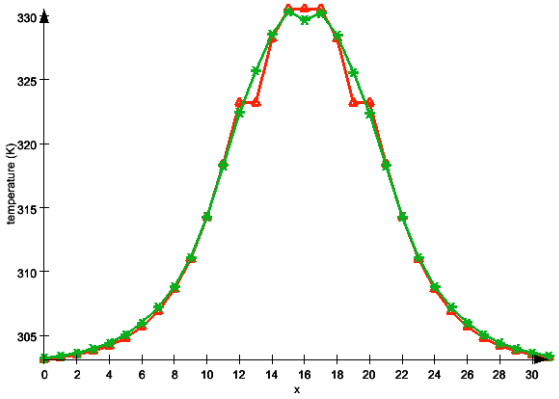

Fig. 4. The given temperature distribution (red with triangles) and the temperature distribution corresponding to the identified electrical conductivity (green with asterisks). The values are measured along a line in the vicinity of the applicator through the 3D volume of the temperature distribution. ©Fraunhofer MEVIS

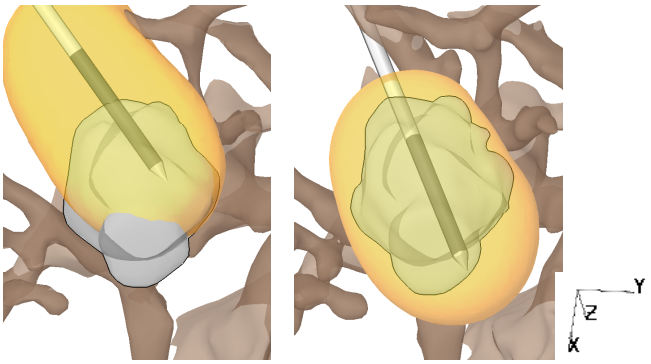

Fig. 5. Optimization for an example based on real patient data with segmented tumor (transparent-gray) and surrounding vascular system (beige-brown). Here, we see a monopolar probe with the corresponding 50°C-isosurface of the temperature (transparent-yellow). On the left, we see our chosen starting placement and on the right, the solution of our proposed optimization method. ©Fraunhofer MEVIS

be obtained by evaluating a suitable objective function. We assume that the tissue is destroyed if temperatures higher than 50°C are reached. At this temperature, the proteins of the tissue and thus tumor cells coagulate within a couple of seconds. In order to get the optimal outcome of the ablation, the temperature in the tumor region shall be high and in particular above this critical temperature.
For the optimization we consider a steady state model of (1) and (2) for the estimation of the coagulation and model a non-cooled applicator. We define the following temperature based objective function [1]:

$$f(T) = \ln\left(\int_{D_t} \mathrm{e}^{-\alpha T(x)} dx\right) \quad \text{with} \quad \alpha > 0 \ . \tag{4}$$

Searching for an optimal probe placement (p,d) that minimizes this objective function means maximizing the minimum temperature inside the tumor region D_t, which yields a uniform tumor heating (again see [1]). The parameters of the probe position (p,d), where p is the center of the electrode's active zone and d the unit normal pointing in the direction of the shaft, only appear in the boundary condition of the electric potential equation (1). Moreover, $\alpha > 1$ yields a stronger penalization of low temperatures in D_t, while $\alpha < 1$ yields a lower penalization of low temperatures in the tumor region. The minimization of the objective function f is performed by a gradient descent method combined with a multi-level approach where the gradient is calculated using shape derivatives [1]. One example of the solution of our optimization method is depicted in Fig. 5.

A. Sensitivity analysis

As already seen in Sect. II-C the modeling of the tissue properties poses a particular challenge, since they are individually different and moreover depend on the current state of the tissue. Values used in simulations are often based on experiments on animal or cadaveric human tissue. Moreover, experimental measurements are always accompanied with a certain range of errors. Consequently, the question arises how sensitive are the results obtained from simulations and optimizations with respect to uncertain tissue properties. In the following, we will analyze the sensitivity of our above described optimization with respect to an uncertain electrical conductivity $\sigma = (\sigma_n, \sigma_t, \sigma_v)$ in native liver tissue, tumor tissue and vessels (see also [1]). Thereto, we assume the electrical conductivity of the three different tissue types to be probabilistically distributed within ranges taken from the literature. Note, that a sensitivity analysis w.r.t. other uncertain tissue properties is completely analog. Substituting the probabilistically distributed values into the PDE-model for the simulation of RF ablation yields a system of stochastic partial differential equations (SPDEs) (as studied in [1]). By evaluating the SPDE system for certain realizations of the electrical conductivity σ, we can analyze the sensitivity of the system w.r.t. variations in σ. For the discretization and interpolation in the stochastic space, we use an adaptive sparse grid collocation (ASGC) approach presented by Ma and Zabaras [6], which combines the power and sampling character of collocating methods with some of the theoretical properties of the generalized polynomial chaos [13]. Moreover, for the sensitivity analysis of the optimal probe orientation we perform a visualization of the probability densitiy function (PDF) by a color coding of the sphere (green colors indicate unlikely orientations, whereas red colors show likely orientations; cf. color ramp on the bottom right of Fig. 6). For the sensitivity analysis of the optimal probe position we consider the covariance matrix of the joint distribution of the probe position's components. The covariance matrix is visualized as an ellipsoid, whose principal axes are aligned with the matrix' eigenvectors and whose extension is scaled with the square root of the corresponding eigenvalues. This can be interpreted as a principal component analysis of the PDF, i.e. large ellipsoids imply that the distribution has a high variance in the corresponding direction, while small ellipsoids indicate narrow distributions. A first result of the sensitivity of the optimal probe position and orientation

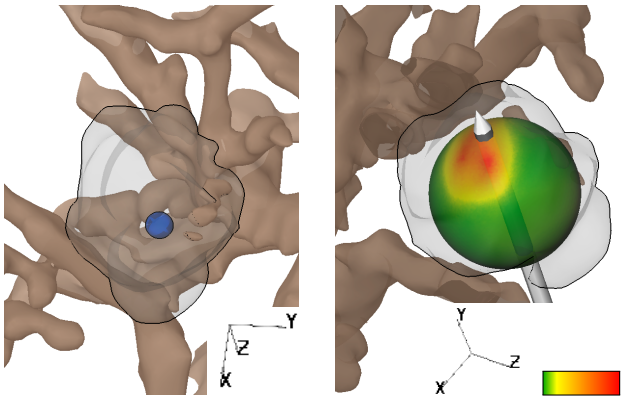

Fig. 6. Visualization of the sensitivity of the optimal probe position and orientation w.r.t. variations in σ. On the left the covariance matrix of the corresponding probability density function is represented via blue ellipsoid. On the right the corresponding probability density function is represented via color coding of the sphere (taken from [1]).

w.r.t. variations in the electrical conductivity is depicted in Fig. 6. Here, we have computed our optimization from above for 8470 different values of σ (which corresponds to a certain refinement level in the stochastic space). For a detailed description of our sensitivity analysis and all parameter settings in the calculation the results of which are shown here, we again refer the reader to [1].

IV. DISCUSSION

We have discussed different approaches for the improvement and extension of the planning of RF ablation. Besides a robust forward simulation an assistance to find the optimal probe placement is needed to achieve the best results for the patient. In our software demonstrator SAFIR [8] (see Fig. 1) the interactive RF applicator positioning and the numerical estimation of the coagulative necrosis are already included. For the simulation of the temperature distribution and therewith the destroyed area, the above described time dependent RF ablation model is used. Especially the vascular structures are important for a realistic and patient individual simulation due to their cooling effects for RF ablation. For a more patient specific and more realistic modeling we are aiming at including all other methods which optimize the outcome of the therapy by means of an improved model e.g. vaporization and patient specific adaption of the model via parameter identification. The presented extended model is solved with a composite finite element method that allows to resolve complicated shaped domains with regular grids and accounts for the anatomical structures, which are given by the preprocessed patient data. The optimization is included already in a simplified way in SAFIR where the RF ablation model is replaced by an approximation. The incorporation of the above described optimization of the probe placement is a further step towards an improved planning system, since an optimization which is based on an approximated temperature distribution is less flexible and does not match the patient individual properties in the way the described PDE model does. However, for a reliable suggestion of the best probe position we need to take into account the surrounding risk structures and anatomical restrictions as ribs, lung, and intestinal system. Further challenging tasks are the validation of the simulation and the speed up in computational time for the forward model and the optimization. Some first validations of the model have been performed [5] but further investigations are needed in particular for all new methods and extensions.

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REFERENCES

[1] I. Altrogge, T. Preusser, T. Kröger, S. Haase, T. Pätz and R.M. Kirby, Sensitivity analysis for the optimization of radiofrequency ablation in the presence of material parameter uncertainty, International Journal of Uncertainty Quantification 2(3), 295-312, 2012.

[2] E.J. Berjano, Theoretical modeling for radiofrequency ablation: state-of-the-art and challenges for the future, BioMedical Engineering OnLine 5:24, 2006.

[3] Y. S. Kim, H. Rhim and O. K. Cho, Intrahepatic recurrence after percutaneous radiofrequency ablation of hepatocellular carcinoma: analysis of the pattern and risk factors, Eur. J. Radiol., 59:3, pages 432-41, 2006.

[4] T. Kröger, I. Altrogge, T. Preusser, P.L. Pereira, D. Schmidt, A. Weihusen and H.-O. Peitgen, Numerical simulation of radio frequency ablation with state dependent material parameters in hree space dimensions, MICCAI (2), pages 380-388, 2006.

[5] K. S. Lehmann, J. P. Ritz, S. Valdeig, V. Knappe, A. Schenk, A. Weihusen, C. Rieder, C. Holmer, U. Zurbuchen, P. Hoffmann, H. .O. Peitgen, H. J. Buhr and B. B. Frericks, Ex situ quantification of the cooling effect of liver vessels on radiofrequency ablation, Langenbecks Arch. Surg., 394(3), pages 475-481, 2009.

[6] X. Ma and N. Zabaras, An adaptive hierarchical sparse grid collocation algorithm for the solution of stochastic differential equations, J. Comput. Phys. 228:8, pages 3084-3113, 2009.

[7] T. Preusser, M. Rumpf, S. Sauter and L.O. Schwen, 3D composite finite elements for elliptic boundary value problems with discontinuous coefficients, SIAM J. Sci. Comp. 33:5, pages 2115-2143, 2011.

[8] C. Rieder, M. Schwier, A. Weihusen, S. Zidowitz and H.-O. Peitgen, Visualization of risk structures for interactive planning of image guided radiofrequency ablation of liver tumors, SPIE Medical Imaging: Visualization, Image-Guided Procedures, and Modeling, 2009.

[9] C. Schumann, C. Rieder, J. Bieberstein, A. Weihusen, S. Zidowitz, J. H. Moltz and T. Preusser, State of the art in computer-assisted planning, intervention and assessment of liver tumor ablation, Critical Reviews in Biomedical Engineering (Special Issue on Thermal Tumor Ablation), 38, 31-52, 2010.

[10] J. Stefan, Ueber die Theorie der Eisbildung, insbesondere ueber die Eisbildung im Polarmeere, Ann. Physik Chemie, 42, 269-286, 1891.

[11] T. Stein, Untersuchungen zur Dosimetrie der hochfrequenzstrominduzierten interstitiellen Thermotherapie in bipolarer Technik, ecomed Verlagsgesellschaft AG & Co. KG, Landsberg, 22, 2000.

[12] H. Tiesler, Identification of material parameters from temperature measurements in radio frequency ablation, PhD thesis, University of Bremen, 2011, http://elib.suub.uni-bremen.de/peid=D00102342 .

[13] D. Xiu, Numerical methods for stochastic computations, Princeton University Press, Princeton, New Jersey, 2010.