Intervention Planning of Hepatocellular Carcinoma Radio-Frequency Ablations

Bernhard Kerbl[1], Philip Voglreiter[1], Rostislav Khlebnikov[1],
Dieter Schmalstieg[1], Daniel Seider[2], Michael Moche[2], Philipp Stiegler[3],
Rupert H. Portugaller[3], and Bernhard Kainz[1]

[1] Institute for Computer Graphics and Vision, Graz University of Technology
{kerbl,voglreiter,khlebnikov,schmalstieg,kainz}@icg.tugraz.at
[2] Department of Interventional Radiology, University Hospital Leipzig
{Daniel.Seider,Michael.Moche}@medizin.uni-leipzig.de
[3] Department of Surgery, Division of Transplantation Surgery,
Medical University Graz
{philipp.stiegler,rupert.portugaller}@medunigraz.at

Abstract. We present a software solution for planning and simulating radio-frequency ablation (RFA) treatment for patients suffering from hepatocellular carcinoma. Our software provides the graphical front-end for the results of the EU FP7 project *IMPPACT*. The main planning application was designed to assist with the identification of minimum-risk setups for RFA probes and generation of evaluable 3D representations of the predicted necrosis zones. Patient-specific mesh data describing the involved anatomic structures are used to individually parameterize the simulation procedure for personalized results. Our software supplies tools for extracting the required anatomic meshes from computed tomography (CT) images and for specifying custom intervention protocols. Data collected during simulations allow for detailed illustration of expected effectiveness and progress of heat-induced necrosis over time. Our software was evaluated positively by medical personnel and has been successfully put into practice at two independent European clinical sites.

Keywords: intervention planning, tumor ablation, simulation, visualization, user-interfaces.

1 Introduction

Hepatocellular carcinoma (HCC) accounts for up to 90% of primary liver cancers [6]. HCC can rarely be resected completely; location of the tumor, limited hepatic reserve or physical condition of the patient are some of the restricting factors [2]. Ablation techniques offer an alternative to conventional methods, targeting the destruction of malignant cells in a minimally invasive way. The physician inserts probes into the patient's body which focus high-frequency alternating current at the tumor. This current causes resistive heating of tissue which leads to necrosis. The effectiveness of the treatment depends on the coverage of the tumor with the eventual heat-induced lesion.

RFA compares favorably with percutaneous ethanol injection and microwave coagulation therapy and can be considered a contestant for the first line treatment in cases of HCC [3]. However, this form of therapy has three major drawbacks. First, large vessels and neighboring organs may be accidentally perforated during insertion of the probe. Therefore, the surgeon must carefully determine the ideal path for placing the probe inside the patient's body. Second, the exact extent of the caused necrosis cannot be reliably predicted by image guidance only. And third, the means for assessment of the results during or right after the procedure are very limited [9].

The main objective of the EU FP7 project *IMPPACT* was the development of a patient-specific intervention planning system (IPS) for RFA interventions based on parametrization and simulation of the procedure to allow assessment of suitable probe setups in clinical applications. A graphical user interface was designed for displaying, examining and processing anatomic meshes and multi planar reconstructions (MPR) obtained from CT scanners. The challenge of accurately predicting the lesions caused by the intervention was addressed using the finite element method (FEM) for solving the equations in an elaborate mathematical model.

2   Related Work

Early research on RFA demonstrated that numerous factors, such as the heat sink effect, need to be considered in order to accurately predict the progress of coagulation [5]. Numerical approaches for a realistic model were assessed by Tungjitkusolmun et al. by solving the bioheat equation with FEM for reconstructed three-dimensional geometries [11].

Villard et al. presented their tool *RF-Sim* with a real-time implementation for visualization of lesions, including a technique for automatic optimal needle positioning. Expected necrotic regions were represented by an approximated ellipsoidal field. The vascular cooling effect of veins and arteries with $\varnothing > 2$ mm was taken into account and would cause indentations on the ellipsoid [12].

Schumann et al. investigated requirements and quality attributes for simulation software solutions [10]. Following these guidelines, an RFA planning tool with a user-friendly graphical interface was outlined. Complete reconstruction of the anatomy and volume visualization were included in order to enable the user to freely navigate and choose arbitrary probe setups [8]. The need for sophisticated applications capable of planning and simulating RFA interventions is also annotated in a later publication by Rieder et al. [7].

3   Clinical Workflow

3.1   Material and Data Acquisition

The planning application and the mathematical simulation model were designed for intended use with the RITA StarBurst ablation needle. The probe is equipped with an umbrella-shaped array of 9 electrodes that can be extended variably.
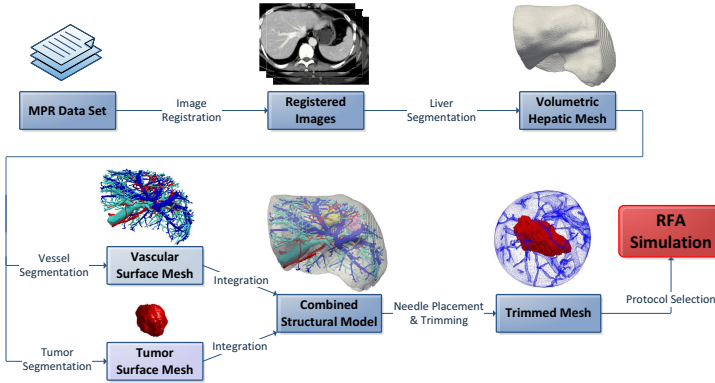
Fig. 1. Illustration of the required steps preceding RFA simulation in a patient-specific environment. Based on the pose of the RFA probe, the combined structural model of the hepatic anatomy is trimmed to the area of interest to reduce the complexity of the solving process. Suitable protocols are selected to simulate recommended procedures including periodic changes in probe position and extension of electrodes.

The determined protocol for patient data acquisition provides that at least two sets consisting of three multi planar CT images each are obtained from patients: one prior to the intervention and another following removal of the probe. Each set contains one native image and two images with applied contrast agents for enhanced vessel visibility during hepatic arterial and venous phase. Additional scans are often necessary to confirm correct placement of the RFA probe before heating.

3.2   Image Processing

The key element to virtually plan, simulate and evaluate results of RFA intervention on a patient is a processable 3D model of the individual hepatic anatomy. Surface meshes representing the internal structures serve as visual clues and alleviate the task of identifying effective probe positions. Furthermore, the major thermal influences in modern bioheat models are assumed based on the shape of the liver and imminent presence of vascular branches.

The intended sequence for creating processable anatomic meshes for RFA simulation from CT is shown in Figure 1. The basis for the image processing phase is given by a pre-interventional set of three CT scans as described in Section 3.1. Image registration is performed in order to compensate for deformations and visual disagreements caused by patient movement between the three consecutive scans. The liver segmentation procedure creates a volumetric mesh fully automatically from the registered images. The boundaries of the liver can be used to parameterize the ensuing steps and reduce the required runtime significantly.

For extraction of the portal vein and hepatic vessels, a new single-seeded method devised by Alhonnoro et al. [1] is employed. The algorithm detects and

combines tubular structures extending from a freely selected starting point. The accuracy of the extracted vascular tree can be improved as required by repeatedly choosing seeds in areas where additional examination is desirable. Detection of tumors residing in the liver is performed semi-automatically.

The extracted structures are combined to form a unified mesh that serves as an input to the mathematical solving procedure. The computational domain for RFA simulation is reduced to a spherical volume surrounding the ablation zone that is assumed to enclose the entire area affected by the heating process. This optimization leads to reduced computation time, while preserving the accuracy of the result.

3.3   RFA Simulation

Following the image processing phase, the simulation is initiated with the resulting trimmed mesh and a suitable intervention protocol (see Figure 1). The protocol defines probe-specific parameters and scheduled actions during interventions, such as planned cool-off phases, repositioning of the probe or extension of the electrodes. These specifications can be customized to comply with the recommended instructions of the manufacturer for treatment with the employed medical equipment. The prediction of the necrosis zone is based on a FEM solving system that calculates the certainty of cell death using an adaptation of the bioheat equation [4].

4   Implementation and Clinical Application

4.1   Graphical User Interface

The user interface of the IPS supports multi-volume and MPR rendering to enable assessment of the entire setup and detailed visualization of particular image layers at the same time in a partitioned widget consisting of multiple adjustable views. Patient CT data are displayed in the four separate sections of the widget, each representing a different viewing perspective with enabled zooming: one freely rotatable 3D view and three 2D layered axial views along the transversal, coronal and sagittal axes respectively. The data set can be traversed on each axis by scrolling through layers. In 2D, volumes and surface meshes cannot be visualized in their entirety; instead we display the contours of the cross section at the corresponding layer. Alterable intensity ranges allow for augmented discriminability of structures in the CT images with specific density (e.g. bones). The 3D representation of the RITA StarBurst is an inherent feature to the graphical interface and can be positioned freely to create a custom interventional scenario (see Figure 2).

4.2   RFA Simulation Using the IPS

The IPS project files are initiated using the acquired CT image sets. The image processing phase was implemented by integrating the developed algorithms into
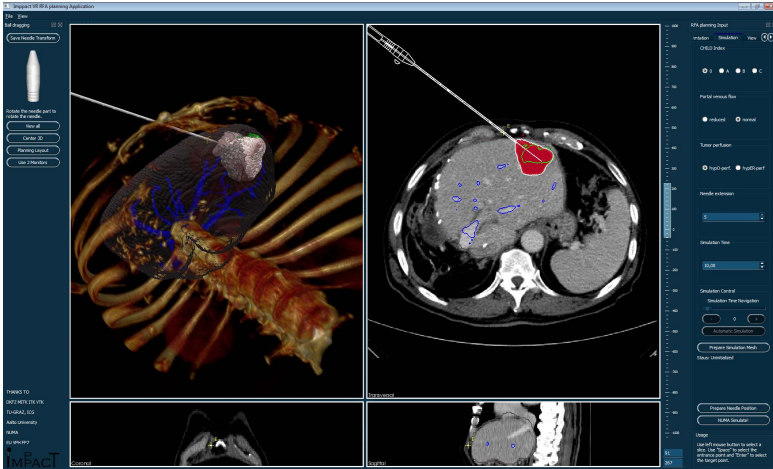
Fig. 2. Graphical user interface of the IPS including 3D volume rendering and multi planar 2D display of patient data. The model representing the RFA probe (**white**) can be freely positioned. The portrayed example displays the anatomy of a sample patient exhibiting a hepatic tumor (**green**) and an overlay of the predicted coagulation area for the selected probe setup (**red** for 2D, **pink** for 3D).

the IPS and providing means for parameterizing the semi-automatic methods accordingly. The meshes that are returned by the extracting functions are instantly displayed in the multi-view widget. All methods are invoked from within the IPS, thus requiring no external tools or procedures. Placement of the RFA needle is performed by selecting two points in 3D space defining the alignment of the needle shaft. The rotation of the probe as well as the extension of the emitting electrodes can be altered to modify the initial parameters of the simulation. Distorting effects caused by the presence of the probe and related influences on the coagulation process are assumed to be small because of the relatively still consistency of hepatic tissue. This assumption has been confirmed during the validation stages of the project (porcine experiments and retrospective MRI). Probe setups and related risks are easily categorized by the user based on proximity of the needle shaft to organs or major vessels. Intervention protocols can be set up or loaded from disk to simulate physical interaction during the treatment. After selecting a suitable protocol, the RFA simulation can be started.

4.3   Investigation and Uncertainty Visualization of Necrosis Zones

Once the FEM calculations have finished, cross sections of the eventual coagulation area are displayed as red overlays in the respective 2D views. In the 3D section, the necrosis zone is represented by a distinctly colored surface mesh (see Figure 2). The lesion can therefore be compared directly with the shape and size of the targeted tumor. For detailed investigation of the coagulation area, we

created an immersive environment for stereo projection using head tracking to determine the position and orientation of the viewer. In contrast to simple 3D navigation in the corresponding view, the stereoscopic system enables the user to actually experience the structural data in three dimensions. Based on the numerical results of the simulation, the certainty of cell death at each location may be conveyed to the observer by adapting the local transfer function accordingly.

An exemplary configuration for computer-assisted RFA intervention is shown in Figure 3. The IPS supplies the patient data and probe parameters for the simulation of the treatment. Stereoscopic images of the affected region are displayed on the projection wall. The implied 3D viewing effect enhances the spatial perception for the observer. Patient dummy and augmented reality devices are part of the training program that was conceived to acquaint trainees with the procedure and correct use of the IPS.
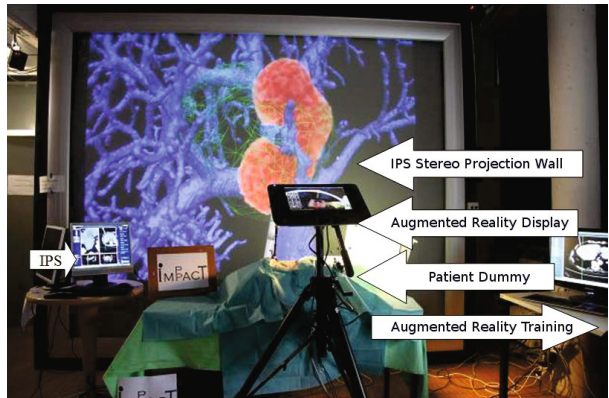

Fig. 3. The RFA training setup at our lab that uses the IPS for stereoscopic projection of predicted lesions

5   Results

5.1   Application Assessment

During the research phase with porcine test subjects at the Medical Universities of Graz and Leipzig, histology slides were obtained from the organs of the animals to provide control data for evaluating the accuracy of predictions made by the solver model. The simulation results could thus be validated post-operatively for these subjects by comparing cross sections of the predicted lesion to the sectioned slides of the resected liver. Furthermore, medical doctors evaluated the tool with a retrospective study on a dozen of HCC ablations with clinical patients, where they compared the predicted lesion size quantitatively and qualitatively with MRI control scans of the patients one week after the intervention. This study is currently under review and will be published in the future.

Personal communication revealed that the tool has high potential to make the planning process more secure and facilitate the elaboration of patient-specific intervention protocols.

5.2   Simulation Times and User Effort

Our system is currently used at two clinical sites: Medical University Graz and University Hospital Leipzig. At these sites, the IPS is used on standard clinical workstations as well as on high-performance laptops. In Table 1 we compare the average times for the separate steps for 10 different ablations on standard clinical workstations – usually Intel Core 2 Duo with 4GB RAM and basic graphics acceleration – with average times for the same procedures on a PC from our Lab (Intel Hexa-Core with 16 GB RAM and Nvidia Quadro 6000 GPU). Except for the visualization of the results, none of the used algorithms exploit GPU acceleration yet. This is mainly due to the absence of required hardware in standard clinical workstations.

Table 1. Average processing times range of planned procedures, including user interaction at clinical workstations (WS) compared to processing times measured on a high end PC from our lab

	clinical WS	high-end PC	user effort
automatic registration	15-25 s	7-12 s	none
liver segmentation	4-6 min	1-2 min	none
tumor segmentation	3-5 min	2-3 min	low
arterial vessel segmentation	10-20 min	10-18 min	medium
venous vessel segmentation	10-20 min	10-20 min	medium
needle placement	1-2 min	1-2 min	low
protocol selection	1-2 min	1-2 min	low
simulation	3-5 h	20-90 min	none
total	209-355 min	45-137 min	–
actual RFA intervention	45-120 min	–	high

6   Conclusion

We have presented and discussed an RFA planning application for HCCs, resulting from the EU FP7 project *IMPPACT*. A graphical user interface for clinical use has been developed with an emphasis on easy and fast examination of multi-layered CT images. Required processing steps for creating patient-specific conditions in RFA simulations have been identified and were successfully integrated into the program. Additional parameters for the definition of conclusive interventional scenarios were added using intervention protocols and a freely adjustable model of the RITA StarBurst ablation needle. Planning and simulation of RFA treatment could be completed within an hour by trained personnel using the IPS on high-end computer systems. Intuitive visualization of the certainty of cell death and extent of the resulting lesion was achieved using a combination of displaying techniques, including stereoscopic projection. The application has been evaluated and employed in two European medical institutions. One major challenge for any comparable planning application is the delicate task of balancing simulation precision and required computation time to suit clinical use.

Future research will be directed towards further increase in efficiency and harnessing of computational power and GPU acceleration to advance the feasibility of reliable online monitoring of lesion formation and progress of necrosis during RFA interventions.

The software is open-source and freely available. The framework may be obtained by contacting one of the authors because of its physical size.

References

1. Alhonnoro, T., Pollari, M., Lilja, M., Flanagan, R., Kainz, B., Muehl, J., Mayrhauser, U., Portugaller, H.: Vessel segmentation for ablation treatment planning and simulation. In: Händler, W., Spies, P.P. (eds.) Rechnerstrukturen und Betriebsprogrammierung. LNCS, vol. 13, pp. 45–52. Springer, Heidelberg (1974)
2. Carr, B.I.: Hepatocellular carcinoma: Current management and future trends. Gastroenterology 127, 218–224 (2004)
3. Lau, W.Y., Lai, E.C.: The Current Role of Radiofrequency in the Management of Hepatocellular Carcinoma: a Systematic Review. Annals of Surgery 249(1), 20–25 (2009)
4. O'Neill, D.P., Peng, T., Payne, S.J.: A two-equation coupled system model for determination of liver tissue temperature during radio frequency ablation. In: Proc. IEEE Engineering in Medicine and Biology vol. 2009, pp. 3893–3896 (2009)
5. Pennes, H.H.: Analysis of tissue and arterial blood temperatures in the resting human forearm. Journal of Applied Physiology 1(2), 93–122 (1948)
6. Pricher, A., Medinger, M., Drevs, J.: Liver cancer: Targeted future options. World Journal of Hepatology 3(2), 38–44 (2011)
7. Rieder, C., Altrogge, I., Kröger, T., Zidowitz, S., Preusser, T.: Interactive Approximation of the Ablation Zone incorporating Heatsink Effects for Radiofrequency Ablation. In: Proc. of CURAC, pp. 9–12 (2010)
8. Rieder, C., Schwier, M., Weihusen, A., Zidowitz, S., Peitgen, H.O.: Visualization of risk structures for interactive planning of image guided radiofrequency ablation of liver tumors. In: Proc. SPIE Medical Imaging, vol. 7261, pp. 726134-1–726134-9 (2009)
9. Rieder, C., Weihusen, A., Schumann, C., Zidowitz, S., Peitgen, H.: Visual support for interactive post-interventional assessment of radiofrequency ablation therapy. Computer Graphics Forum 29, 1093–1102 (2010)
10. Schumann, C., Rieder, C., Bieberstein, J., Weihusen, A., Zidowitz, S., Moltz, J.H., Preusser, T.: State of the art in computer-assisted planning, intervention and assessment of liver-tumor ablation. Critical Reviews in Biomedical Engineering 38(1), 31–52 (2009)
11. Tungjitkusolmun, S., Staelin, S.T., Haemmerich, D., Tsai, J.Z., Webster, J.G., Lee Jr., F.T., Mahvi, D.M., Vorperian, V.R.: Three-dimensional finite-element analyses for radio-frequency hepatic tumor ablation. IEEE Transactions on Biomedical Engineering 49(1), 3–9 (2002)
12. Villard, C., Soler, L., Papier, N., Agnus, V., Thery, S., Gangi, A., Mutter, D., Marescaux, J.: Virtual radiofrequency ablation of liver tumors. In: Ayache, N., Delingette, H. (eds.) IS4TM 2003. LNCS, vol. 2673, pp. 366–374. Springer, Heidelberg (2003)