DATA ACQUISITION FOR RADIOFREQUENCY ABLATION SIMULATION

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Abstract: One approach to treat liver tumors is local destruction of the tumor for example by radiofrequency ablation. In this intervention an electrode is placed into the tumor and dissipates radiofrequency waves, thereby heating up the surrounding area. The heated tissue coagulates and cells in this region die. The treatment is successful if all tumor cells are destroyed. A computational description for this procedure would allow a better planning, safer performance and a lower rate in local recurrence of tumors. It would therefore be highly desired, but is hard to achieve as it is both difficult to model and open research in many related areas.
For building a computational model the first step is to take a close look at the procedure to understand in detail what the model has to predict. At the same time, a good understanding of the information gained from patients during the procedure is necessary to see what is available for an experimental validation of a created model. Existing gaps in verification then have to be filled with phantom or animal experimental studies. The paper gives an overview over the procedure with an emphasis on the gathered data and a conceptual evaluation of the data's suitability for automatic processing and computational modeling.

1. Introduction

Radiofrequency (RF) ablation of liver tumors is a quite new approach for cancer treatment. First patients were treated in 1993 [1]. It is based on the following procedure: a needle is placed in the tumor and destroys it from the inside by delivering energy in form of radiofrequency electromagnetic waves into the tissue thereby heating the tissue. Cells that are heated above approximately 50º C degenerate and die in this procedure, the tissue coagulates. The final result is a necrosis zone which – for the treatment to be successful – has to encompass all tumor cells [2, 3].

The procedure shows several challenges to the skilled surgeon or radiologist. Support by information technology and especially augmented reality could be used in many subtasks of the procedure: starting from choosing a good position where to place the needle, going on with performing the placement and controlling the effects of the intervention while treatment goes on, up to assessing the results of the treatment.

For planning as well as assisting in monitoring the procedure a model of the RF ablation process that shows how the heat is distributing through the tissue is needed. Establishing a model that is able to do prediction in difficult situation is an unsolved scientific problem. The model is demanding in knowledge in more than one research area. A complex liver geometry needs a patient specific reconstruction into a virtual model. Computation then has to be based on finite element analysis. The correct biophysical properties are likewise patient specific and descriptive mathematical equations are still open research. Especially from a biochemical point of view the changes in cells during the coagulation process are only partially understood so far. A good model has to compute the heat sink effect by proximity to close vessel and the attraction of RF current towards the vessels as shown in [4]. Furthermore it should model the heat distribution in inhomogeneous tissue. Its suitability has to be verified in experimental settings and needs to be cross-compared to available data of performed interventions.

Building a mathematical model for a real process can be done in two ways: First by theoretical derivation from existing formulas, or second, by building an empirically correct description without theoretical base. For RF ablation a description cannot be derived completely from existing physical and chemical equations. The process is not well enough understood in those sciences. The model therefore has to be validated experimentally and to some extend found empirically by providing a computation that reproduces results from findings in experiments. The strength of the model thereby depends on the information that is available to build it: the basic ground truth.

Describing the procedure in detail is the first step to understanding what the model has to compute. At the same time it is necessary to gain an overview over the data collected from patients during the procedure. The data is by far not sufficient to build a computational model, but even with filling gaps by using phantoms or animal studies, the data collected from patients is the only contribution, which later on helps in transferring findings from other studies into models for patients. The following sections therefore describe

which data is available from real procedures, how it is collected, and what needs to be gathered in other ways to build a model with experimental verification. The description is based on findings in papers, discussions with doctors and watching ongoing procedures. Variations therefore might be found in clinical procedures performed by other doctors.

2. Related Work

An overview over the procedure is described by several medical doctors, for example in [5, 2, 3]. A good overview over the engineering perspective is given in [6]. There exist many studies by doctors on local recurrence of tumors. Especially Mulier et al. [7] performed a meta-study to collect long-term results. Yet another approach focusing purely on the human factors perspective and unfortunately lacking a feasibility study can be found in [8].

Many authors describe the process of RF ablation in an abstract way and compute heat distribution for artificially generated situations which are not taken from patient data. Most advanced simulations of this kind can be found in [4, 9, 10]. This approach is useful when regarding abstract questions like the validity of bio-physical equations or electrode design.

Another approach is the simulation for ablation with the aim to create a patient specific planning tool. A major step into this direction was accomplished by Butz et al. [11] who proposed a planning tool for cryo-ablation. Computing the ablation zone has been done by estimating an ellipsoid. Tumors which are too big to be destroyed by one single needle can be killed using overlapping coagulations and several needles. Using ellipses to estimate the resulting coagulation areas the authors computed the best needle positions for creating overlapping coagulation areas in this publication.

Villard et al. [12, 13] made the same approach (predicting ablations as ellipsoid) for RF ablation and created a tool called RF-Sim which allows a detailed planning for needle placement, including computing the best needle position for a percutaneous approach. Ellipses for predicting the necrosis zone of an RF ablation are an idealized assumption. Villard et al. take deformations of the ellipse by nearby vessels into account in [14].

The physical validity of the RF-Sim model is still limited. Liver tissue is inhomogeneous at different scales and distributes heat in more complex shapes. Sheu et al. compute a mathematical model for RF ablation based on physical properties and bio-physical equations with blood perfusion effect in [15]. It is unfortunately not compared to patient data from a real intervention.

A similar model is computed by Kroeger et al in [16]. Though the model shows many properties that fit reality, the experimental validation lacks persuasion, as the result is compared to an image taken from a patient two months after the intervention. Using this model for computing the optimum needle placement is presented by Altrogge et al. [17]. A bio-physically based patient specific description of the ablation process with experimental validation is to the best of the author's knowledge not published.

3. Data acquired from patients during the procedure

Taking a close look at the procedure is best done by describing the workflow. In the following section the emphasis lies on information sources (acquired images and other) used by the performing radiologist or surgeon in their task due to two reasons: first it shows why simulating RF ablation is desired, second – as it describes the information gathered in clinical practice – it shows which information collected from patients can be used for building a computational model and validating a simulation.

The process of planning and executing the procedure leads to image acquisition in different modalities. Additionally the RF generator takes measurements that help the doctor in controlling the ongoing procedure. The following paragraphs describe the information gathered from patients in each phase of the procedure.

3.1. Pre-operative phase

A patient with a tumor in the liver has first to be diagnosed by a radiologist. This can be done with different imaging modalities, for example using Ultrasound (US), Computed Tomogram (CT), or Magnet Resonance (MR) imaging. If the diagnosis points to a tumor in the liver, which needs to be destroyed by RF ablation, the next thing is to plan the intervention pre-operatively. This is done using either CT or MR images, as those give the best visual representation of the tumor location. Ideally the images used for planning the procedure are acquired no more than 3 to 4 weeks prior to the intervention. In that case there is

a fair chance, that the images show all tumors with approximately the size which will be found during the intervention. If possible images that were taken for diagnosing are reused for planning purposes. If these images are not suited new images are acquired. In case the intervention is guided by ultrasound, an examination with ultrasound is performed one day before the procedure.

The needle has to be placed on a path that does not hit any vessel or bile duct of relevant size. Unfortunately, wherever a tumor grows it will draw blood support to it. Hence there will be vessels growing to the tumor and therefore in close proximity to the area where the needle has to be placed and where the ablation will be performed. Avoiding all vessels is not a simple task. CT or MR images for tumor diagnosis are taken with contrast agents. They show all the inner structures in the liver: the vessel trees, the big bile ducts, the gall bladder, and - of course - the parenchyma. These images give the radiologist all information needed for needle placement.

Besides deciding for the best needle path, the doctors have to agree on details of needle type and ablation protocol. There exist different models of needles used for this kind of intervention. The exact desired position for the needle tip depends on many factors. Besides the anatomical and imaging technology requirements, the used ablation protocol and needle layout also have to be taken into account.

The monopolar or bipolar versions consist of one electrode that dissipates RF waves. These needles create coagulations with an elliptical shape in small size (about 1.6 cm diameter [3]). Another possibility is to arrange electrodes parallel, so they are placed together, which increases coagulation size. Finally, there exist needles with an extendable array of electrodes, as for example the LeVeen Needle by Boston Scientific or the StarBurst by RITA Medical Systems follows this design (see Figure 1). They can deploy up to 5 cm wide and have the ability to measure temperature in part of their electrodes during the procedure. Their lesion shapes are given as spheres by the manufacturers but reported in in-vitro experiment as barrel or mushroom formed [10].

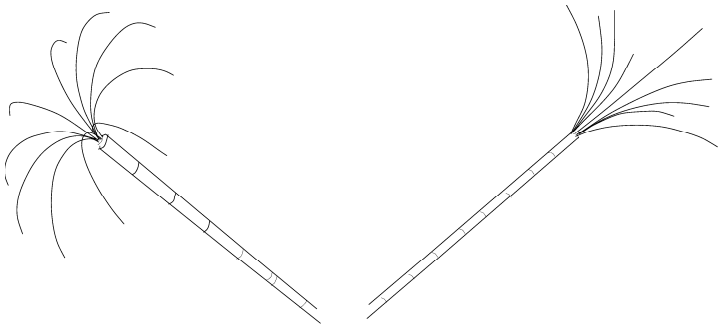


Figure 1. Schematics of needles with deployable arrays. On the left side the LeVeen device has an umbrella shape. On the right side the StarBurst is less curved and sometimes referred to as 'Christmas tree' shaped.

The data used by the doctor for his decision process is the patient specific MR or CT images, if acquired US images, and his knowledge on performing the procedure – based on the device manuals. This information, though absolutely sufficient to a skilled radiologist or surgeon, is hard to process automatically. US images can be recorded when acquired, but – as ultrasound presents a 2D slice through the tissue – what can be seen is absolutely dependent on the position and orientation of the ultrasound sensor. This location information is not recorded in clinical practice. The US data can therefore not be used for machine processing as the cutting plane in the image is unknown. Furthermore US images are quite noisy and automatic processing is therefore difficult.

For MR or CT images computers need a higher contrast than doctors to be able to correctly segment a liver and its inner structure. Segmentation of bile ducts out of those images is open research. If vessel trees are not segmented completely they might not be reconstructed correctly and one fragment might be connected to the wrong vessel tree in the reconstruction process. The segmentation of tumors cannot be done automatically and is a radiologist's task. The result for image processing on such an image is a virtual model of a patient's liver that is in best case incomplete – worst case wrong. This is to a certain extend acceptable for a model that is already known for computing correct. As ground truth for building a model it is insufficient.

3.2. Intra-operative phase

The result of the pre-operative phase is a detailed plan on the desired needle position, needle type, and placement path. During the intervention the needle has to be placed along this chosen needle path. The placement can be done under US or CT guidance.

US images are generated in real time, but are blocked by solids and gas. So US will not work behind the ribs or through the lung. Therefore not every needle path can be chosen. If the needle is placed using US guidance the images are taken with contrast agent (micro bubbles) to highlight vessels and tumor. A few seconds after inserting the contrast agent first the vessels highlight up then the tumor in the parenchyma is visible. The time window for watching these structures is approximately 10 seconds. Then the micro bubbles are gone and another injection will be necessary if the structures need to be visible again.

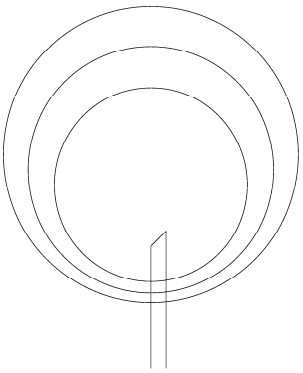
Alternatively, a single CT image can be acquired in near real time and is not limited by bones or air, but only shows an axial slice of the patient. So for placing the needle under CT guidance a path in between the ribs and through the lung could be chosen, but the path has to stick to the same plane that is recorded in the CT fluoroscopy image.

After the needle is placed in the desired position, destruction of the tumor can begin. The generator is switched on and, if deployable, the array of electrodes is deployed according to the device manuals. The following example describes this part of the procedure in detail and shows how to create a coagulation zone in the size of 5 cm using a RITA StarBurst:

The exact desired position for the needle tip is described in the manual and depends on the size the coagulation should have in the end. According to the instruction manual to achieve 5 cm diameter for the coagulation the needle tip has to be placed at 1.5 cm distance from the tumor. The created lesion will then extend over the whole tumor and the safety margin as explained in the datasheet for this needle [18].

The RF generator can be set to different control modes (automatic temperature control mode, infusion mode, power control mode, etc.) and needs various parameters (power to be used and time for running the generator) [19]. Figure 2 shows a schematic of the created coagulation together with the ablation protocol suggested.

According to the device manuals, in the beginning the electrode array is deployed 2 cm wide. Then the generator is switched on and step by step the array is deployed further (3cm, 4cm, and 5cm) following the decided ablation protocol.



For a 5 cm ablation:

Deploy to:	For a Duration of:
2 cm	Until Target Temp is reached, then deploy to 3 cm
3 cm	Until Target Temp is reached, then deploy to 4 cm
4 cm	7 minutes at Target Temp then deploy to 5 cm
5 cm	7 minutes at Target Temp the goto Cool Down

Figure 2. On the left side a schematic for a deployable needle is shown and the expected coagulations created with deploying the array step by step as described in the StarBurst Device Placement Diagram [18]. Details on how to perform the ablation are written in the RFA for Liver Tumor Protocol [20]. The manual thereby suggests an ablation protocol as in an excerpt described in the table right beside.

For the whole procedure the RITA Medical Systems' RF generator is able to measure the temperature in every other electrode in the array. It shows temperature information, time, and used power in raw numbers as well as in graphics. Furthermore, it computes the efficiency which is a measurement for conductivity of the tissue. An example graphical output of a beginning procedure is shown in Figure 3.

If the tissue is heated up too much it carbonizes, thereby changing its electrical conductivity to isolation. In this state it is not possible to create big coagulation zones. Whenever the efficiency drops the power is reduced to avoid carbonizing. Therefore, the upper graph in Figure 3 shows a rise temperature until the impedance grows too much. Then the power is shut down and temperatures as well as impedance are falling with it.

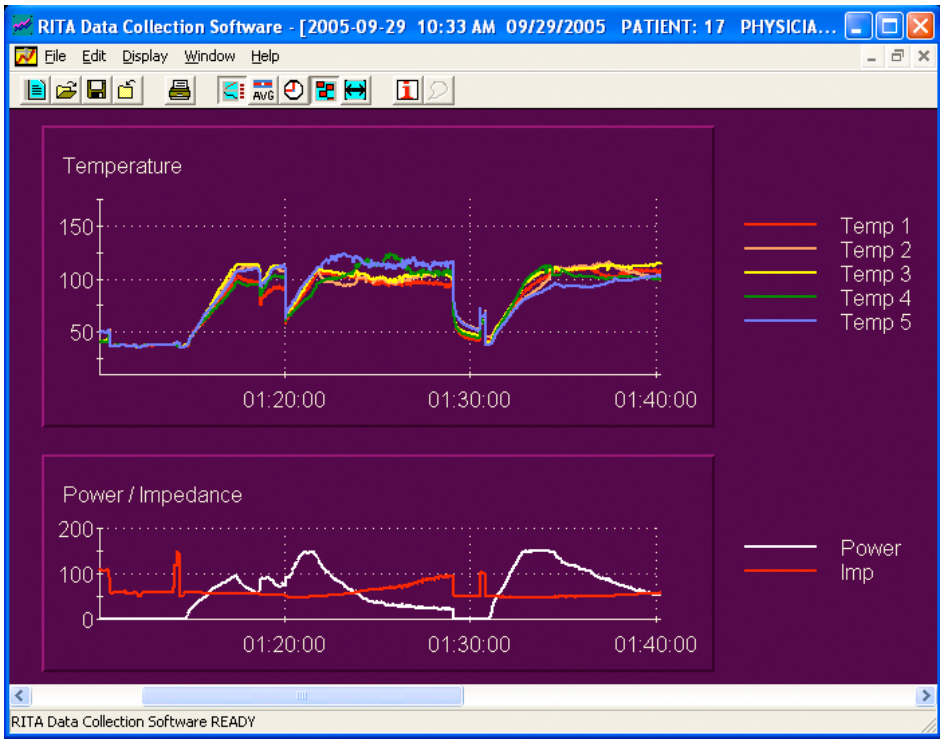


Figure 3. Example of graphical output of the RITA RF generator measurements during RF ablation (Courtesy of Lars Frich). Note as impedance rises the power is dropped and with it temperature and impedance fall (shortly before the 1:30 mark).

Furthermore, the graphs show the temperature as measured in the 5 measuring electrodes. These are 5 spots at the rim of the desired coagulation that represent the temperature in the whole area. Ideally, all 5 electrodes show the same temperature measurements. In this case, one has reason to believe the assumption that the heat distribution is even as planned. If one line drops and does not reach the same temperature as the others, the tissue is probably cooled by a nearby vessel. This is a hint of not evenly distributed heat. If one line rises more than the others, this specific tip might be sitting in an area that is not as much cooled as the others, i.e. an area that is not as perfused.

Whenever the array is deployed further, the temperature in all electrodes drops as they are extended into not yet heated up tissue. RF waves are then dissipated from the new position and the new treatment region is heated up. According to the ablation protocol in the final extension the generator keeps running for a set time. Finally, the RF generator is switched off.

During the whole procedure the radiologist watches the ongoing ablation in US. As cell fluid evaporates there is no clear view of the ongoing ablation. The possibility to watch the coagulation growing is therefore very limited. When the RF generator is finally switched off, the radiologist waits for the evolving micro bubbles to disappear so he will once again have a clear look. This takes about 10 minutes. Then he does an early assessment using contrast enhanced US. In this assessment the radiologist can see the coagulation as it was produced during the procedure. As heat conduction in the liver is patient specific the result might differ from the planned and expected coagulation. For example, though the coagulation size might have been planned for a size of 5 cm diameter for some patients the result has only 3 cm.

If the radiologist is not satisfied with the result he can perform another ablation. Sometimes he might even plan from the beginning to create several overlapping coagulations to treat a tumor that is too big to be treated by one ablation. Whenever the needle is taken out, the generator is running on low power. Heating up the needle path like this, serves the killing of possibly carried along tumor cells as well as the closing of small vessels along the path so there will no bleeding. Some radiologists do an overview CT scan right after the procedure is completed, mainly to show that there is no bleeding in the liver. Neither this first US nor an overview CT scan can be used to assess if the tumor was really treated successfully. The necrosis zone is not yet defined.

During this part of the procedure a lot of data is gathered, but a lot of information is also not available for building a computational model. US images once again have the same limitations as in the pre-operative phase (missing location information) and can, therefore, not be used to establish a computational model. The exact location of the needle can only be acquired if the needle placement is performed under CT guidance. Still, the location of the extended electrodes remains unknown. As the ablation protocol might even lead to a change in electrodes' positions during the procedure the model has to assume needle positions. This is once again acceptable if applying a model that is already known as being correct to do a prediction. It is insufficient for building a ground truth.

If temperature measurements are taken by the equipment during the procedure, this information is most desirable, as this is a very good chance to validate computations. Furthermore, a detailed protocol of applied power and computed efficiency is very helpful in computational reproduction. Most obviously, information on extension and shape of the coagulation zone right after taking out the needle is not available. Images acquired at that time are not meaningful for assessment of tumor treatment and therefore not taken. Unfortunately, this would be the most important information for validating a computational model that can only simulate heat distribution to this point. But assessment of patient treatment is done post-operatively.

3.3. Post-operative phase

An image acquired right after the procedure does not show the ablation in its final shape. It would also not show parts of the tumor that might have survived. The necrosis develops over a couple of days after the ablation and changes shape during that time. The liver tissue swells as a first reaction and also the process of cell destruction is carried on after the intervention. An evaluation of the procedures success is therefore done by taking images 2 weeks or 1 month after the procedure in CT or MR. Contrast agents show the current shape and extension of the necrosis zone. This is the first chance to detect if a tumor grows again.

Follow-up scans are taken in intervals of 3 months to find early indications of recurrences (local or somewhere else in the liver). Comparing the treatment result in those images shows that over time the necrosis zone is getting smaller as the destroyed tissue builds a scar. New liver tissue grows back, but some rest of the necrosis remains visible in the tissue forever.

As the goal of a good computational model should be to predict treatment success, reproducing results from the first images that are taken for treatment assessment has to be the goal. Those images are obviously taken a few days up to one month after the procedure. But in these images other effects like regrowth of liver tissue are also visible. The computation therefore cannot be proven to be correct by correlation to these images.

4. Discussion and Conclusion

Modeling a real process (physical, chemical, biologic, or medical) is a question of which part of the process to watch and describe and on which scale. So gathering data or setting up an experiment also means that the computational model has to describe the same procedure. The intervention as described above is very complex. Computations with the aim to predict the result of this treatment is therefore difficult and as much information as possible needs to be incorporated into the model. At the same time, data collected from patients during the procedure is often either not suitable for automatic processing or incomplete. Conclusively the model cannot be build from patient data only.

Building the computational model demands several steps which require data acquisition. The following listing defines the requirements and explains from where to acquire the data.

1. Reconstruction of a virtual patient specific model of a liver with its inner structures: though image data of a patient's liver and its inner structure is acquired from patients during the pre-operative phase, this data is only partially suited for the task. Comparably low contrast between the three vessel trees and the liver makes segmentation difficult. Acquiring information on all vessel trees in one image makes automatic reconstruction of the vessel trees difficult as fragments might be aligned wrong. Bile ducts are especially difficult to segment. Tumors have to be segmented manually, but then can be easily integrated into the virtual model. Conclusively the virtual model has to be established from images acquired in phantom or animal studies.
2. Annotation of the reconstructed tissue with physical properties: electrical and thermal conductivity as well as blood flow rate in the vessels are never acquired for patients. These

can be taken as estimates from literature. For a phantom or animal they could be acquired. In both cases applying the final model to a patient's dataset has to be done without the exact thermal and electrical tissue parameters. There exists no way to gather these parameters without dissecting part of the liver.

3. Ablation protocol and parameters: building the model has to be done by starting with simple tasks and adding complexity on the way. A complete ablation protocol as done for patients is, therefore, not well suited for the beginning. Especially, if the needle electrodes are extended during the procedure, the results of several coagulations are overlapping and the effects can hardly be assigned to their causes.
4. The resulting coagulation/necrosis: The shape of the necrosis develops over days after the ablation. Therefore, no image acquired from patients will show the coagulation at the time when the RF generator is switched off. But images that are acquired later show the developed necrosis including beginning liver tissue regrowth. Though predicting this situation is the final goal of the computation those images are useless for validation without the intermediate step that shows the coagulation right after switching off the RF generator. Establishing the ground truth in this case can only be done by using phantoms or animal experiments.

Many of the steps described above need data acquisition from other sources than patients. As computational models are already able to take the heat sink effect and the attraction of RF current towards perfused vessels into account, an experimental validation has to model the same conditions. Therefore, data acquisition from experimental settings has to use a replication of a perfused liver. Everything below this level is not able to validate state of the art computational models.

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