Towards Validation for Physiological Models in Intervention Planning

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Abstract. Computer supported treatment planning systems aim at predicting treatment results. Recently attacked challenges base not only on anatomical findings, but include physiological processes. This way, interventions which are highly depending on patient physiology become predictable and can be supported in computer based planning. Though the necessity to validate computations used for treatment planning is unquestioned available models lack validation. This contribution discusses challenges for designing a validation study for the example intervention of radiofrequency ablation (RFA) in the liver.

Keywords. intervention planning, physiological modeling, model validation, radiofrequency ablation

Introduction

Designing a medical study to validate an engineering model is difficult and demands new approaches on almost every level. Different research areas have to collaborate and leave their typical path of thinking to contribute to a common solution oriented on the challenge. For those interventions where a prediction is most desired the intervention result cannot be seen in radiological images. Therefore, evaluating data collected from patients in clinical practice is not sufficient.

While conducting preclinical studies for validation purposes opens up possibilities and opportunities, it also demands to be aware of consequences of decisions. Data in this case will be collected exactly for the reason of validation of a simulation model. It therefore has to fit different requirements than if acquired for medical research only. At the same time treatment planning aims at serving medical personnel. The validation therefore has to be accepted in the medical community.

After giving an overview over radiofrequency ablation as the example medical procedure and the state of the art in computer supported RFA intervention planning the contribution discusses measurement possibilities and resulting study design decisions.

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This research was partially funded by MRTN-CT-2004-512400 and ICT-223877.

1. Related Work

RFA is a minimally invasive treatment of liver tumors. In this intervention a needle electrode is placed inside the tumor and surrounding tissue is heated up through dissipation of electromagnetic waves. Results of the intervention are hard to plan and impossible to image during or right after the intervention. Furthermore, the process of cells dying from heating goes on for a couple of days after the intervention. A detailed description of the procedure can be found in Goldberg et al. [1] (from a clinical perspective) and Organ [2] (for engineering purposes).

Different models for predicting the result of this intervention exist. An important first approach was taken by Villard et al. [3]. A more advanced simulation based on a physiological model was created by Kroeger et al. [4]. To the best of the authors' knowledge an experimental validation is missing for all RFA simulation models.

2. Approach

A study for validation of models used in planning treatment results has to be designed carefully. If the study is to prove anything the model and its validation have to reflect the same situation. So a first decision concerns the separation into major effects that, if modeled, have to exist in the validation study and minor effects, which can be neglected in the computation though present in the study. For RFA the most dominating effect is the heat sink effect by close-by vessels under perfusion. The necessity to validate this effect leads to a perfused organ and therefore to an in-vivo animal study. A minor and therefore neglectable effect is inhomogeneity due to bile ducts in the liver. Those do not carry rapid flowing fluids and therefore do not contribute to heat sink.

Computational prediction of treatment results relies on radiological images. Image acquisition in the validation study has to be oriented on data processing for anatomy reconstruction. Any error derived in this step should be kept as small as possible. The generated data is an input to further processing and errors will propagate through the subsequent computations.

Images in the study are to be processed by machines and therefore should be taken oriented on best chances for low errors in processing. The goal of the image acquisition and processing is a three dimensional anatomy reconstruction in high resolution, showing all inner structures that contribute to the major effects. Structures in this reconstructed anatomy have to be identifiable as they have to carry associated functionality as for example flow rate, which differs for the contributing vessel trees. Therefore the study was designed combining results from three CT scans in the imaging protocol. Images are acquired in approximately the same breathing state.

Acquiring subsequent images to highlight one single structure at a time demands image to image registration to reconstruct one single volume. Deformations in between the images should be kept as low as possible to prevent big uncertainties and possibly big errors. While the use of fiducial markers during image acquisition enhances accuracy in the registration steps, it potentially influences the intervention result and either has to be reflected in the simulation model or else introduces a new error source. Applied image processing techniques therefore have to be oriented on natural features. The need for high accuracy might possibly lead to the application of semi-automatic techniques. In the context of registering subsequent images based on natural features contrast, resolution, and slice thickness are most important features.

Last but not least, for a resulting predictive model to be accepted in the medical community it has to be proven according to sound research methodology in the medical research community. As medical research and clinical practice cannot image RFA intervention results during or after the intervention a validation has to rely on histological examinations of the tissue harvested in an animal study. Here animals of a relevant size and with a physiology close to human physiology are preferred. Therefore a validation study will be carried out in porcine model. Fusing data from histological examinations and radiological prediction concerns computer science research. The necessary registration step is difficult but solvable as long as the radiological images show a high resolution and a thin slice thickness. These conditions allow natural features to be found in both radiological images and histological examinations.

3. Study Design Decisions

While the demand to validate an engineering model in a medical study leads to different challenges in the study design, computers offer more possibilities to process subsequent images and also allow integration of additionally acquired data.

For validating a simulation for the RFA process the study was planned along four major demands:

- In the computational model major effects have to be separated from minor ones. Only the major ones have to be available for computation as well as validation.
- Image processing should be based on natural features to avoid additional error sources introduced by fiducial markers.
- Image processing performed by computers leads to different specifications for the optimum imaging protocol.
- For interventions where the result cannot be imaged in radiological images histological examinations have to be fused into the same data set.

The described study has been approved by the respective ethics committee and is scheduled to be performed. As medical research methodology compares results from more than one experiment to gain statistics on the success the study encompasses the use of 20 pigs. Different key parameters for the simulation model will vary in the study.

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