Contents

1 Introduction

In flight pilot training, the computer-aided simulation of virtual training scenarios was established early. In the next few years, the visuo-haptic simulation of surgical interventions in virtual reality (VR) training and planning systems has the potential to become an important cost and risk reducing standard tool in the education of medical students [28]. In addition, VR trainers could assist the surgeon in the spatio-mental planning of real procedures with personalized virtual body models.
Firstly, the patient-specific VR training method concept summarized in this text comprises methods for patient-individual patient body modeling. Secondly, visuo-haptic presentation methods for the feedback to the operator, taking into account the soft image deformation, e.g. by breathing or instruments. Especially punctures of the upper liver or lower lung close to the pelvis can be strongly influenced by respiratory displacements up to 5 cm [29] and make needle navigation even more difficult.

1.1 Motivation

As a medical field of application, here the needle puncture of pathological liver structures is considered. The emphasis lies on cholestatic bile ducts caused by the obstruction of the endoscopic access by tumors or scar formation [30]. Cholestasis is mainly accompanied by jaundice, as well as pale stools, low appetite, tiredness, itching and nausea [31]. Fluoroscopically,

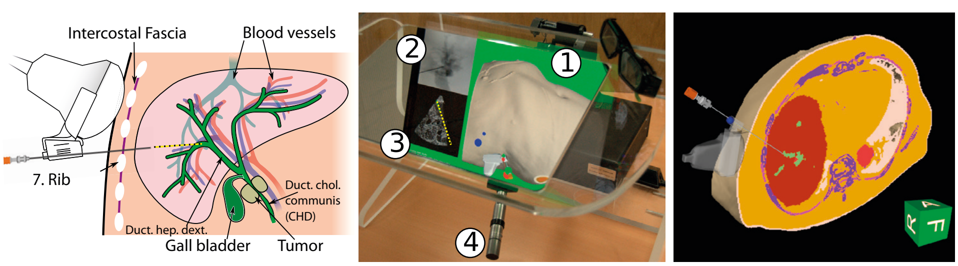

Figure 1.1: Simulated ultrasound (US)-guided needle puncture of a cholestatic bile duct: Left: US-supported needle puncture of a cholestatic bile duct. Middle: Hardware with stereo glasses and semi-transmissive mirror for improved hand-eye coordination and user interface: (1) 3D stereo main view, (2) fluoroscopy simulation, (3) ultrasound view with target line (dashed yellow), and (4) needle steering and force output device. Right: 3D main view (1) of the simulator with section along the US plane and target structure (green). From [1].

the disease can be minimally invasively visualized by intravascular contrast agent injection using "percutaneous transhepatic cholangiography" (PTC) and treated with an additional catheter drainage ("percutaneous transhepatic cholangiodrainage", PTCD) of the punctured bile vessel [32, 33]. Both interventions are abbreviated by PTC/D from now on. They are mainly defined by difficult minimally invasive needle navigation, often between the sixth and seventh rib to the congested bile ducts. Currently, these punctures are often supported by ultrasound imaging (US) as a navigation aid (Fig. 1.1, left) [34, 33].
The aim of this work was a patient modeling and VR method concept for the patient-specific virtual training of needle navigation to a moving target structure, new specialized methods to this aim and the prototypical implementation and evaluation of important aspects of the system. Hardware, visualization and controls of an adequate PTC/D-VR training system are shown in Fig. 1.1 (center).
The success of puncture of a bile vessel with navigational support by simulated fluoroscopic images (Fig. 1.1, center (2)) is indicated outspreading contrast agent held under pressure in the needle catheter. It is difficult to navigate with this imaging technique and it burdens with additional radiation exposure due to continuous X-ray control, increased navigation precision errors and a higher number of needle repositionings [28, 35].
For this reason, needle-based navigation is increasingly conducted with US-guided methods. These provide increased accuracy and precision, reducing the average number of needle repositionings, thereby helping the patient recover more quickly [34, 33]. A needle guide rail is often attached to the side of the US head (Fig. 1.1, left), the linear extension of which on the US image monitor corresponds to a needle path target line (Fig. 1.1, middle (3)).
The methods presented in this work enable visuo-haptic VR simulation of needle intervention under fluoroscopy control and US-assisted navigation in breathing virtual patients. The training progress and planning insights achievable with the system could benefit both the student and the surgical doctor. They cover anatomy imaging in X-ray and US imaging, US head positioning for optimal navigation and puncture. Within the limits of the available hardware equipment, attention is paid to the most realistic or plausible visuo-haptic immersion [36] possible at this time. With time-efficient patient-specific preparation of breathing virtual body models, the doctor could improve the efficiency and effectiveness of his treatment for the benefit of patients by preparing a surgical intervention.

1.2 State of Research and Research Needs

Today, virtual reality systems are used in teaching, training and entertainment [37]. Medical education and practice [38] also benefits from this development. The increasing amount of high-resolution 3D and 4D image data for diagnostics, therapy and surgical planning as well as novel VR methods will allow the regular use of VR systems in everyday medical training and clinical practice. Novel highly immersive visuo-haptic imaging techniques allow more accurate and precise 3D interactions in virtual bodies with reduced user fatigue [39].

So far, patient-specific VR training systems rarely find practical use in medicine. Among other things, this is currently due to the considerable time required for data preparation. In particular, the patient-specific segmentation of anatomical organs and structures accounts for the majority of the time in the preprocessing process chain. To this day, only in first prototypical studies the support of the training of physicians by VR systems without patient-specific virtual body models was examined [40, 41, 42, 43].

The basis of the patient-specific VR simulation is formed by 3D or 4D CT image data of the patient. In general, the semi-automatic segmentation of the image data should be possible in the clinical routine with little time expenditure. Conventional modeling methods may take about 32 to 63 hours of time per 3D image [22, 23, 44]. For this reason, many current VR systems often do not offer an intervention simulation on newly acquired patient data. In addition to efficient patient modeling, the visual and haptic representation (visuo-haptic rendering) is an important topic in this work.

None of the currently existing systems offers so far simplifications of the necessary and very time-consuming process for semi-automatic segmentation of the patient image data. In this work, the addressed structures were divided into large-volume filling structures, which are passed by the needle on the way to the target, or relevant key or risk structures. The latter should either be reached or not be punctured. Rapid real-time classifiers were presented for the filling structures, and organ-specific, optimized methods were used for the target structures to be segmented, resulting in organ segmentation masks that partially filled the image space.

In the gaps between organs, in this work, large-volume filling structures such as air, skin, soft tissue and bone were segmented by transfer function heuristics in real time. High-precision semiautomatic methods for bony structures were presented in [10, 11, 45]. Unfortunately, there is little literature on efficient, automatic segmentation of these background structures, since they are not in the center of the research communities' interest and are often handled with standard methods [46, 44].

A target organ containing other target structures was the liver in this work. There are two significant ongoing contests for their segmentation. Current results on liver segmentation have been published in [47, 25, 48]. Currently, depending on the database used, DICE coefficients [24] clearly above 0.9 can be achieved semi-automatically. Currently, new segmentation methods are being tested in the VISCERAL challenge, current values for liver segmentation with fully automatic methods are here at a maximum with a DICE coefficient of 0.93[1]. Because of its robustness, for the VR-based training of interventions presented here, the multi-atlas-based segmentation approach [49] for the organ group liver, spleen, pancreas and kidneys [47, 25, 50, 51, 52, 53, 54, 55] is adapted. By averaging many segmentation estimates, it has the potential to robustly segment different important organs of the abdominal target area

[1] `http://visceral.eu:8080/register/Leaderboard.xhtml` visited 5/14/16 (CT, liver)

by concurrent semantic-numeric data integration, which is conceptually also useful in this work.
The segmentation of vascular structures in general has been studied by several authors. Most of the methods are methodologically based on the analysis of local 3D Hessian matrices [56, 57]. The eigenvector belonging to the largest eigenvalue indicates the assumed course direction of the currently considered vessel branch and forms a probability map [58, 59, 56, 57]. Unfortunately, no running competitions are available for these difficult to segment vascular tree structures. Realistic DICE coefficients from the literature are in the range of 0.5, which are already good for tree structures with thin vessel branches [26]. In a phantom study that was not relevant for clinical image data, DICE coefficients of more than 0.9 were achieved [60].
The various possible uses of VR systems in medicine are presented in [61]. On the hardware side, the immersion of the user into virtual reality is supported by stereoscopic and haptic input and output devices [62]. Especially eye-hand coordination in the treatment of anatomically complex body areas is an important field of training [40, 41, 42, 43]. Various authors [63, 62, 64, 65] summarize the developments of VR systems with a patient-related approach. VR systems for virtual endoscopy are the most advanced. In the case of virtual body models, fully manually created segmentations of individual organs and structures dominate, and together with triangulated surface or volume element models FEM simulation methods are popular [66]. The applications of marketed VR training systems [67] cover endoscopic [68, 69, 70, 71, 72, 73, 74, 75] and surgical interventions [76, 77, 78, 79, 80, 81].
Earlier and more recently, VR simulators for needle-based interventions have been proposed by several research groups for various indications: (1) lumbar puncture [82, 83, 84, 85, 86, 87, 88, 89, 90]; (2) biopsies [91, 92, 93, 94, 65, 95, 96, 97]; (3) blood samples [98, 99, 100, 101, 102]; (4) injections [103, 104, 105, 106]; (5) brachytherapy [107, 108] and (6) radiofrequency ablation [109, 110, 111]. Respiratory motion simulation has so far only been considered rudimentarily on surface models by simple respiratory motion models with sinusoidal amplitude modulation and the Chainmail deformation algorithm [91, 112, 113, 114]. The visualization of dynamic effects such as the deformation of the tissue by used instruments and by realistic breathing movements was not available there. Surrogate-controlled breathing models from the analysis of 4D CT image phases, as presented in [115, 116], have not yet been part of published simulator concepts.
Currently, the simulation of minimally invasive needle puncture interventions with real-time and increased, high-quality immersion into virtual reality is a field of research [91, 107, 98, 99, 92]. This development is driven by the advancement of PC hardware with fast multi-core processors and GPGPU computing. Regarding methodology, the work presented here for direct haptic volume rendering has provided new impetus to the sparse state of research [117, 118, 119, 120]. This is among other reasons due to the new use of personalized partial segmentation and respiratory motion models. A new evaluation approach has been proposed for the new haptic algorithms. In this special simulation context, the developed haptic-visual coupling and the consideration of the realistically simulated respiration in

a common, efficient deformation framework are also new for the required visual rendering methods. The methods developed by the author and his team are an innovation in the field of GPU-based direct 4D volume rendering [121, 122, 123, 124, 125, 126] and 4D motion model transfer for dose saving VR simulations [18, 19, 20, 21].

1.3 Research Questions, Target and Focus

The research topic of this thesis is to provide methods for a sufficiently plausible, patient-specific liver puncture training simulation with reduced patient modeling effort, which is accepted by a representative user group and provides a motivating training experience.

This publication summary focuses on innovative key methods of the presented VR-based, patient-specific needle puncture training simulator: (1) efficient methods for modeling virtual patients, (2) algorithms for the efficient calculation of visuo-haptic representations, (3) new haptic evaluation methods, and (4) quantitative method assessments and a user study for the qualitative evaluation of the system in a medical application with a complicated target structure (cholestatic bile ducts):

(1) The first focus is the creation of generic and derived patient-specific virtual patient atlases by means of selected, application specific accurate, structure specific sub-segmentation methods featuring a reduced time effort to a few hours. Such a full volume segmentation concept [1, 6, 7] for VR application has not been presented in the literature yet.

(2) The real-time capable, GPGPU-assisted and voxel-grid-based methods of visuo-haptic volume rendering of the image data [2] support the targeted navigation of the needle in simulated breathing virtual patients [5, 3]. A special US viewport in the simulator GUI allows the training of this precise navigation method. This topic also includes the presentation of a new, more plausible force output method at organ boundaries [2]. Needle punctures supported by a guide rail attached to the side of the US probe are also supported. So far, deformations of the patient's body were rather simulated with FEM-based methods [66].

(3) In order to be able to quantitatively evaluate the force output, a new *in silico* evaluation method for force output algorithms is presented [27, 4]. The aim is to use suitable quality measures to compare the force output [8] based on partially segmented virtual patients in comparison to manually fully segmented and already positively evaluated virtual patient. The force output based on a fully segmented patient was checked for plausibility with puncture experienced physicians and was refined in this work for the PTC/D intervention [27, 2, 23].

(4) Medical application example of the VR simulation methods is the bile duct puncture with fluoroscopy assist and, above all, US-guided PTC/D with needle guide rail. Qualitatively, the plausibility of the VR simulation is evaluated by a user study with medical students. Quantitatively, the system is evaluated under various specific aspects such as segmentation quality, speed [1, 7] and temporal performance of the rendering modules [2].