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Towards 4DCT-US image fusion for liver motion monitoring

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***Abstract*— High-intensity focused-ultrasound (HIFU) is a promising technique for treating liver tumors. However, liver motion due to breathing imposes a real-time monitoring of the treatment. To reach this goal and following on previous work, we propose to encase an ultrasound (US) imaging probe into an extracorporeal HIFU device, such that the imaging plane is aligned with the HIFU acoustic axis. Because the tumor itself may not always be visible on US images, we plan to rely on a pre-operative 4D-Computed Tomography (CT) model to infer the tumor location during treatment, using intensity- or feature-based registration techniques. In order to study the feasibility of US guidance according to a pre-operative planning image, we decided to perform US acquisitions on patients after informed consent. These patients undergo radiotherapy treatment and have a 4D-CT image for planning (Philips Brillance), with injected contrast-agent. A hand-held US imaging probe was used to provide 2D images sequences in the coordinate system of the CT scanner thanks to an optical tracking system. No device was available to record a breathing signal during US acquisitions. A breathing signal was estimated for each US sequences using Principal Component Analysis. Inhalation versus exhalation was identified by the user, and the respiratory phase was estimated from the breathing signal using the Hilbert transform. Using this signal and the information from the tracking device, it was possible to approximately register both modalities spatially, and throughout the respiration cycle.**

Keywords*— *Multimodal image fusion, Image-guided therapy, High-intensity Focused Ultrasound

I. Introduction

High-Intensity Focused-Ultrasound (HIFU) is a promising technique for treating liver tumors, thanks to its non-ionizing nature and its potential to coagulate the targeted tissue quickly and in a non-invasive way. However, the practical implementation of this technique raises two major issues: i) the design of the HIFU probe, which must deliver the planned thermal dose to the targeted tissues, which can represent a substantial volume, whilst minimizing the heating of heterogeneous intervening tissues: skin, ribs, fat, muscle, liver tissue and blood vessels, and ii) the localization of the lesion itself, which must be monitored in real-time since the liver is subject to motion, induced mainly by the respiration, but which can be affected by multiple other sources such as deformations due to the probe pressure, or motions of the patient. Tumor motion is particularly important to monitor in real-time, first in order to target the cancerous tissue and sparing healthy areas, but also to ensure the proper thermal dose is delivered. This is obvious in the context of a continuous insonification, but techniques relying on gating must take also into account tissue cooling effects such as perfusion or diffusion.

To reach this goal and following on previous work [1, 2], it was decided to place an ultrasound (US) imaging probe in the center of an extracorporeal HIFU transducer, such that the imaging plane is aligned with the HIFU acoustic axis. Because the tumor itself may not always be visible on US images, we plan to rely on a pre-operative model derived from so-called 4D imaging (3D + time) to generate a patient-specific pre-operative model of the motion of the liver and tumor. We plan to rely on intensity or feature-based registration techniques [3] between the pre-operative data and the real-time US images to estimate the tumor location during the treatment.

In this paper, we report our data acquisition protocol and early experimental results toward such real-time tumor localization. Namely, we employ 4D-Computed Tomography (4DCT) to reconstruct an average respiratory cycle, exploiting contrast-enhanced CT when possible to image the liver vessels, and a tracked 2D ultrasound imaging probe emulating the forecasted treatment conditions. We then propose a framework based on non-rigid image registration to generate a time-continuous periodic respiratory motion model of the liver based on the 4DCT data, before presenting our preliminary results for fusing the ultrasound image sequence with a 4DCT model.

II. Materials and methods

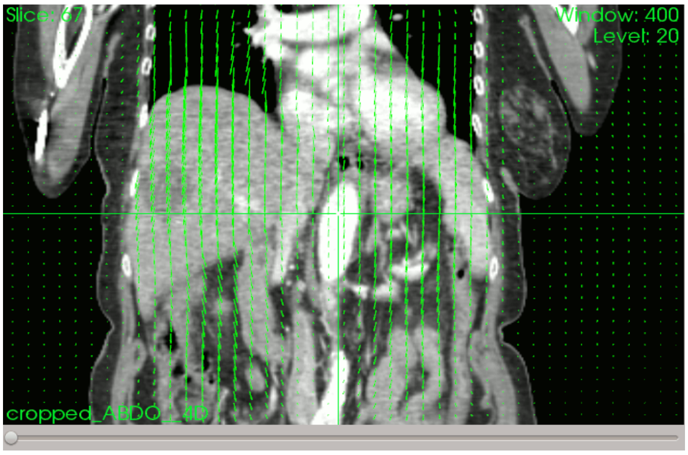
A. Image acquisitions

In order to study the feasibility of US guidance according to a pre-operative planning image, it was decided to perform US acquisitions on 12 patients undergoing radiotherapy treatment and having a 4D-CT image for planning (Philips Brillance). Informed consent for the study was obtained from all patients. Nine patients were imaged with an injection of iodine based contrast agent. In such cases, a first CT scan was performed before the injection and a second one at portal time. 4DCT reconstruct an averaged respiratory cycle from a continuous acquisition covering between 10 to 15 cycles, using a helical acquisition and phase-tagging of respiratory signal acquired with a respiratory belt. Ten 3D volumes were reconstructed representing the anatomy of the patient at evenly distributed phases of the respiration.

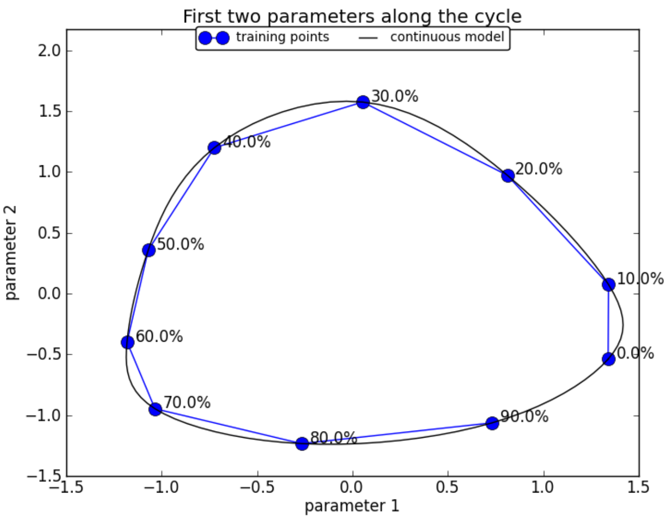
A hand-held US probe (Clarity, Elekta) was available, providing 2D images sequences in the coordinate system of the CT scanner thanks to a calibrated optical tracking system. However, no device was available to record a breathing signal synchronized to the US acquisitions. US images were acquired by a radiologist just before or after the 4DCT, with the request to i) apply the least possible pressure to avoid deformations, while maintaining a good image quality ii) target for characteristic structures such as sus-hepatic or portal veins, or the gallbladder, which are expected to be visible on contrast-enhanced 4DCT images and iii) keep the probe fixed with respect to the patient during a free-breathing acquisition.

The 4DCT and US acquisitions were performed in the same session, asking the patient to remain as still as possible during and between the examinations, so as to minimize any motion or deformation.

B. 4DCT patient specific motion model



(a)



(b)

Fig. 1. (a) Coronal slice through the 4DCT acquisition at maximum exhalation, with overlaid deformation vector field estimated between the maximum exhalation and inhalation phases. (b) Parametric representation of the breathing model, the first 2 components of a PCA model are displayed, with linear and spline interpolation between the reconstructed phases.

Although representing a single, averaged respiratory cycle, the 4D-CT data enables us to build a patient-specific 3D model of the liver, and of its typical deformations induced by breathing. Deformation vector fields were estimated between the reconstructed phases using an image-intensity-based non-rigid registration method capable of preserving the sliding motion [4] between the rib cage and the lungs, but also with the liver, as demonstrated on Fig. 1(a). The sets of coefficients of the deformation fields relating each phase with the reference (maximum exhalation) were analyzed using Principal Component Analysis in order to define a simple parametric space for the deformation model, and a cyclic spline interpolation is computed to define a time-continuous, periodic model of the breathing motion.

C. Ultrasound data analysis

Since no respiratory signal could be recorded simultaneously to the ultrasound image sequence, such a signal was estimated retrospectively from the images themselves. To do so, we relied on the assumption that the probe was fixed with respect to the patient. Under this hypothesis, the only cause for variability within the images of the ultrasound sequence is the motion of organs, which is mostly due to breathing. Following the ideas proposed in [5], a PCA model was estimated from the pixels of the sequences, and assimilated the breathing signal to the coefficient corresponding to the main component of the PCA. In order to accelerate this process, only pixels within a mask defined by bright and time-varying pixel intensities were retained. The discrimination of inhalation versus exhalation was performed visually by an expert, and the respiratory phase was estimated from the breathing signal using the phase of the Hilbert transform (Fig. 2).

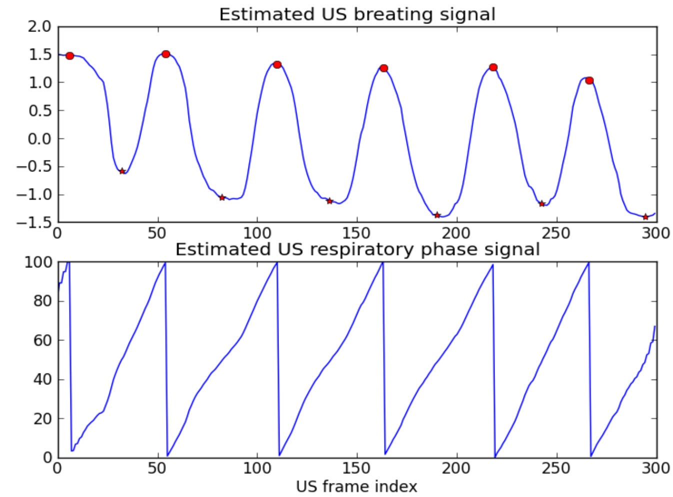


Fig. 2. (upper row) Main component of the PCA model generated from an ultrasound sequence, and identified local maxima. (bottom row) Corresponding breathing phase signal.

D. Preliminary 4DCT-US image fusion

Based on the breathing signal estimated for the ultrasound image sequence, and the time-continuous breathing motion model, it is possible to synchronize the ultrasound and CT model with respect to the respiratory phase. Furthermore, since the US images were acquired in the coordinate system as the CT thanks to the optical tracking of the ultrasound probe, it was possible to fuse the modalities spatially and throughout the respiration.

III. Results

The non-rigid registration and spline interpolation between the reconstructed phases allowed generating a continuous 4D model of the liver motion during an average respiratory cycle, as displayed in Fig. 1. This model provides a periodic motion of the anatomy. Together with the segmentation of the 4DCT data, in particular of the liver, liver vessels and the tumor, this respiratory motion model enables a comprehensive planning of the treatment. The retrospective estimation of a breathing signal from the US image sequence was found to be strongly correlated with the observed motion, with a frequency ranging between 14 to 30 cycles per minute and coherent with the signal recorded with the respiratory belt during the 4DCT acquisition. The effect of selecting pixels with high or varying intensity had negligible impact on the resulting signal, while significantly speeding-up the analysis. The simple fusion strategy developed here, relying exclusively on the tracking device information and the estimated breathing signal allowed a first visualization of the datasets, which showed coherent motions of similar structures. However, it also appears that the matching between structures visible in CT and US is not perfect, and the resulting data cannot be used as a reference for evaluating registration accuracy in experiments involving patient repositioning.

IV. Discussion

The present work is preliminary, and several challenges remain to be tackled. Nevertheless, the proposed framework for generating a 4D model provides an interesting basis for planning and real-time monitoring of a HIFU treatment of liver tumors.

The PCA analysis of the ultrasound image sequence also proved to be interesting for compensating the lack of a respiratory signal synchronized with the images, and was found to be robust to a limited sliding of the probe. Relative motions between the probe and the patients were also easily detected, which can be of interest to detect unexpected events which may affect the treatment delivery such as motion, substantial evolution of the breathing patterns or coughing. Furthermore, the selection of a limited number of pixels of interest during a preliminary training phase can enable a real-time evaluation, though further investigation would be necessary to balance between signal estimation accuracy, ability to detect abnormal events, and computational costs.

While the proposed data fusion was observed to provide coherent motion of identifiable structures across modalities, the matching quality is insufficient to consider such a fusion as a reference for automated registration as would be required in a patient treatment setup, even after performing acquisitions with 12 patients. This suggests that even with a very short delay between the acquisitions and no patient repositioning issues, motions of the patient, deformations of its anatomy and/or variations in the breathing patterns impose to consider fusion strategies involving non-rigid registration. A population-wide model, or a model incorporating multiple breathing cycles based on 4D-MRI acquisitions, may be of interest in this respect. The proposed PCA-based methodology is known to scale up well for such a task. Statistical model based matching methods, which can also provide confidence estimate for structures not directly visible in the images [6], could then be employed for estimating the tumor location. Real-time tracking of vessels in the ultrasound sequence, as proposed in [7] could provide the necessary information for such feature-based registrations.

Compared to the motion freezing methods, tumor-tracking techniques potentially offer additional benefits such as higher delivery efficiency and less treatment time. These factors may be particularly important in HIFU treatment of abdominal tumor sites, where a large treatment area is created [7, 8]. It is well-known that for the treatment of abdominal tumors, respiratory motion induces important consequences such as secondary lesions in adjacent organs. Our long-term objective is to combine HIFU treatment with motion tracking and correction to reach the threshold for necrosis much more quickly and accurately than without this correction [9]. Thus, treatment times and, consequently, the total acoustic intensity delivered could be decreased significantly.

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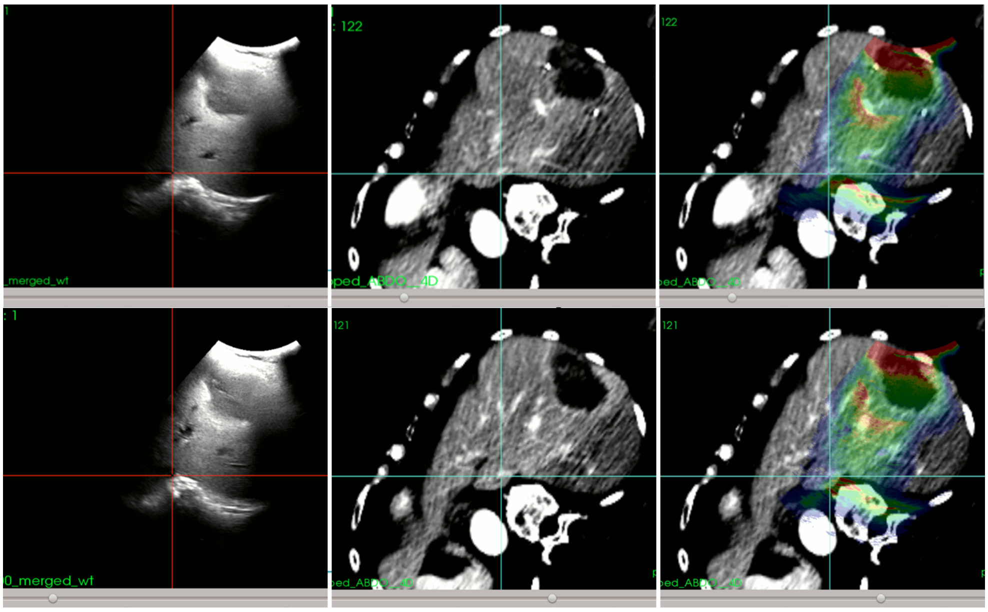

Fig. 3. (left) US image, (middle) slice of the 4DCT data at the corresponding respiratory phase and section plane, (right) fusion with US in color overlay. Top and bottom rows represent two different time steps.