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Simultaneous acquisition of 4D ultrasound and wireless electromagnetic tracking for *in-vivo* accuracy validation

Abstract: Ultrasound is being increasingly investigated for real-time target localization in image-guided interventions. Yet, *in-vivo* validation remains challenging due to the difficulty to obtain a reliable ground truth. For this purpose, real-time volumetric (4D) ultrasound imaging was performed simultaneously with electromagnetic localization of three wireless transponders implanted in the liver of a radiotherapy patient. 4D ultrasound and electromagnetic tracking were acquired at framerates of 12Hz and 8Hz, respectively, during free breathing over 8 min following treatment. The electromagnetic antenna was placed directly above and the ultrasound probe on the right side of the patient to visualize the liver transponders. It was possible to record 25.7 s of overlapping ultrasound and electromagnetic position data of one transponder. Good spatial alignment with 0.6 mm 3D root-mean-square error between both traces was achieved using a rigid landmark transform. However, data acquisition was impaired since the electromagnetic tracking highly influenced the ultrasound equipment and vice versa. High intensity noise streaks appeared in the ultrasound scan lines irrespective of the chosen frequency (1.7-3.3 MHz, 2/4 MHz harmonic). To allow for target visualization and tracking in the ultrasound volumes despite the artefacts, an online filter was designed where corrupted pixels in the newest ultrasound frame were replaced with non-corrupted pixels from preceding frames. Aside from these artefacts, the recorded electromagnetic tracking data was fragmented and only the transponder closest to the antenna could be detected over a limited period of six consecutive breathing cycles. This problem was most likely caused by interference from the metal holder of the ultrasound probe and was solved in a subsequent experiment using a 3D-printed non-metal probe fixation. Real-time wireless electromagnetic tracking was compared with 4D ultrasound imaging *in-vivo* for the first time. For stable tracking, large metal components need to be avoided during data acquisition and ultrasound filtering is required.

Keywords: Image guidance, motion compensation, 4D ultrasound tracking, radiotherapy, liver SBRT

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1 Background

With the emergence of matrix array transducers and higher computational power, fast volumetric (4D) ultrasound imaging has become feasible. The low risks and high spatiotemporal resolution make 4D ultrasound a promising candidate for a range of image-guided procedures as it enables continuous real-time target localization in 3D. Especially abdominal tumours can move and even deform with respiration, potentially reducing therapeutic efficacy [1].

In contrast to many of the current motion compensation strategies in radiation therapy [2], ultrasound tracking does not rely on surrogate markers such as external breathing curves or implanted markers. The direct visualization provides measure of the actual tumour motion without invasive marker implantation or correlation model approximation. While ultrasound tracking accuracy has been investigated in a number of phantom experiments, e.g. [3]–[5], *in-vivo* validation of real-time target localization remains challenging due to the difficulty to obtain a reliable ground truth. So far, this has either been restricted by the inter- and intra-observer variability of manual annotations, which are difficult to obtain in ultrasound volumes [6], or been limited

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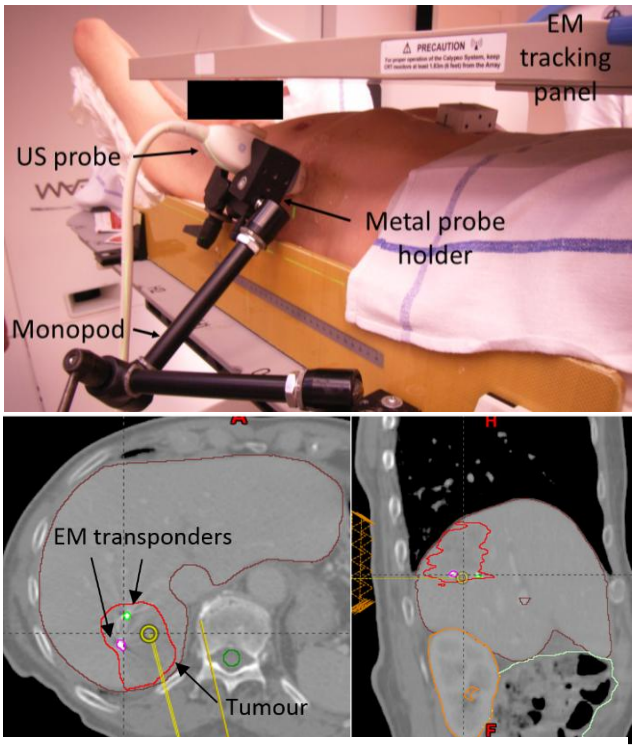

Figure 1: Top – Setup for simultaneous acquisition of 4D ultrasound imaging and electromagnetic tracking. The ultrasound probe was attached to the patient couch to continuously visualize the target region. Bottom – Two (out of three) implanted transponders in the liver surrounding the tumour.

to static scenarios where the setup accuracy of ultrasound is compared to another target localization modality [5, 7].

The goal of this study was the first simultaneous acquisition of two real-time motion signals – 4D ultrasound and electromagnetic (EM) tracking – to assess ultrasound tracking accuracy *in-vivo*. This is a crucial step for clinical implementation of ultrasound guidance and ultimately could also lead to a better understanding of relative motion between (implanted) surrogate markers and "true" target motion.

2 Simultaneous acquisition

The experimental setup for simultaneous acquisition of real-time 4D ultrasound and wireless EM tracking is shown in Figure 1. The ultrasound probe was manually positioned to visualize the target region in the liver and was fixed to the treatment couch using a monopod (Magic Arm, Manfrotto, Italy) and a metal clamp.

Ultrasound imaging was performed with a 4D ultrasound station (Vivid 7 Dimension, GE Healthcare, US) modified for real-time tracking and volume streaming. Volumes were acquired at 12 Hz during free breathing immediately after treatment in a liver patient receiving stereotactic body radiotherapy (SBRT). For future evaluation of different ultrasound tracking approaches, volume data were stored for offline analysis.

Simultaneously, the positions of three EM transponders implanted around the tumour were recorded at 8 Hz per transponder (24 Hz total) using an EM tracking panel (Calypso, Varian Medical Systems Inc., US) placed directly above the patient. The wireless EM system has been investigated in a number of clinical trials for real-time motion compensation, e.g. in prostate and liver SBRT [7, 8].

2.1 Impact of EM tracking on ultrasound

The EM tracking signal highly influenced the ultrasound image acquisition as can be seen in Figure 2 (left). High intensity noise streaks appeared in varying locations in 20-30% of the scan lines per volume, replacing the image information. Varying the ultrasound imaging frequency (1.7-3.3 MHz, 2/4 MHz harmonic) led to no notable differences in artefact appearance. Due to superior soft tissue visualization, the *in-vivo* experiments were performed at 2/4 Mhz.

To allow for target visualization and tracking in the ultrasound volumes despite the artefacts, an online filter reducing random high-intensity streaks was designed. The current volume i and the i-k previous volume(s) were compared on a voxel-by-voxel basis. If the voxel intensity in the current volume was considerably higher than the intensity in one of the previous volumes, the voxel value was replaced.

A higher filtering factor k will lead to better artefact suppression as can be seen in Figure 2. However, the image parts replacing the artefacts were taken from previous time points. The resulting tracking information using the filter will include data from older volumes and could therefore over- / underestimate target motion. To minimize the amount of "temporal distortion" while at the same time achieving an acceptable amount of artefact reduction, a value of $k = 2$ was chosen for the tracking experiments.

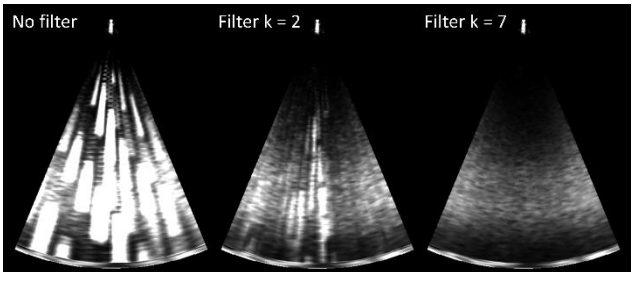

Figure 2: Effect of Calypso signal on ultrasound images (left) and result of an increasing amount of temporal filtering (k = 2, ...,7).

2.2 Impact of metal parts on EM tracking

EM tracking systems are generally sensitive to metal components within the measurement volume. Initially, the aluminium probe holder was placed in close proximity to the antenna, leading to failed tracking attempts. The probe was then repositioned to increase the distance to the antenna (see Figure 1) and an ultrasound sequence of 8 min duration was acquired. However, no continuous EM tracking signal could be acquired during this time due to the interference. The longest partial EM trace contained six consecutive breathing cycles (25.7 s) with overlapping ultrasound and EM position data of the transponder located closest to the antenna (see Figure 4a). The signals of the remaining two transponders were too fragmented for further analysis and could not be used.

In a follow-up experiment, a plastic extension for probe positioning was designed to minimize the amount of metal below the antenna. This simple replacement allowed for undisturbed acquisition of EM tracking and ultrasound imaging, so long as the probe itself was not placed directly below the EM antenna panel.

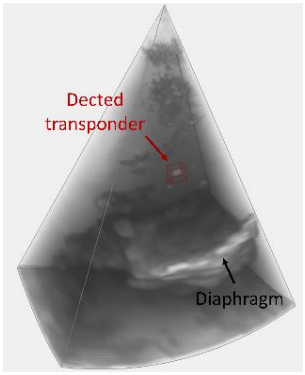

Figure 3: EM transponder in an ultrasound volume, detected using template matching. The diaphragm is clearly visible.

3 Simultaneous tracking

The primary goal of this study was to test the feasibility of simultaneous acquisition of real-time 4D ultrasound and EM tracking for *in-vivo* accuracy validation studies in the future. Since the tracking algorithm itself was not in the focus, a simple template matching approach with a single pattern was chosen for target localization in ultrasound. Template matching was calculated with sub-voxel accuracy. This increased the tracking latency substantially, but real-time tracking capability had a lower priority than highly accurate tracking results in this retrospective feasibility study.

The transponder was manually identified in the first volume and used for template generation. It was tracked over the entire 8 min sequence using the EM artefact filter described in Section 2.1. For comparability, temporal and spatial alignment of the tracking results from ultrasound and EM tracking is required as both run on different systems with different system clocks and in different coordinate systems.

3.1 Temporal synchronization

Retrospective synchronization of EM and ultrasound tracking data was achieved by adapting the sampling rates, iteratively shifting one trace relative to the other and calculating the normalized cross correlation between the coordinate axes with the highest motion amplitude of each respective coordinate system. Figure 4a shows the temporally aligned traces. The sparsity of the EM tracking signal is evident and was likely caused by metal interference (see Section 2.2).

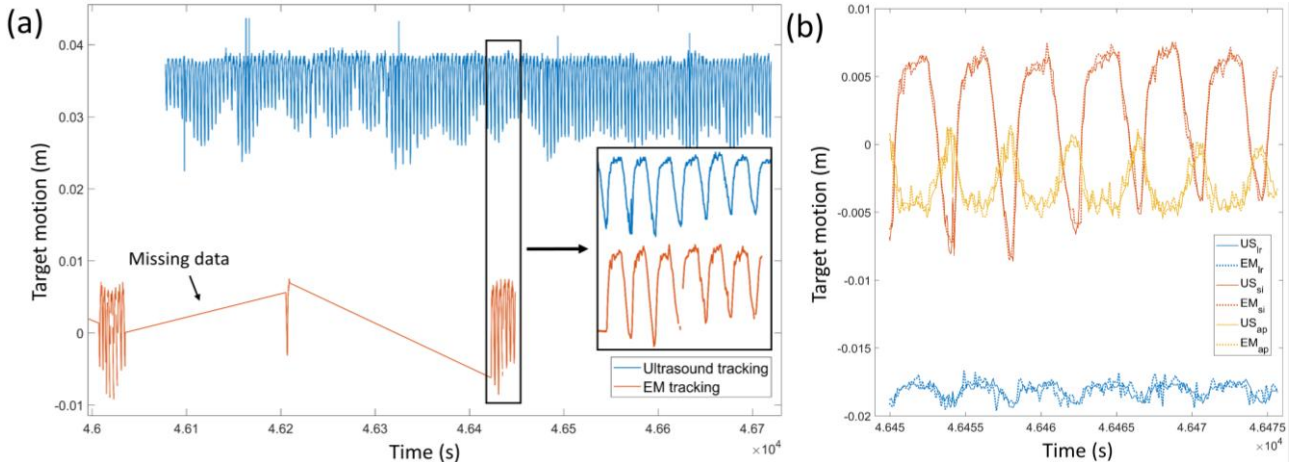

Figure 4: (a) Temporal synchronization of ultrasound and EM tracking data. Interference from metal components disturbed the EM tracking system, leading to missing data points. (b) The spatially aligned transponder trajectories measured with ultrasound and EM tracking.

3.2 Spatial alignment

To align the EM and ultrasound tracking data in the same coordinate system, only the 25.7 s time interval with simultaneous acquisition (see Figure 4a) was considered. By interpreting the data as 3D point clouds, a rigid landmark transformation was performed on the temporally aligned traces, determining the rotation and translation between the EM and ultrasound coordinate systems. Figure 4b shows the temporally and spatially aligned tracking results of EM and ultrasound tracking for the only trackable transponder. The root-mean-square (rms) error between the two aligned traces was 0.55 mm. An additional affine matching step showed little to no scaling errors between the two traces. Wireless EM tracking has a reported accuracy of < 1 mm for prostate and < 2 mm for lung traces [9]. The intra-observer error for manual annotations in ultrasound typically lies between 1-2 mm [6]. The low rms error in this study suggests that both modalities observed the same target with no substantial discrepancies.

4 Conclusion

Ultimately, our goal is to use 4D ultrasound imaging for direct tumour localization in real-time without relying on surrogate signals, invasive marker implantation or ionizing radiation. However, ultrasound tracking accuracy needs to be assessed *in-vivo* for safe clinical implementation. To date, there is no published data comparing 4D ultrasound with another real-time tracking modality *in-vivo*.

The results of this preliminary study have shown the feasibility of a direct comparison between EM and ultrasound tracking in a liver patient during free breathing, warranting further investigation. Due to mutual interference effects between both systems, only one out of three transponders could be detected in ultrasound and EM simultaneously. We found that this can be further improved by using less metal in the setup and by filtering the ultrasound volumes to remove the EM artefacts for stable tracking. While in the current study, the signals were recorded in two separate coordinate systems that were spatially aligned afterwards, in the future they should be aligned in the same treatment coordinate system prior to the measurements by external calibration for better comparability.

While ultrasound holds the potential for tracking the actual tumour translations, rotations and even deformations, direct tumour tracking has not been investigated at this stage. In future experiments, the target area surrounding the tumour will be identified in addition to the implanted markers to compare the tissue motion to the output of the marker-based tracking method for evaluation of current surrogate-based methods. Relative motion between markers and tumour could be investigated in a real-time *in-vivo* setting for the first time.

Author's Statement

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References

[1] Korreman SS. Motion in radiotherapy: photon therapy. Phys Med Biol 2012; 57(23):R161–R191.
[2] Schweikard A, Glosser G, Bodduluri M, Murphy MJ, Adler JR. Robotic motion compensation for respiratory movement during radiosurgery. Comp. aided Surg., 2000; 5(4):263–77.
[3] Ipsen S, Bruder R, O'Brien R, Keall PJ, Schweikard A, Poulsen PR. Online 4D ultrasound guidance for real-time motion compensation by MLC tracking. Med Phys 2016; 43(10):5695–5704.
[4] Prall M, Kaderka R, Saito N, Graeff C, Bert C, Durante M, Parodi K, Schwaab J, Sarti C, Jenne J. Ion beam tracking using ultrasound motion detection. Med Phys 2014; 41(4):41708.
[5] O'Shea TP, Garcia LJ, Rosser KE, Harris EJ, Evans PM, and Bamber JC. 4D ultrasound speckle tracking of intra-fraction prostate motion: a phantom-based comparison with x-ray fiducial tracking using CyberKnife. Phys Med Biol 2014; 59(7):1701–20.
[6] Harris EJ, Miller NR, Bamber JC, Symonds-Tayler JRN, Evans PM. Speckle tracking in a phantom and feature-based tracking in liver in the presence of respiratory motion using 4D ultrasound. Phys Med Biol, 2010; 55(12):3363–3380.
[7] Foster RD, Solberg TD, Li HS, Kerkhoff A, Enke CA, Willoughby TR, Kupelian PA. Comparison of transabdominal ultrasound and electromagnetic transponders for prostate localization. J Appl Clin Med Phys, 2010. 11(1):57-67.
[8] Poulsen PR, Worm ES, Hansen R, Larsen LPS, Grau C, Høyer M. Respiratory gating based on internal electro-magnetic motion monitoring during stereotactic liver radiation therapy: First results. Acta Oncol, 2015; 54(9):1445-52.
[9] Sawant A, Smith RL, Venkat RB, Santanam L, Cho B, Poulsen P, Cattell H, Newell LJ, Parikh P, Keall PJ. Toward Submillimeter Accuracy in the Management of Intrafraction Motion: The Integration of Real-Time Internal Position Monitoring and Multileaf Collimator Target Tracking. Int. J. Radiat. Oncol. Biol. Phys, 2009; 74(2):575–582.