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ORIGINAL ARTICLE

Feasibility of tracked ultrasound registration for pelvic–abdominal tumor navigation: a patient study

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Abstract

Purpose Surgical navigation techniques can guide surgeons in localizing pelvic–abdominal malignancies. For abdominal navigation, accurate patient registration is crucial and is generally performed using an intra-operative cone-beam CT (CBCT). However, this method causes 15-min surgical preparation workflow interruption and radiation exposure, and more importantly, it cannot be repeated during surgery to compensate for large patient movement. As an alternative, the accuracy and feasibility of tracked ultrasound (US) registration are assessed in this patient study.

Methods Patients scheduled for surgical navigation during laparotomy of pelvic–abdominal malignancies were prospectively included. In the operating room, two percutaneous tracked US scans of the pelvic bone were acquired: one in supine and one in Trendelenburg patient position. Postoperatively, the bone surface was semiautomatically segmented from US images and registered to the bone surface on the preoperative CT scan. The US registration accuracy was computed using the CBCT registration as a reference and acquisition times were compared. Additionally, both US measurements were compared to quantify the registration error caused by patient movement into Trendelenburg.

Results In total, 18 patients were included and analyzed. US registration resulted in a mean surface registration error of 1.2 ± 0.2 mm and a mean target registration error of 3.3 ± 1.4 mm. US acquisitions were 4 × faster than the CBCT scans (two-sample *t*-test $P < 0.05$) and could even be performed during standard patient preparation before skin incision. Patient repositioning in Trendelenburg caused a mean target registration error of 7.7 ± 3.3 mm, mainly in cranial direction.

Conclusion US registration based on the pelvic bone is accurate, fast and feasible for surgical navigation. Further optimization of the bone segmentation algorithm will allow for real-time registration in the clinical workflow. In the end, this would allow intra-operative US registration to correct for large patient movement.

Trial registration: This study is registered in ClinicalTrials.gov (NCT05637359).

Keywords Surgical navigation · Ultrasound · Registration · Electromagnetic tracking · Pelvic malignancies · Bone

Introduction

In 2020, the worldwide incidence of cancer was approximately 19.3 million [1]. One of the primary curative treatment methods for cancer is surgery. Long-term survival after surgical treatment depends on complete cancer tissue removal with adequate resection margins and malignant lymph node clearance [2]. However, intra-operative localization of malignant tissue is challenging, especially in patients with adhesions, fibrosis or shrunken tumor tissue due to (chemo)radiotherapy. Therefore, image-guided surgery (IGS) and intra-operative navigation techniques could aid the surgeon in localizing tumors or malignant lymph nodes. In addition, IGS could be used to define surgical resection margins more accurately and reduce complications from damaging critical structures, such as vessels, ureters and nerves, which might improve patient outcomes [3].

IGS is widely applied in surgical procedures with rigid structures, such as orthopedic and neurosurgery, which has already resulted in commercially available systems [3, 4]. As a more specific application, IGS proved to be of additional

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value in abdominal cancer surgery at the Netherlands Cancer Institute (NKI) [5–7]. Pelvic–abdominal malignancies, e.g., rectal recurrences or pelvic lymph nodes, are relatively fixed to bony structures due to surrounding fibrotic tissue, enabling rigid tissue navigation. An in-house developed navigation setup is currently applied as standard of care for complex open surgical procedures in the pelvic–abdominal cavity. This setup implements an electromagnetic tracking system (EMTS) with sensors attached to the patient's skin to match and monitor a preoperative model with the patient's position in the operating room (OR). This registration procedure is essential to enable IGS and highly influences the accuracy and usability of surgical navigation systems [8].

Currently, for patient registration in abdominal tumor navigation at the NKI, a cone-beam CT (CBCT) scan is made in the OR—after patient positioning, prior to surgical draping—and matched with a 3D model derived from preoperative (CT and MRI) images [5]. However, this registration method has several limitations. Firstly, a workflow interruption of approximately 15 min is required during the surgical preparation phase, while staff needs to leave the OR during CBCT scanning. Secondly, a CBCT is a relatively expensive device and exposes patients to radiation. But most importantly, a CBCT scan cannot be reacquired during surgery to correct for patient movement caused by, for example, retractor placement or tilting of the surgical bed into Trendelenburg. These intra-operative movements often lead to pelvic shifts that are not measured by the patient sensors on the skin, since the pelvic bones can move in relation to the skin. As a correction, the CBCT registration can be manually adjusted during surgery, but this is a subjective method and cannot correct for rotational errors [7]. Therefore, a new registration method is essential.

Ultrasound (US) registration could overcome these problems. US acquisitions can easily be performed after (re)positioning the patient, and intra-operative reacquisition is possible to correct for patient movement. Furthermore, US is a relatively cheap and noninvasive method causing minimal workflow interruption, since staff members are not obliged to leave the OR during acquisition. Tracked US has already proven to be a viable method for patient registration in IGS using the bone surface as a registration target, such as the femur, tibia, spine or pelvis [9–15]. On the pelvis, for example, Barrat et al. achieved a target registration error (TRE) of 1.6 mm using a self-calibrating US bone registration algorithm [9] and Hacihaliloglu et al. applied a Gaussian mixture model resulting in a bone surface fit error of 0.62 mm [10]. While these studies show feasibility of US-based registration, most of them were performed on phantoms or cadavers, which is not entirely representative to the intra-operative patient setting. Additionally, the clinical focus of these studies lies on computer-assisted orthopedic surgery, in which the surgical target is the same as the registration target, namely bone. Therefore, the applicability of tracked US registration for accurate navigation toward tumors in the pelvic–abdominal cavity still needs to be investigated.

In this patient study, we collected percutaneously tracked US images of the pelvic bone in the OR to explore the clinical feasibility of an US bone registration method during surgical navigation procedures. We computed the accuracy of the US registration method by comparing it to the ground truth, which is CBCT registration, and also compared the acquisition times of both methods. Moreover, we made an additional US scan while the patient was in Trendelenburg to quantify the influence of an alternate patient position on the registration accuracy.

Materials and methods

Study design

A prospective observational pilot study was conducted at the NKI, Amsterdam. The study protocol was approved by the institutional review board in May 2020 (IRBd20-141) and all patients provided informed consent. Patients scheduled for navigated open surgical resection of pelvic–abdominal malignancies with intra-operative CBCT scan were included between July 2020 and December 2021.

Surgical navigation system

For each patient, a 3D model was made based on preoperative imaging data, such as CT and MRI scans. In the OR, real-time tracking was done with the NDI Aurora V2 EMTS (Northern Digital Inc., Waterloo, Ontario, Canada) combined with the planar or tabletop field generator, a surgical pointer and three patient sensors (Philips Nederland B.V., Eindhoven, the Netherlands). These patient sensors were taped to the patient's skin prior to the surgical procedure: two on the back at the height of L5 and one on the front at the lateral side of the iliac crest. Afterward, patient registration was done using an intra-operative CBCT scanner, either the Philips Allura Xper system (Philips Nederland B.V., Eindhoven, the Netherlands) or the Ziehm Vision RFD 3D (Ziehm Imaging, Orlando, FL, USA). The CBCT scans were rigidly matched with the preoperative CT scan based on the voxel intensity of the pelvic bone. Subsequently, the patient sensor positions on the CBCT scan were registered with the real-time electromagnetically (EM) tracked position of these sensors, enabling surgical navigation using in-house developed software SurgNav (NKI, Amsterdam, the Netherlands). The root-mean-square error (RMSE) of the CBCT registration was defined as the root-mean-square Euclidean distance between the registered and EM tracked patient sensors. This CBCT registration method

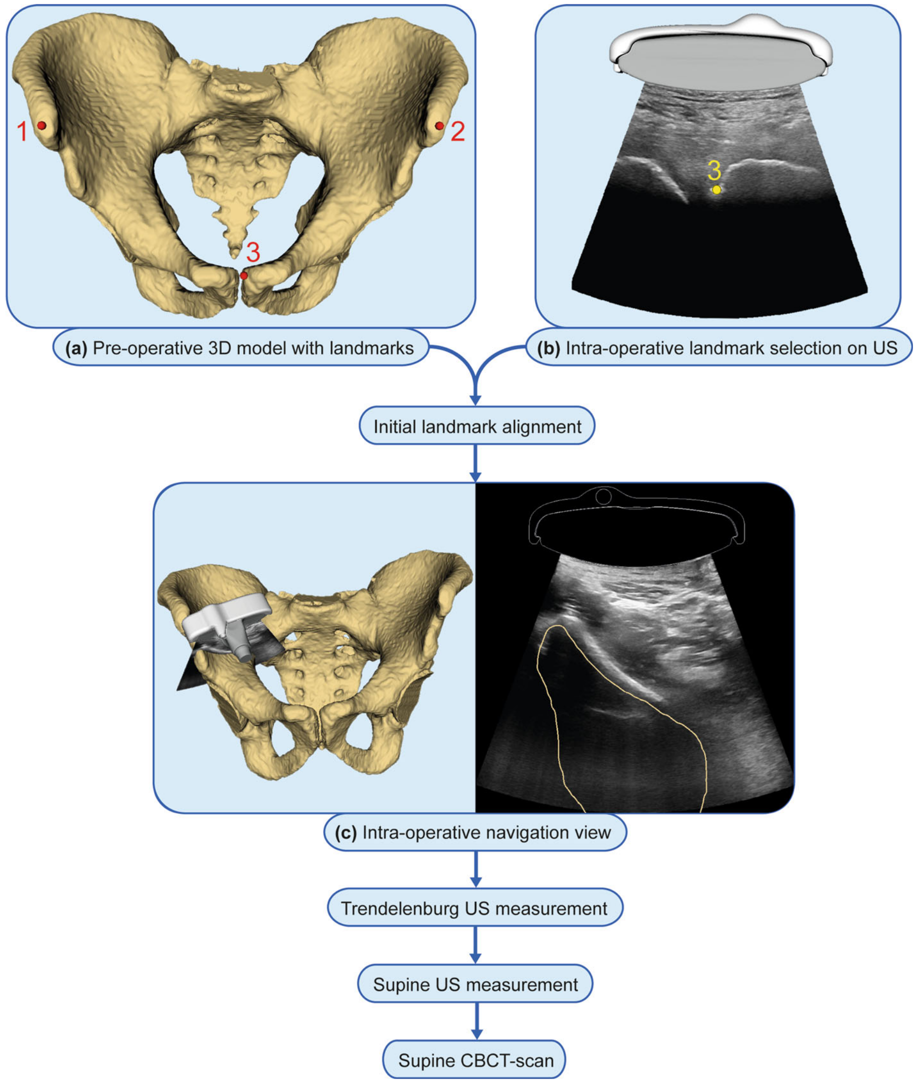

Fig. 1 Overview of the study workflow. The tracked ultrasound (US) (**b**) was initially aligned with the preoperative 3D bone model (**a**) resulting in an intra-operative navigation view (**c**) during the US measurements

was used as a reference to compute the US registration accuracy in this study.

Study measurements

An overview of the study workflow is shown in Fig. 1. Preoperatively, the pelvic bone of each patient was semi-automatically segmented using 3D Slicer software (version 4.10–4.11, www.slicer.org) [16]. Three landmarks were defined on the 3D model: at the left and right anterior superior iliac spine and inside the cleft of the pubic bone (Fig. 1a).

In the OR, a T-shaped US transducer (I14C5T, BK Medical, Denmark) was tracked using a clip-on tool with embedded EM sensor specifically designed for this transducer by Smit et al. [17]. The US plane has been calibrated with the EMTS using the tracked pointer method, which enabled real-time US imaging in EMTS coordinates [18, 19]. All US and EM tracking data were streamed into 3D Slicer using PLUS (www.plustoolkit.github.io) and SlicerIGT (www.slicerigt.org) software [20, 21]. Data were visualized in 3D Slicer during the measurements and recorded for postoperative analysis.

US acquisition was done after patient anesthesia but before sterile draping. First, an initial alignment of the EMTS with the preoperative model was performed. Using tracked US, all three preoperatively defined landmark locations were percutaneously imaged in the patient and a corresponding set of landmarks were manually selected by a second researcher on the streamed US image in the 3D Slicer software (Fig. 1b). The EMTS was then aligned with the 3D model by registering the intra-operative with the preoperative landmarks using the “Fiducial registration wizard” in 3D Slicer, which uses the rigid iterative closest point (ICP) algorithm from VTK. Landmark placement was not critical, since the initial alignment served as an approximate registration to enable real-time visualization of the US plane relative to the

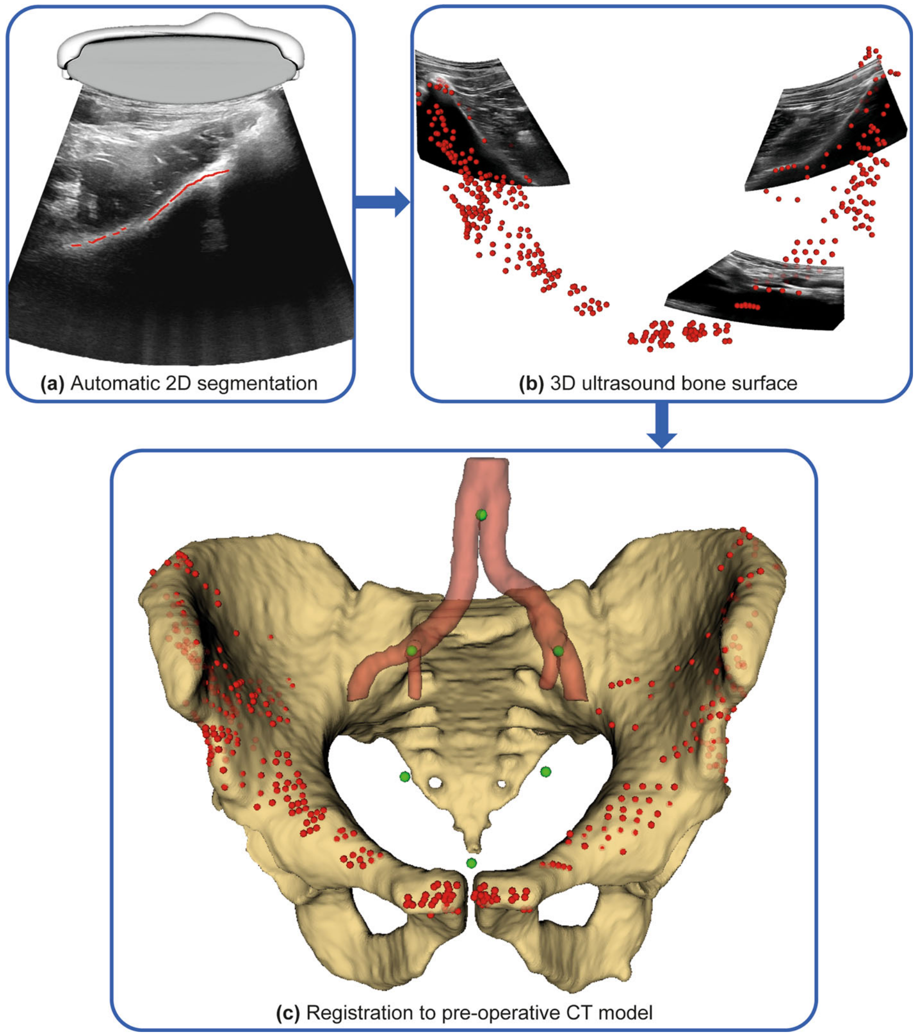

Fig. 2 Overview of the ultrasound bone registration method. 2D ultrasound images were automatically segmented (**a**), converted into a 3D point cloud (**b**) and registered to the preoperative CT bone model (**c**). Six target points (green) were used to compute the target registration error

preoperative bone model (Fig. 1c). This interface helped to correctly position the US transducer on the patient during the subsequent measurements.

After initial alignment, two US measurements were acquired for each patient: firstly in Trendelenburg (tilt of 10 degrees) and secondly in supine patient position (tilt of 0 degrees). In both measurements, three structures of the pelvis were percutaneously visualized, namely the left and right iliac crest and the pubic bone. The iliac crests were scanned at the lateral and medial side in a cranial–caudal sweeping motion, while the pubic bone was scanned ventrally from different angles by tilting the US transducer. During scanning, the US transducer was positioned orthogonally to the bone surface to maximize its intensity on the acquired US images. The goal of these measurements was to visualize most of the pelvic bone surface on US, which was postoperatively used for registration and accuracy assessment. Tracked US data and acquisition times were recorded per US measurement. After the data collection phase, the normal surgical workflow continued including the CBCT scan in supine patient position and surgical navigation.

Analysis

All data were analyzed postoperatively in 3D Slicer and using custom MATLAB scripts (R2019a; The MathWorks Inc., Natick, MA, USA). To correct for possible patient movement due to compression of the US transducer, real-time patient tracking was applied using the EM tracked patient sensor positions. In this way, all (Trendelenburg and supine) US images were corrected to the same time point, enabling fair comparison between registration methods.

For the segmentation of bone surface from US imaging, the Shadow Peak segmentation algorithm developed by Pandey et al. was implemented in 3D Slicer, enabling semiautomatic segmentation [11]. This algorithm computes a real-time segmentation of 2D US images (Fig. 2a). The 2D segmentation was then converted into approximately 5 (range 3–7) 3D points at relevant US frames. The segmentation threshold (range 0–1), Gaussian filter sigma (range 2–6) and clip box were altered during the segmentation process to reduce the number of false positives, and any remaining false positives were manually removed. After selecting approximately 60 frames per US recording, this resulted in a 3D point cloud with a median of 300 (range 151–432) points (Fig. 2b), which was registered to the preoperative CT bone model using VTK's ICP algorithm implemented in the "Fiducials to model registration" module in 3D Slicer (Fig. 2c). The resulting root-mean-square distance between the registered point cloud and CT bone surface was defined as the surface registration error (SRE). This process was done for the supine and Trendelenburg measurement separately, resulting in two different US registrations per patient.

To evaluate the accuracy of the US registration method, the CBCT registration was used as a reference. Therefore, it was important that the patient was not repositioned between the (supine) US measurement and the CBCT scan. Six target points were defined on the preoperative CT scan where tumors or malignant lymph nodes are frequently located (along the vessels, pre-sacral or close to the rectum), namely the aortic bifurcation, both arterial iliac bifurcations, ventral of the coccyx and on both lateral sides of the proximal rectum (green points in Fig. 2c). Then, the accuracy of the US registration method was computed with the TRE, defined as the Euclidean distance between the target points registered with the supine US registration and the target points registered with the reference.

Similarly, the target registration error in Trendelenburg (TRE_{tren}) was computed to evaluate the influence of altering the patient position into Trendelenburg on the navigation accuracy at the defined targets. TRE_{tren} was defined as the Euclidean distance between the target points registered with the Trendelenburg US registration and the target points registered with the supine US registration. Assuming that both US registrations are correct, TRE_{tren} measured the registration error caused by Trendelenburg positioning that cannot be compensated by the patient sensors on the skin.

Statistically, the Shapiro–Wilk test was used to test whether data were normally distributed. Normally distributed data were reported as the mean ± standard deviation. Also, the differences between the mean acquisition time of the US measurements and CBCT scans were compared using a two-sample unequal variance t-test and data correlation was tested using Spearman's rank correlation. Values of $P < 0.05$ were considered to be statistically significant.

Table 1 Patient characteristics ($N = 18$)

Characteristic	N (%)	Mean ± standard deviation
Gender		
Male	10 (56)	
Female	8 (44)	
Age at surgery (years)		55 ± 10
BMI (kg/m^2)		27 ± 3
Tumor type		
Recurrent	11 (61)	
Lymph node metastasis	4 (22)	
Residual	2 (11)	
Primary	1 (6)	
Pretreatment		
Surgery and (chemo)radiotherapy	12 (66)	
Only (chemo)radiotherapy	3 (17)	
Only surgery	2 (11)	
None	1 (6)	
Surgical procedure		
Resection local recurrence rectum	5 (27)	
Para-aortic, iliac or mesenterial lymph node dissection (LND)	4 (22)	
Total pelvic exenteration	4 (22)	
Total mesenteric excision (TME)	2 (11)	
Open abdominoperineal resection (APR)	1 (6)	
Open low anterior resection (LAR)	1 (6)	
Debulking	1 (6)	

Results

Patient characteristics

In total, 23 patients were included in this study. Two patients were excluded from further analysis because one or more EM sensors were outside the EM tracking volume during the measurements. Three patients were excluded since they required repositioning between the US measurements and the CBCT scan on the surgical bed, which caused patient movement, thus preventing further analysis. Patient characteristics of the remaining 18 patients are listed in Table 1. Most patients were scheduled for resection of local tumor recurrence (mostly rectal) or lymph node metastasis, often preceded by prior surgical treatment and/or (chemo)radiotherapy. No correlation between the patient characteristics and other outcome parameters was found.

Ultrasound registration accuracy

The mean RMSE of the CBCT registration, which was used as a reference in this study, was 1.0 ± 0.5 mm. There was some inter-patient variability, since the three highest RMSEs were 2.3, 1.7 and 1.4 mm.

The mean SRE of the US registration was 1.2 ± 0.2 mm in supine and 1.3 ± 0.2 mm in Trendelenburg patient position, and the mean TRE of the (supine) US registration was 3.3 ± 1.4 mm. However, there was a large inter-patient variability, since three patients had a mean TRE higher than 5.0 mm (Fig. 3a). These three patients also had the highest RMSE of the CBCT registration: 2.3 (patient 5), 1.7 (patient 1) and 1.4 (patient 15) mm.

Over time, the mean TRE per patient decreased toward the end of the study (Fig. 3a). Testing the correlation between the patient order and mean TRE resulted in a Spearman's correlation coefficient of − 0.58, which is significantly less than zero ($P = 0.007$).

The mean directional TRE was highest in dorsal direction of the patient: 2.2 ± 1.7 mm (Fig. 3b). In caudal–cranial direction, the error was 0.9 ± 1.2 mm and in right–left direction, it was 0.3 ± 1.2 mm. Notably, the mean ventral–dorsal error was directed dorsally for each patient.

Registration error in Trendelenburg

The mean TRE_{tren} between the supine and Trendelenburg US registration was 7.7 ± 3.3 mm with a large inter-patient variability (Fig. 4). The directional error of this TRE_{tren} was mainly cranially of the patient, 7.0 ± 2.9 mm, as visualized in Fig. 5. In dorsal–ventral and left–right direction, the mean TRE_{tren} was 1.7 ± 2.1 mm and 0.4 ± 1.6 mm, respectively.

Acquisition time

The mean duration of the pelvic bone US acquisitions was 4.0 ± 0.8 min in Trendelenburg and 3.5 ± 0.8 min in supine patient position. In contrast, the mean CBCT scanning time was 16.9 ± 6.9 min, which is significantly higher than the mean US acquisition time in Trendelenburg ($P = 0.001$) and supine patient position ($P = 0.000$). However, the CBCT scanning time was only recorded for 8 of the 18 included patients. Postoperatively, semiautomatic segmentation of bone surface from US took approximately 15 ± 5 min per US registration.

Discussion

In this patient study, we investigated the clinical feasibility and accuracy of US pelvic bone registration as an alternative to CBCT registration for surgical navigation. US registration proved to be fast and feasible with a mean target registration accuracy of 3.3 ± 1.4 mm at surgically relevant locations. Notably, tilting the surgical bed into 10 degrees Trendelenburg position caused a mean shift of 7.7 ± 3.3 mm at these targets compared to the registration in supine position, mainly in cranial direction.

The TRE found in our study is in line with results from other studies using tracked US registration methods based on the pelvic bone. Pandey et al. achieved a mean TRE of 3.22 mm in a phantom using Shadow Peak US bone segmentation and normalized cross-correlation [11], and Salehi et al. reached a median TRE of 2.76 mm in two cadavers [12]. Higher accuracies have been reported at the pelvic bone surface itself, such as a mean bone surface error of 1.7 mm in three cadavers [13] and a surface fitting error of 0.62 mm in 23 patients [10]. These values are consistent with the SRE of 1.2 ± 0.2 mm found in our study. However, these studies were designed to target bone in orthopedic surgical procedures, while our navigation system focuses on malignancies located inside the pelvic cavity. Therefore, the TRE provides a more relevant indication of the clinical navigation accuracy compared to the SRE. Limited literature is available on what accuracy is clinically needed for pelvic–abdominal navigation systems, but based on the size of pelvic–abdominal malignancies, the TRE should be within 5 mm for accurate tumor localization and resection [5]. The found TRE of 3.22 mm after US registration should therefore be sufficient to accurately navigate toward these tumors.

A correlation between the patient inclusion order and mean TRE was found (Fig. 3a), indicating a possible learning curve. During the course of this study, we became more experienced in performing the US acquisition. This might have led to visualization of a larger pelvic bone surface area in patients at the end of the study, resulting in a more accurate registration. On the other hand, the (reference) CBCT registration also affects the computed TRE, since CBCT registration errors could propagate into the TRE. To illustrate this, three patients with the highest RMSE of the CBCT registration also had the highest TRE in our results (patient 1, 5 and 15 in Fig. 3a). However, this is a study limitation only and would not be an issue when clinically applying the US registration method.

While intra-operative US acquisition was 4 × faster than CBCT scanning, i.e., 3.5 ± 0.8 min per registration, postoperative segmentation was still time-consuming. On average, segmentation took 15 ± 5 min, mainly caused by manual case-by-case fine-tuning of parameters to achieve optimal bone surface segmentations. The used Shadow Peak segmentation algorithm works on 2D US images in real time, but because of many false positives (precision of 0.54), this algorithm is not robust enough for fully—unsupervised—automatic segmentation in clinical practice [11]. Alternatively, deep learning-based US bone segmentation methods have shown promising results, for example reaching a mean precision of 0.87 with a fully convolutional neural network [12] and a mean dice coefficient of 93% using a generative adversarial network [22]. Therefore, a real-time deep

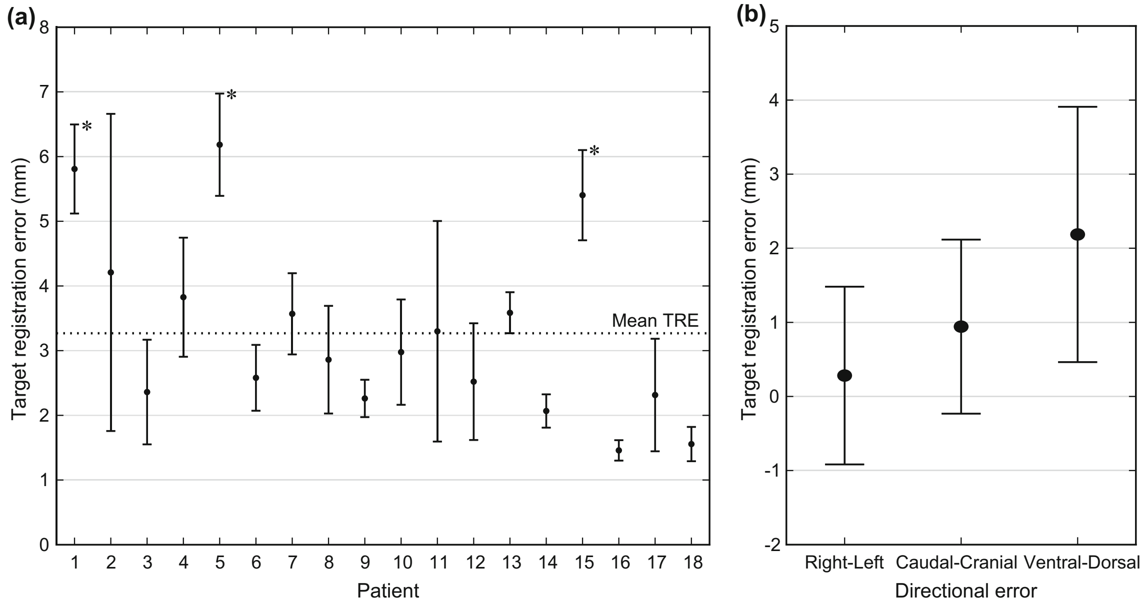

Fig. 3 **a** Mean ± SD target registration error (TRE) of the (supine) ultrasound registration compared to the reference (CBCT). In three patients marked with * the root-mean-square error of the reference was higher than 1.40 mm. **b** Mean ± SD directional TRE

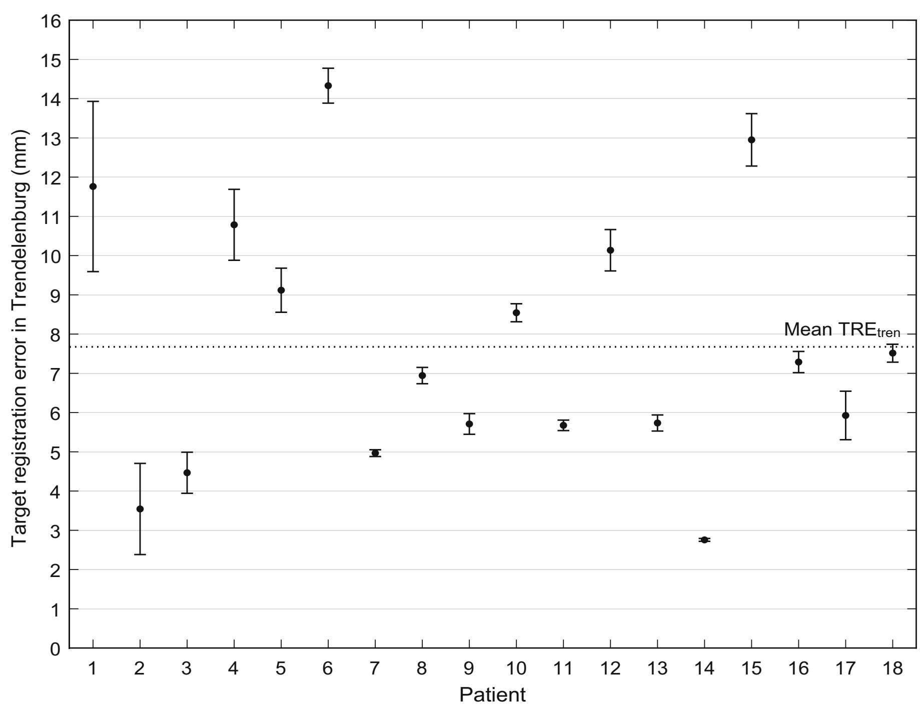

Fig. 4 Mean ± SD target registration error in Trendelenburg (TRE$_{tren}$) between the ultrasound registration in supine and Trendelenburg patient position

learning-based segmentation method should be implemented in our US registration workflow in the future to enable efficient clinical application.

In pelvic–abdominal navigated procedures at the NKI, a manual correction is often required after the CBCT registration, despite constantly tracked patient sensors. Intraoperative traction of the patient's skin probably causes shifts between the patient sensors and internal anatomy. A recent study shows that this correction was needed in 85% of the navigated procedures, mainly in cranial direction because of patient positioning into Trendelenburg with a median of 7 mm [7]. This is in line with our results, since the cranial error was 7.0 ± 2.9 mm when the patient was placed in 10 degrees Trendelenburg position. These results suggest that US registration is an accurate method to compensate for

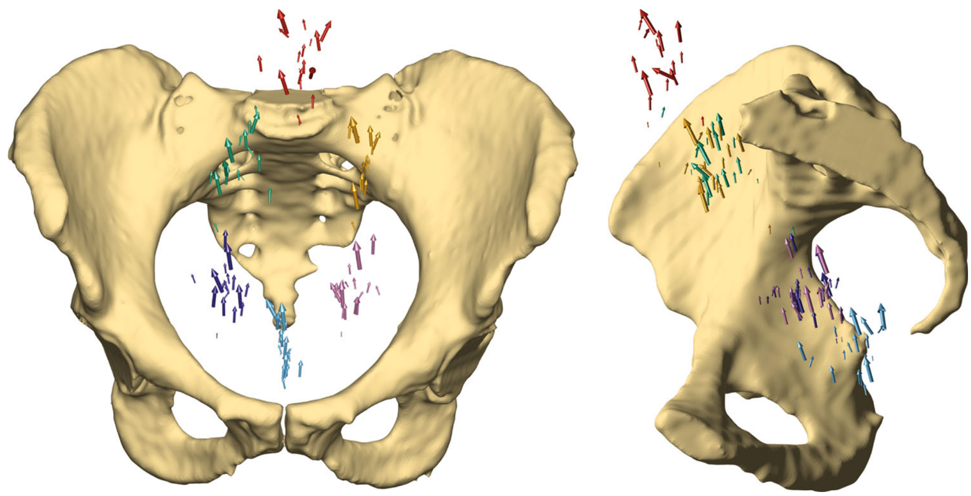

Fig. 5 Directional target registration error in Trendelenburg (TRE_{tren}) between the ultrasound registration in supine and Trendelenburg patient position. The arrow length represents the TRE_{tren} in mm and each color represents one of the six targets: aortic bifurcation (red), both arterial iliac bifurcations (green and orange), on both lateral sides of the proximal rectum (blue and magenta), and ventral of the coccyx (cyan)

errors caused by patient movement. In addition, US acquisition can generally be performed in the final surgical position, eliminating the need for rescanning. If required, rescanning the patient with US will take less than 5 min, which is acceptable in a clinical workflow. For that reason, US registration is preferred over CBCT registration in surgical procedures with alternate patient positions to achieve a higher navigation accuracy.

While the results of this study are promising, US-based registration also has some challenges. Firstly, US acquisition is user dependent and some experience is required to optimally (orthogonally) visualize the bone surface. Intuitive software, such as the intra-operative navigation view (Fig. 1c) helps to minimize the user dependency, but it could be further improved by training new users on phantoms or test subjects first. US acquisition was mainly difficult on patients with high BMI, especially at the medial and lateral iliac crest, but no correlation between the patient's BMI and computed TRE was found in this study. Secondly, compression of the US transducer might induce patient movement. In part, this has been corrected for using the tracked patient sensors, but some movement might not be optimally tracked since these sensors are attached to the skin instead of the bone itself. Still, this error will be negligible if compression is minimal during US scanning. Lastly, small registration errors could have been induced by the speed of sound variation in human tissue. For example, fat tissue has a speed of sound of 1,450 m/s while the US device assumes a speed of sound of 1,540 m/s. Since tissue between the skin and pelvic bone is mostly fat, this speed of sound difference could result in structures appearing deeper in the US image than they physically are, e.g., 3 mm deeper at 5 cm imaging depth [23]. This might explain why the mean directional TRE was directed dorsally for each patient with 2.2 ± 1.7 mm. Application of a speed of sound correction algorithm might improve the accuracy of the bone surface location, such as the algorithm suggested by Fontanarosa et al. [24]. While the mentioned limitations could be further improved, we think that the influence of these limitations on the final clinical navigation accuracy would be minimal.

In this study, US registration was done percutaneously before surgical incision. In the future, additional sterile intra-abdominal US acquisition could further increase the accuracy during surgery, since more parts of the medial pelvic bone surface are accessible, such as the sacrum. We will validate this in a separate clinical study while optimizing the current bone segmentation and registration algorithm. As such, we expect to replace the CBCT with US for pelvic–abdominal tumor navigation at the NKI. In the end, this would result in a fast, accurate and noninvasive registration method, which has the potential of implementation in other clinical institutes as well.

Conclusion

We showed that US registration of the pelvic cavity is feasible with an accuracy of 3.3 ± 1.4 mm to apply for surgical navigation in a clinical patient setting. Additionally, US registration is a fast method which can objectively correct for patient movement by simply acquiring a new US scan. After improvement of the bone segmentation algorithm and software pipeline, US registration could be applied in future pelvic–abdominal tumor navigated surgical procedures.

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Author contributions All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by MAJH, WJH and HCG. The first draft of the manuscript was written by MAJH, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Declarations

Conflict of interest T.J.M. Ruers is involved as Chief Medical Officer of a company in surgical navigation, Bcon-medical. The other authors have no relevant financial or non-financial interests to disclose.

Ethical approval This study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of the Netherlands Cancer Institute (IRBd20-141).

Informed consent Written informed consent was obtained from all individual patients included in the study.

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