Strategy for accurate liver intervention by an optical tracking system

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Abstract: Image-guided navigation for radiofrequency ablation of liver tumors requires the accurate guidance of needle insertion into a tumor target. The main challenge of image-guided navigation for radiofrequency ablation of liver tumors is the occurrence of liver deformations caused by respiratory motion. This study reports a strategy of real-time automatic registration to track custom fiducial markers glued onto the surface of a patient’s abdomen to find the respiratory phase, in which the static preoperative CT is performed. Custom fiducial markers are designed. Real-time automatic registration method consists of the automatic localization of custom fiducial markers in the patient and image spaces. The fiducial registration error is calculated in real time and indicates if the current respiratory phase corresponds to the phase of the static preoperative CT. To demonstrate the feasibility of the proposed strategy, a liver simulator is constructed and two volunteers are involved in the preliminary experiments. An ex-vivo porcine liver model is employed to further verify the strategy for liver intervention. Experimental results demonstrate that real-time automatic registration method is rapid, accurate, and feasible for capturing the respiratory phase from which the static preoperative CT anatomical model is generated by tracking the movement of the skin-adhered custom fiducial markers.

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1. Introduction

Image-guided minimally invasive interventions are increasingly applied in clinical procedures for histopathological diagnostics and tumor therapy. Percutaneous radiofrequency ablation (RFA) has become an accepted alternative to surgical resection in the primary treatment of hepatocellular carcinoma (HCC) and other liver tumors [1, 2]. Several methods based on different modalities, such as ultrasonography (US), magnetic resonance (MR), and computed tomography (CT), are available to guide a puncture needle to reach a tumor target [3, 4]. A real-time method based on ultrasonography imaging modality can continuously track the position of a puncture needle. However, this method is not always available or sufficient for guiding the procedure because the tumor target is not always identified in 2D US images. Alternatively, the method based on CT imaging is often implemented to check the location of a puncture needle after the needle is inserted into the tissue. In this case, the surgeon has to “mentally” register the patient with the preoperative 3D CT image to transfer the planned
trajectory to the patient. To verify whether the needle reaches the tumor target along the planned trajectory, the needle position is repeatedly checked in control CT scan, thereby leading to high radiation exposure for patients and prolonging procedure time.

The current state of the art for liver tumor localization is guiding a puncture needle to target the tumor based on the optical or electromagnetic tracking systems, as an alternative solution to the traditional methods [5–8]. Optical or electromagnetic tracking systems have been successfully applied on rigid structures in clinical applications, such as the skull and otolaryngology [9, 10]. To transform the puncture needle into the image space coordinate frame, the intraoperative physical anatomy has to be registered to a preoperative 3D image data set (i.e., CT and MR). A point-based registration method is often used in the existing tracking systems. Fiducial markers used for point-based registration can be localized by the tracking systems and easily detected in image space. However, the liver is a soft-tissue organ that exhibits significant deformation due to respiratory motion, cardiac motion, and peristalsis; the said motions cause liver motion ranged from 1 cm to 2.5 cm in shallow breathing. To accurately target the tumor within the liver, several approaches are proposed to compensate the liver motion [11, 12]. Some groups have proposed methods to characterize the internal organ motion and deformation over a respiratory cycle by tracking external skin fiducials [13, 14]. However, the accuracy of these methods could be suspect. Another strategy of tracking liver motion is to combine the external and internal fiducials. Krücker et al. [15] used six needles inserted in the liver and six skin fiducials for liver motion compensation by the electromagnetic tracking system. Maier-Hein et al. [5, 6] presented a liver motion compensation method by an optical tracking system based on a combination of inserted fiducial needles and skin markers. This method proved that the accuracy of using an inserted needle combined with skin fiducials was higher than that of using skin fiducials alone.

Therefore, a technique with simple equipment and real-time tracking fiducials is required to accurately compensate the liver motion and to be conveniently applied in RFA. To this end, we develop a strategy of accurate needle placement on the basis of an optical tracking system and skin-adhered fiducial markers to guide the needle insertions. This method allows the navigation of puncture needles to be conducted without breathing control and minimizes the invasiveness of the intervention via the tracking skin-adhered fiducial markers during the procedure to automatically detect the respiratory phase, which match the preoperative 3D image data set. This study aims to perform optimal percutaneous liver interventions, which is relevant to the liver motion compensation during RFA treatment.

The remainder of this paper is structured as several sections. Section 2 presents the strategy of automatic real-time registration to find the respiratory phase, which the static preoperative CT was performed, and describes experiments of implementation and evaluation in detail. Section 3 presents the experimental results. Finally, Section 4 presents the discussion and conclusion.

2. Materials and methods

An image-guided surgical navigation (IGSN) system for percutaneous liver interventions has been developed, which consists of an optical tracking system and an image processing system. The proposed strategy is based on the real-time automatic registration of image and patient fiducials. The optical tracking system is used to track the positions of the fiducial markers in patient space real time and continuously capture the changes of the marker positions. A color bar depicts the amplitude of the fiducial registration error (FRE) in real time to indicate the mapping between the current positions of fiducial markers in patient space with the positions of the fiducial markers in preoperative image data set. A holder mounting three mounted retroreflective spheres is attached onto a puncture needle. The
calibration of the puncture needles is performed so that the optical tracking system can obtain the transformation between the three retroreflective spheres and the tip of the puncture needle, and track the tip of the puncture needle through the transformation in real time. A custom skin-adhered fiducial marker is designed to automatically detect the preoperative image data set accurately, which can eliminate user bias and improve the registration accuracy. A scheme is illustrated in Fig. 1.

![Fig. 1](image.png)

(a) Scheme for navigating the placement of the puncture needle. (a) Prior to the intervention, a set of custom fiducial markers is glued onto the surface of the liver simulator. A CT scan is then acquired, and the custom fiducial markers are automatically localized in the image space. Finally, the respiratory controlling system functions to make the liver simulator generate respiratory movement. During the experiments, custom fiducial markers are continuously localized by an optical tracking system. The real-time calculation of FRE is continuously performed to find the respiratory phase corresponding to the preoperative CT scan in a respiratory cycle. A robotic arm is used to hold the puncture needle and touch the target points. (b) Diagram of the respiratory movement of the liver simulator.

2.1 Tracking fiducial markers in patient space

To date, various skin-adhered fiducial markers, such as retroreflective spheres or disks, are available for registration [17, 18]. However, all these markers fail to be automatically detected in both patient and image spaces, whereas large user error is introduced by manually picking fiducials. These factors reduce the registration accuracy and have a significant effect on the navigation result. To address this problem, a custom skin-adhered fiducial marker is constructed to implement automatic and real-time registration, which is the prerequisite for the proposed liver motion compensation method. The custom fiducial markers are conveniently glued onto the patient’s skin before the CT scan. Manual intervention is not necessary during the procedure because the registration procedure is fully automatic.

The custom fiducial marker is composed of a retroreflective sphere (Northern Digital Inc., Canada) and a pedestal that is glued onto the patient’s skin and mounted on the retroreflective sphere, as shown in Fig. 1. The pedestal is an axisymmetric geometry with a height of 7 mm, a maximum radius of 5.75 mm, and a minimum radius of 1.05 mm. The area of flat pedestal bottom is sufficient large to place double-sided adhesive tape and glue onto the patient’s skin firmly. A CT scan is taken after the custom fiducial markers are glued onto the patient’s skin. During the procedure, the NIR light from the illuminators of two NIR cameras is directly reflected back to the cameras by the retroreflective spheres that have a retroreflective coating on their surface. Each NIR camera has an NIR narrow band-pass filter placed between the lens and the complementary metal oxide semiconductor (CMOS) digital image sensor to prevent visible light from being detected by the CMOS sensor [16]. Therefore, only the NIR
light reflected by the retroreflective spheres can be captured by the two cameras. To track the positions of retroreflective spheres rapidly and continuously, an automatic algorithm is developed to process the images captured by the two cameras and to extract the coordinates of the retroreflective sphere centers in the camera images. The workflow of the algorithm is depicted in Fig. 2.

![Image](image_url)

**Fig. 2.** Workflow of detecting retroreflective spheres in the patient space and stereo matching of two subpixel sets from the left and right images to compute 3D coordinates with an optical tracking system. In the middle sub-figure of the bottom line, the blue circle represents the retroreflective sphere center searched in the compressed image; the red cross represents the retroreflective sphere center searched in the original image.

2.1.1 Processing of images captured by the left and right cameras

As illustrated in Fig. 2, images are first obtained from left and right cameras with a resolution of 1280 × 1024 pixels. Directly processing these images would be extremely time-consuming. Therefore, the width and height of these images are compressed by a factor of 1/8 to reduce the computing time. The resolution of the compressed images is 160 × 128 pixels, which speeds up the image processing. Given the existing obvious image contrast between the retroreflective spheres and the background in the compressed images, the boundary of the retroreflective spheres could be extracted from the compressed images by a simple gradient-magnitude-based method as follows:

\[
\left\| G(i, j) \right\| = \sqrt{G_x^2 + G_y^2},
\]  

(1)

\[
G_x = I(i+1, j) - I(i-1, j),
\]  

(2)

\[
G_y = I(i, j+1) - I(i, j-1).
\]  

(3)

where \(i\) and \(j\) are the pixel indices in the \(x\) and \(y\) directions of the compressed image; \(I\) and \(G\) are the pixel intensity and gradient magnitude, respectively. Some noise exists in the gradient-magnitude image computed from the compressed image. This noise could significantly affect the subsequent steps; thus, a Gaussian filter is introduced on the gradient-magnitude image to...
eliminate the noise and smooth the image. After Gaussian filtering, the gradient-magnitude image is noted as $I_g$.

2.1.2 Tracking of the retroreflective sphere centers

The gray of retroreflective sphere is greater than the background. Therefore, a gray threshold value $t$ is applied to $I_g$ to extract the regions of spheres. The localized pixels at the boundary of each retroreflective sphere are then searched. All the pixels inside the boundary of each retroreflective sphere are labeled, and the retroreflective sphere centers are determined. The number of pixels inside the boundary of a retroreflective sphere is designated as $m$. The coordinate of a pixel inside the boundary of the retroreflective sphere is $q = [q_x, q_y]$. We then calculated the coarse coordinate $\mathbf{q}$ of the retroreflective sphere center as follows:

$$\mathbf{q} = \frac{1}{m} \sum_{i=1}^{m} \mathbf{q}_i. \quad (4)$$

The accurate coordinates of the retroreflective sphere centers on the left and right images are automatically computed in the original images via the following process. A subimage with a size of $80 \times 80$ pixels is cropped from original image, with the center lying on the coordinate of the retroreflective sphere center extracted from the compressed image. A Gaussian filter is introduced to restrain the noise in the sub-images and to improve the reliability of the extracting retroreflective sphere centers. A threshold $\tau$ is applied to separate the region of retroreflective sphere from the subimage. The accurate coordinate of a retroreflective sphere center is computed using Eq. (4).

2.1.3 Stereo matching using the coordinates of the retroreflective sphere centers in the left and right images

The left NIR camera coordinate frame $F^l$ with $(X_l, Y_l, Z_l)$ as its three coordinate axes is established. Likewise, the right NIR camera coordinate frame $F^r$ with $(X_r, Y_r, Z_r)$ is built. The global coordinate frame $F^g$ with $(X_g, Y_g, Z_g)$ is determined by the two NIR cameras. The details of the coordinate frames can be referred to our previous work [16, 19, 20]. If the 3D coordinate of a retroreflective sphere center is expressed by $\mathbf{P}_g$ in $F^g$, $\mathbf{P}_l$ in $F^l$, and $\mathbf{P}_r$ in $F^r$, the relationships among $F^l$, $F^r$, and $F^g$ are expressed as

$$\mathbf{P}_g = R_g \mathbf{P}_l + T_g, \quad (5)$$

$$\mathbf{P}_g = R_g \mathbf{P}_r + T_g. \quad (6)$$

Where $R_g$ and $T_g$ are the transformations from $F^l$ to $F^g$, whereas $R_g$ and $T_g$ are the transformations from $F^r$ to $F^g$. The 3D coordinate of a retroreflective sphere center can be computed using Eqs. (5) and (6). All the markers are found in the patient space.

2.2 Automatically extracting the retroreflective sphere centers in image space

The localization of fiducial markers glued on the patient requires accurate identification of the corresponding retroreflective sphere centers in the preoperative medical image data set. Several localization methods of fiducial markers in image space have been widely reported [17, 21–23]. The automatic localization method we developed is similar to that proposed by Zheng et al. [23] The said method proposed by Zheng et al. [23] is semi-automatic. To realize the ease of use, this said method is improved and made fully automatic in the present paper.
2.2.1 Searching for pedestals of the fiducial markers in CT images

As shown in Fig. 6, the CT value of the pedestals is greater than that of most tissues or the liver simulator. If two suitable band-pass CT threshold values are set, most parts of the liver simulator are removed from the images. $S_c$ is set to be the CT image set. Subsequently, two band-pass threshold values, $T_{low}$ and $T_{high}$, are applied to separate the pedestals and some parts of the liver simulator from $S_c$ shown in Fig. 3(a). A morphology-based method of erosion operation is applied on the 3D image data set after band-pass filtering operation to eliminate 3D clusters of noisy voxels. A dilation operator is then applied to allow the large 3D connected regions (including the pedestals and some parts of the liver simulator) return to their original size before the erosion operation. All the remaining connected regions that were filtered with Gaussian filter are labeled, as shown in Fig. 3(b). The voxels inside each connected region are also labeled. The number of the labeled voxels inside each connected region is computed, such that the volume of each connected region is obtained. The volume of the pedestal model is used to identify the pedestals from all the connected regions by comparing their volumes. In some cases, the volumes of some bones are approximately equal to the volume of the pedestal model, which are incorrectly counted as pedestals. To exclude these cases, a constrained condition is introduced to remove these objects, that is, a comparison of the maximum and minimum distances of two points on the surface of the connected regions with those of the pedestal model. All the pedestals are correctly detected and shown in Fig. 3(c).

![Fig. 3. Workflow of the automatic extraction of retroreflective sphere centers in the image space. (a) Three-dimension reconstruction model of the liver simulator built from the CT image data set. (b) 3D reconstruction after applying two band-pass threshold values $T_{low}$ and $T_{high}$ and implementing erosion and dilation operations. (c) The right pedestals are obtained after comparing their volumes with that of the pedestal model. (d) The point cloud of pedestal model sampled from the surface of the pedestal model. (e) Image after the ICP algorithm is implemented to register the point cloud sampled from the 3D pedestal model surface to one of the pedestals searched in the image space. (f) Retroreflective spheres are labeled with gray balls.](image)

2.2.2 Construction of a point cloud of the pedestal model surface

The pedestals of the fiducial markers are custom made according to their geometries. Therefore, a point cloud of the pedestal model surface can be easily constructed. A 3D pedestal model is first built using the Visualization Toolkit (Kitware, Inc.) according to the geometries of the pedestal model. A point cloud is then sampled from the 3D pedestal model surface, which includes enough points to represent the 3D pedestal model. This point cloud is
imported into the CT image space as the pedestal model to be coregistered with the searched pedestals in the image space.

2.2.3 Registration of the point cloud of the 3D pedestal model surface with searched pedestals in the image space

Matching is first performed by moving the point cloud of the 3D pedestal model surface to the pedestals searched in image space through overlapping their respective centroids and principal axes. A standard iterative closest point (ICP) matching algorithm is used along with a $k$-$d$ tree structure to iteratively match the point cloud of the 3D pedestal model surface with the fixed point clouds that consist of all the voxels inside each pedestal [24]. The accurately matched results are shown in Fig. 3(e). The ICP algorithm is a robust and efficient method for model-based matching. However, the method can be easily trapped in local minima and is highly dependent on the original relationship of position between the pedestal model and the pedestals searched in image space [25]. Moving the centroids and principal axes of the two point clouds together aids in avoiding them to be trapped in local minima. In order to remove objects with density that similar to pedestal, the mean squared error of the two point clouds after ICP is computed and compared with the given error tolerance. The iterations are stopped if the change in error is smaller than 0.05 between two iterations or if a maximum number of 150 iterations has been reached.

2.2.4 Computation of the coordinates of all the retroreflective sphere centers in image space

A set of rotation matrix $R$ and translation matrix $T$ is obtained related to the ICP matching result of two point clouds. The matrices are the transformations that transfer the original position of pedestal model to the position of the pedestals being searched in the image space. The coordinates of the retroreflective sphere centers relative to the original position of the pedestal model in the image space are known. Therefore, rigid transformation is adopted to obtain the new coordinates of the retroreflective sphere centers through the set of $R$ and $T$. These new coordinates are counted as the centers of the retroreflective spheres and are mounted on the pedestals searched in the image space. The results are shown in Fig. 3(f), which are labeled with gray balls.

2.3 Automatic coregistration of two point sets of the retroreflective sphere centers in image and patient spaces

After the retroreflective sphere centers in the 3D image data set are detected, two point sets of the retroreflective sphere centers in the image and patient spaces need to be coregistered. The automatic assignment of the two point sets may cause wrong point-to-point assignments that would lead to significant registration error. Consequently, a simple point-distance-based method is used to find the proper assignment of the two point sets before coregistration:

\[
\begin{align*}
Q_p &= \{q_{p1}, q_{p2}, \ldots, q_{pn}\} \quad \text{is the point set of the retroreflective sphere centers tracked in patient space.} \\
Q_i &= \{q_{i1}, q_{i2}, \ldots, q_{in}\} \quad \text{is the point set of the retroreflective sphere centers detected in image space.} \\
D_p &= \begin{bmatrix}
d_{p1} & d_{p2} & \cdots & d_{p(n-1)}
\end{bmatrix} \\
D_i &= \begin{bmatrix}
d_{i1} & d_{i2} & \cdots & d_{i(n-1)}
\end{bmatrix}
\end{align*}
\]

These are $(n-1) \times (n-1)$ matrices. The $j$th column vectors $d_{pj}$ and $d_{ij}$ represent the distances between the $j$th point and other points in the patient and image spaces, respectively. Each element of $D_p$ and $D_i$ is computed as $d_{pk} = q_{pk} - q_{pk}$ and $d_{ik} = q_{ik} - q_{ik}$ ($l \neq k ; l, k = 1, 2, \ldots, n$), respectively. The elements of every column vector are sorted in descending order to acquire two new matrices: $\tilde{D}_p = \begin{bmatrix}
\tilde{d}_{p1} & \tilde{d}_{p2} & \cdots & \tilde{d}_{p(n-1)}
\end{bmatrix}$ and $\tilde{D}_i = \begin{bmatrix}
\tilde{d}_{i1} & \tilde{d}_{i2} & \cdots & \tilde{d}_{i(n-1)}
\end{bmatrix}$. To find the proper assignment of the two point sets, the distance error matrix $E = [e_1, e_2, \ldots, e_{n-1}]$ between $\tilde{D}_p$ and $\tilde{D}_i$ is computed as follows:
\[ e_i = [e_{i1}, e_{i2}, \ldots, e_{i(n-1)}] (i = 1, 2, \ldots, n-1), \]

(7)

\[ e_g = \| \bar{d}_{g} - \bar{d}_{gL} \| = \sqrt{\sum_{b=1}^{n-1} (\bar{d}_{g(b)} - \bar{d}_{gL(b)})^2}. \]

(8)

The row and column indices of the minimum element of each column vector \( e_i \) represent the point index number in the point set of patient space and the corresponding point index number in the point set of image space, respectively. For example, \( e_{i4} \) is the minimum element of vector \( e_i \), which means that the first point in the point set of patient space corresponds to the fourth point in the point set of image space. When two fiducial points have the same or very similar distances with respect to other fiducial points, their distances to the respective fiducial configuration centroid in both coordinate frames are compared to eliminate this case. However, symmetric fiducial configurations are avoided, which can confound this method.

A least-squares-based algorithm is used to estimate the rigid transformation matrix between the patient coordinate frame and the image coordinate frame according to the proper assignment of two point sets computed by the method implemented above. All fiducials glued on the patient and mounted on surgical instrument are tracked in real time and mapped to the image space through this transformation matrix. The 3D coordinates of the three retroreflective spheres mounted on the surgical instrument are separated from all the tracking coordinates by using the code of distances method published in our previous work [16]. Consequently, a one-time procedure of registration is completed.

### 2.4 Implementation and evaluation of the experiment

#### 2.4.1 Experimental setup

A liver simulator is constructed with an airbag inserted inside it. The inflation of the airbag is controlled by an air pump system to simulate the respiratory movement, as shown in Fig. 1. A dual-source CT system (SOMATOM Definition; Siemens Medical Solutions, Forchheim, Germany) is used to acquire image data sets for the liver simulator. A self-developed optical tracking system is constructed, which includes two CMOS cameras (MV-130UM; Microvision, China), two NIR light illuminators, and a puncture needle attached to a holder with three mounted retroreflective spheres. An NIR narrow band-pass filter (BD-940; Compass Optical Tech., China) is placed between the lens and CMOS digital image sensor to prevent visible light from being detected by the CMOS sensor [16]. Each of the NIR light illuminator is made of an annulus aluminum substrate. A total of six high-power light-emitting diodes, each with a wavelength of 940 nm, are welded to the surface of this substrate. The optical tracking system can track up to 50 passive retroreflective spheres with an accuracy of 0.1 mm for the root mean square (RMS) in real time. Our self-developed image processing software functions with the optical tracking system that runs on an Intel(R) Core(TM) i5-3470 CPU (3.20 GHz) with 4 GB RAM running under Windows 7.

#### 2.4.2 Fiducial marker distribution and experiments of registration accuracy

The distribution of fiducials for point-based registration mainly depends on the target location and patient position in the clinic. Recent advances in the study of point-based registration have proven that the target registration error (TRE), which is the most valuable estimate of the accuracy in IGSN, is influenced by the FLE as well as the number and geometrical distribution of fiducials [26–31]. Fitzpatrick et al. [27, 31] first proposed a method to calculate the expected TRE in point-matching registration. West et al. [26] improved the method proposed by Fitzpatrick et al. and predicted the distribution of the theoretical TRE for three hypothetical fiducial marker configurations. Omara et al. [28] evaluate the TRE distribution in three configurations of different combinations of nine anatomical landmarks in eight real clinical surgeries.
In this study, nine custom fiducial markers (denoted as $FM_1$ - $FM_9$) are glued onto the surface of the liver simulator [see Fig. 4(a)]. All the nine fiducial markers that were used as fiducial points can be clearly captured by the cameras. These nine markers are placed approximately symmetrically along the cranio-caudal axis of the liver simulator, but the configurations of the different combinations of nine fiducial markers do not confound the point–distance-based pairing method because they are not truly symmetric because of manual placement bias. A total of 21 small-circle surface patches are distributed around the surface of the liver simulator. The center of each patch draws a black solid point, which functions as the target point for needle pointing. The diameter of the small surface patch is approximately 5 mm, as shown in Fig. 4(a). The patches are distributed in seven regions to test the target accuracy in different positions. Three patches are placed in each region. The corresponding position of each patch center is manually localized eight times in the image space. The average is defined as the “true” position in the image coordinate frame. The liver simulator is scanned after the custom fiducial markers are glued onto its surface [see Fig. 4(b)]. Four configurations of the fiducial markers are designed to perform the registration:

a) Configuration 1: All nine custom fiducial markers are used.

b) Configuration 2: Six custom fiducial markers including all nine markers are used, except $FM_1$, $FM_2$, and $FM_3$.

c) Configuration 3: Six custom fiducial markers including all nine markers are used, except $FM_4$, $FM_5$, and $FM_6$.

d) Configuration 4: Six custom fiducial markers including all nine markers are used, except $FM_7$, $FM_8$, and $FM_9$.

The procedures of targeting typically place the tip of the needle on the black solid point in the center of the small patch in patient space. All the configurations are performed at about 1200 mm distance to the tracking system.

Fig. 4. (a) Nine custom fiducial markers are glued onto the surface of the liver simulator in the patient space. (b) 3D reconstruction model of the liver simulator in the image space.
2.4.3 Volunteer study

To study the feasibility of the proposed method, two volunteers participate in the experiments. Nine custom fiducial markers are glued onto the surface of each volunteer’s abdomen. Before the experiments, two volunteers are asked to practice quiet free breathing. When the breath of the volunteers is stable, the experiment commences, and the optical tracking system starts working. To perform this automatic registration method while avoiding unnecessary CT scans of the volunteers, the center positions of the nine custom fiducial markers are recorded once. These points are defined as the positions of the fiducial markers localized in the preoperative CT image data when the volunteers are breathing during the expiration phase. The displacement of each fiducial marker and the FRE value are continuously recorded for more than 1 min. The experiments are performed thrice for each volunteer (see Fig. 5).

2.4.4 Ex-vivo porcine liver model for accuracy assessment

An ex-vivo porcine liver model is employed to further verify the strategy for liver intervention in the presence of the liver motion. The airbag controlled by the air pump system is used to simulate liver motion in vivo. The livers are placed inside a plastic container supported with foam. The airbag is placed between the livers and the foam so that the inflation of the airbag exert on the livers and make the livers move. Several custom fiducial markers are glued on the surface of the livers. The lateral, anterior, and posterior walls of the liver are supported, only allowing the superior wall to move freely. Such efforts are made in order to maximize the amount of superior/inferior similar to that found in vivo. Twelve small steel balls of 19 gauge are percutaneously implanted through a guide sheath into three sets of livers to serve as targets. The intervention of each target is repeated three times in different puncture points. After intervention, CT scan is performed and the image data set is loaded into the image processing system in order to compute 3D distances between the needle tip and target points. TRE assessment is performed by these 3D distances, as shown in Fig. 6.
Fig. 6. Intervention result assessment on ex-vivo porcine liver model. The localization of the needle tip and target are defined in image space using the image processing system. The 3D distances between the needle tip and target points are computed for each run. The unit of blue grid marks is centimeter.

3. Results

The performance of the described automatic registration method was successful, and the experimental results are presented as follows. Given that no interaction is required during registration, the registration step is always ready to start within a few seconds. The total time required for a one-time registration is $0.08 \pm 0.01$ s for all the experiments. Therefore, at least 10 instances of registration are completed in 1 s, which is sufficiently rapid to track the fiducial markers for real-time automatic registration and to capture the continuous change of the liver simulator in real time.

The curves in Fig. 7 show an example of the maximum, minimum, and averaged displacements of all nine custom fiducial markers that changed over time in Configuration 1 for 1 min in the liver simulator and volunteers. The displacements of the custom fiducial markers recorded in the liver simulator and volunteers have a similar changing trend within this period. In the inspiratory phase, the maximum displacement in the liver simulator is stable, with a standard deviation of 0.56 mm in 1 min, whereas that in the volunteers is less stable, with a standard deviation of 1.14 mm. However, the minimum and averaged displacement of the liver simulator and volunteers are both stable in the inspiratory phase. In the expiration phase, the displacements of all the custom fiducial markers in the liver simulator and volunteers are approximately the same under 0.5 mm. The FRE curves of the custom fiducial markers in the liver simulator and volunteers changed over time in Configuration 1, as shown in Fig. 8. The FREs of the custom fiducial markers in the liver simulator and volunteers present a similar changing trend within this period, which is similar to the displacements of the custom fiducial markers. The FRE in the liver simulator presents the maximum value of $1.37 \pm 0.18$ mm in the inspiratory phase, which drops to the minimum value of $0.08 \pm 0.02$ mm in the expiratory phase. Meanwhile, the FRE in volunteers has a lower stability than that in the liver simulator, such that the FRE curve fluctuates within a small range in the inspiratory phase, and the FRE value is less than 0.6 mm in the expiratory phase.
Fig. 7. Curves of absolute displacement errors of all nine custom fiducial markers change over time in Configuration 1 for 1 min. The green curve represents the maximum displacement of the nine markers; the red curve represents the minimum displacement of the nine markers; and the blue curve represents the averaged displacement of the nine markers. The black dash line called inspiratory phase line indicates that the current phase is inspiratory phase when the value of displacement is lower than this line. The points of three displacements in the middle of dotted box indicate the expiratory phase. The different displacements are recorded for (a) the liver simulator and (b) the volunteers.

Fig. 8. FRE change over time in Configuration 1 for 1 min. The black dash line called inspiratory phase line indicates that the current phase is inspiratory phase when the value of FRE is lower than this line. The phases of curve pointed by purple narrows indicate the expiratory phases. The curve of FRE is recorded for (a) the liver simulator and (b) the volunteers.

The TREs of the automatic registration method in the liver simulator is measured in seven regions, as shown in Fig. 9. The TREs of the automatic registration in the seven regions range from 0.02 mm to 1.49 mm. The maximum mean TRE is observed in Region 4, with a mean TRE of 0.74 ± 0.17 mm. The minimum mean TRE is observed in Region 2, with a mean TRE of 0.51 ± 0.24 mm. The comparison of the TREs measured in four configurations in the expiratory phase is shown in Fig. 10. The TREs measured in four configurations follow the same trend. The minimum averaged TRE is 0.64 ± 0.25 mm in Configuration 1, and the maximum averaged TRE is 0.66 ± 0.27 mm in Configuration 3.
Fig. 9. Measured TRE values in different regions for the automatic registrations in the expiratory phase in liver simulator. For all boxplots, the central line mark represents the median TRE; the box represents the 25th and 75th percentiles; the small square within the boxplot represents the averaged TRE; and the whiskers indicate the range in TRE.

Fig. 10. Comparison of measured TRE values in different configurations for the automatic registration in the expiratory phase in liver simulator. For all boxplots, the central mark represents the median TRE; the box represents the 25th and 75th percentiles; the small square within the boxplot represents the averaged TRE; and the whiskers indicate the range in TRE.

Table 1 shows the TREs between the needle tip and target points for each set. All of 12 interventions on ex-vivo porcine liver present accuracy suitable for intervention on a tumor with diameter more than 1 cm. The mean value of TREs associated with 12 interventions is 3.59 mm with a square deviation (SD) of 1.09 mm.

| Material | Min  | Max  | Mean ± SD | RMS |
|----------|------|------|-----------|-----|
| Set 1    | 1.65 | 3.30 | 2.75 ± 0.65 | 2.83 |
| Set 2    | 2.36 | 5.17 | 3.80 ± 1.34 | 4.03 |
| Set 3    | 2.41 | 4.51 | 3.72 ± 0.80 | 3.81 |
| Total    | 1.65 | 5.17 | 3.42 ± 1.09 | 3.59 |
4. Discussion and conclusion

The proposed strategy of real-time automatic patient-to-image registration may be beneficial for accurate needle insertions in radiofrequency ablation of liver tumor. To realize the real-time automatic registration, custom fiducial markers are accurately localized in image space by the automatic localization method and tracked in the patient space in real time by the optical tracking system we constructed. The proposed strategy is found to be sufficient for respiratory motion detection. This study aims to develop a reliable method for instructing interventional radiologists to perform needle insertions and to reduce the operation time.

The automatic registration method presented in this study considerably improves the registration time to approximately 0.1 s when custom fiducial markers are used. Consequently, this method can track the movement of external fiducial markers in real time. Real-time 3D imaging is desirable in various image-guided interventions for real-time tracking of target tumors. Currently available 3D imaging modalities are too slow for reconstructing the 3D anatomical structure; thus, only the surrogate method could be used rather than the continuous imaging method during a procedure. In this paper, a novel concept is presented (1) to track the movement of external fiducials glued onto abdomen skin in real time and (2) to use the fiducial tracking data to register the fiducials obtained in a preoperative CT scan to find the respiratory phase in which the static preoperative CT scan was performed by calculating the \( \text{FRE} \) in real time. When this real-time tracking process is repeated at least 10 times per second by the optical tracking system, the anatomy is imaged in real time in patient space, and the right respiratory phase corresponding to the preoperative CT anatomical model can be found. Unlike skin markers that reference the skin surface, marker needles used during liver intervention as fiducials for tracking may reference the target organ itself [5, 6]. However, marker needles are invasive and may cause major complications such as pleural and gastrointestinal perforation. In the work of Meier-Hein et al. [5, 6], the placement of the marker needles required approximately 15 min for skilled operators; this step has been described as the most time-consuming within the workflow.

Paired-point registration calculates the rigid transformation that best aligns corresponding fiducial points in the respective image and patient space. Usually, skin-adhered custom markers are glued prior to imaging. For high accuracy, more than four registration markers should be broadly distributed around the region of interest. The placement of the custom fiducial markers was facile and quick. In this study, nine broadly distributed registration markers are glued on the liver simulator and the volunteers for automatic registration. In all phantom results, the self-imposed \( \text{FRE} \) of \(<0.6\) mm could be achieved. Results of phantom experiments and volunteer study showed that the motion of the liver simulator is more regular than that of the volunteers because the movement of the liver simulator is controlled by a pump, whereas that of the volunteers is captured during quiet free breathing. Liver tumor ablation is usually performed under general anesthesia; thus, patient breathing is more regular than quiet free breathing. The results of \textit{ex-vivo} porcine liver model provided an acceptable accuracy for intervention on a tumor with diameter more than 1 cm. Therefore, the proposed strategy will perform better in clinical applications compared with other strategies. The critical problem of the IGSN system for percutaneous liver tumor RFA is the synchronization of a respiratory phase for which the static preoperative CT anatomical model is generated. When a shape-conserving mattress is used, which can help to reduce the deformation caused by respiration, the observation of marker movement and the real-time \( \text{FRE} \) calculation help in the selection of the best respiratory phase for needle insertion.

In summary, the proposed strategy of real-time automatic registration shows the feasibility of capturing the respiratory phase from which the static preoperative CT anatomical model was generated by tracking the movement of skin-adhered custom fiducial markers. This technique is potentially applicable to liver interventions that require minimum invasiveness. Our future work will mainly focus on applying this strategy in clinical study for soft-tissue interventions. If a surgical robotic arm used in clinic is available, the strategy combined with the clinic robotic system can also accurately navigate the other soft-tissue surgery such as
kidney and lung interventions. Currently, the custom fiducial marker is only used for CT. It can be modified for use in other imaging devices in the future, such as the cone-beam CT and MRI.

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