Automatic Doppler Volume Fusion of 3D Ultrasound using Point-based Registration of Shared Bifurcation Points

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Abstract We previously proposed the use of acoustic microbubble delivery in blood vessels as a therapeutic application of microbubbles to improve the efficiency of high-intensity focused ultrasound and the efficacy of acoustic targeted drug therapy. Among the technical requirements for this technique is detailed visualization of the blood vessel network for navigation around a target such as a tumor. For this purpose, three-dimensional (3D) Doppler volumes, which can be acquired by matrix array imaging probes, are quite convenient because they allow the blood vessel structure to be extracted without segmentation. However, the achievable volume is limited and incomplete because the Doppler signal depends on flow direction. To compensate for these issues, an ultrasound volume fusion technique is required. In this study, we propose a blood vessel volume fusion method by automatic registration among shared bifurcations. In addition, we propose a novel 3D ultrasound calibration method, which is needed to determine the initial transformation. Several optical markers are used as fiducial markers in this calibration. To examine the feasibility of the proposed methods, calibration accuracy and volume fusion accuracy assessments were conducted using an artificial blood vessel and in human subjects. Regarding calibration accuracy, the target registration error of the proposed method was 2.2 mm. Regarding volume fusion accuracy in the artificial blood vessel, the mean distance between the shared bifurcations was reduced from 2.4 mm (initial transformation by tracking data) to 0.5 mm (registration of shared bifurcations). Regarding the volume fusion of blood vessels in human subjects, the distance was also reduced from 10.4 mm to 0.3 mm. The results demonstrate that the proposed methods are accurate for constructing large and complete blood vessel networks for navigation of microbubble delivery. Moreover, the methods may also be useful for extracting intraoperative blood vessel network to support minimally invasive surgery or therapy.

Keywords: ultrasound image fusion, ultrasound calibration, 3D blood vessel network reconstruction.

including interpolation and hole-filling processing. Ultrasound calibration estimates the fixed transformation matrix between the B-scan plane position and an attached tracker (infrared-reflective markers or a tracking coil) [13–15]. Although many calibration methods have been proposed for 2D ultrasound, techniques for 3D ultrasound are limited [16, 17]. In addition, previously reported techniques require a well-designed calibration phantom. Ultrasound calibration carries errors of 1–2 mm due to tracking and imaging errors. Therefore, the quality of the reconstructed volume is insufficient to construct blood vessel structure for our navigational purposes.

In this paper, we propose a simple and convenient calibration method for 3D ultrasound and a novel method of automatic Doppler volume fusion to correct fusion accuracy for the construction of an extensive and complete blood vessel network structure. The proposed methods were validated both in vitro and in vivo. The study was approved by the ethics committee of Tokyo University of Agriculture and Technology and informed consent was obtained from subjects.

2. Materials and Methods

We conducted our experiments using an 3D echography (iU22, Philips) and a matrix phased array imaging probe (x6-1, 1.5–5.0 MHz, Philips). To measure the initial transformation, an optical tracking device (Polaris Vicra, 0.3 mm nominal error, Northern Digital Inc.) was used. A rigid object containing four infrared reflective markers was attached to the probe. Before the experiments, ultrasound calibration was conducted. In volume acquisition, the volume position was measured with the tracking device.

2.1 3D Ultrasound Calibration

In our previous work, we used a 3D probe calibration method based on 2D probe calibration, which estimates the B-scan plane position at a 0 degree sweeping angle. Although this method accurately estimates the calibration matrix, the calibration procedure involves careful probe scanning on a calibration phantom and requires approximately 30 minutes to collect sufficient points. As an alternative, we developed a novel 3D ultrasound calibration method using optical markers. The calibration setup is illustrated in Fig. 1. Let Ph, Pr, and Vol be the coordinate systems of the phantom (ΣPhantom), probe (ΣProbe), and volume (ΣVolume), respectively, and Tb is the coordinate transformation from B to A. First, more than four optical markers are placed in a water container, and each marker position PPh ∏m in the phantom coordinate system is measured by an optical tracking device. Second, the container is filled with water at 40°C. The ultrasound volume of the markers is acquired, and the transformation among the probe and the phantom PPTb ∏m is also measured by the tracking device. Each marker is segmented, and its position Vol ∏m in the volume coordinate system is estimated by spherical fitting. Finally, the marker positions in both the probe and volume coordinate systems are used to estimate the transformation matrix between the coordinates PPTv ∏m by point-based registration between the fiducial marker positions in the probe and the volume coordinates (PPh ∏m) and (Vol ∏m).

2.2 Automatic Doppler volume fusion

The accuracies of a position sensor and ultrasound calibration are insufficient for volume fusion because the error is greater than 1.0 mm. Moreover, blood vessel transformation and rotation, which cannot be measured by a tracking device, must be considered for applications in the human body. Therefore, we propose an estimation method with more accurate transformation using point-based registration between shared bifurcations of blood vessels in multiple volumes. A general outline of the method is shown in Fig. 2.

The key technique of the proposed method is point-based registration among the positions of the shared bifurcations in their respective volumes. The method to extract bifurcations has been previously reported [18]. However, point-based registration requires strict pairs of points among the volumes. One possible automatic approach is to find the pairs that result in the minimum registration error, but this approach involves high computational costs. For example, when four bifurcations are picked up from two volumes having 20 bifurcations each, the number of the combinations is more than 563 million (20C4 × 20P4). Even if each point registration requires 1 msec of computation, 156 hours is required. To reduce the computational time, different volume coordinate systems may be integrated into the same coordinate system using tracking and calibration data. Thus, the 3D search range of the shared bifurcations is limited within the tracking and calibration errors.

Let Volumes #1 and #2 be the input volumes and Vol1 ∏p(V1, ..., Vol1Pm) and Vol2 q(Vol2 q1, ..., Vol2 qn) be the bifurcations of the respective volumes. First, Vol2 q is transformed to the volume #1 coordinates using tracking data, and Vol1 q is obtained. Second, automatic registration is conducted using the shared bifurcations. Three points Vol1 pA, Vol1 pB, Vol1 pC (source points) are selected from the bifurcations of volume #1 from three combinations. The candidates for shared bifurcations are then searched in volume #2 for the respective source points. The search range is limited within the predefined initial error of 20 mm (Fig. 3). Let Vol2 qA, Vol2 qB, Vol2 qC be the candidate points of the shared bifurcation Vol1 pA. Next, point registration is performed for all of the candidate points, and their fiducial registration errors (FRE) are obtained. If the FRE is less than 2.0 mm and the smallest, another point Vol1 pD is added to the source points and used to search the corresponding candidate points from Vol2 qD. Then, point registration is performed using four point pairs. In the same way, the number of points for registration is extended to a maximum of seven. Finally, the optimal transformation matrix is obtained us-

![Fig. 1 Setup of 3D ultrasound calibration.](image-url)
ing the largest number of points and minimum FRE.

The final step of the method is volume fusion using the transformation matrix obtained. Volume fusion is processed by a conventional method: 1) transform volume #2 to the volume #1 coordinate system and 2) compound the two volumes. Using registration, we obtained the correct transformation from the volume #2 coordinates to the volume #1 coordinates. For volume transformation, a voxel grid (volume #2) for transformed volume #2 is constructed. The grid has the same origin and spacing as volume #1. Using the transformation, each voxel position of volume #2 is transformed to the volume #2 coordinates, then its voxel value is obtained by trilinear interpolation. Next, volumes #1 and #2 are fused by a binary OR operation.

3. Validations

For validations of the proposed methods, all software for the ultrasound calibration and the volume fusion were implemented in the C++ language (Visual Studio 2012, Microsoft) using an open-source library (the visualization toolkit Kitware).

3.1 Accuracy of 3D ultrasound calibration

The setup for ultrasound calibration is shown in Fig. 4. To validate the target registration error, we prepared an accuracy assessment board consisting of eight markers (Fig. 5).

For basic validation, eight volumes were acquired for the fiducial markers from different probe positions. The spherical fitting errors (SFE) and FRE were then obtained.

For the assessment of calibration accuracy, the target registration errors (TRE) were validated using an accuracy assessment board containing eight optical markers. The board volumes were acquired from 35 probe positions, ranging from 80 to 120 mm in height and from 0 to 150 degrees of rotation around the vertical axis (Fig. 6). First, the position of each marker on the accuracy assessment board was measured by the tracking device. Next, the volumes were acquired, and their probe positions were measured. The volumes were processed using the same calibration methods, and the center positions of the markers in the volumes were obtained. Finally, the centers were transformed to the phantom coordinates using the calibration matrix to obtain the TRE.

3.2 Volume Fusion Assessment using an Artificial Blood Vessel

To validate the basic performance of the proposed fusion algorithm, an in vitro experiment using an artificial blood vessel made of polyvinyl alcohol (Fig. 7) was conducted. An acoustic board was placed in a container, and the vessel was fixed on the board. The container was filled with distilled water, and Doppler fluid
was then perfused into the vessel. Four Doppler volumes were acquired at different azimuths ($\theta$) and elevations ($\phi$), as shown in Fig. 8. In the test, the flow velocity was 30 mm/sec, the depth of the echography was 70 mm, the azimuths were 0 and 30 degrees,
and the elevations were 45 and 90 degrees.

After volume acquisition, two of the four volumes were fused by the proposed method; seven patterns of fusion results were thus obtained. The distances between the shared bifurcations, as well as the numbers of true positive and false positive bifurcations, were analyzed for the validation.

3.3 Blood vessel volume fusion tests in human subjects
To validate the method under practical circumstances, 20 Doppler volumes were acquired from four healthy male subjects aged 23 ± 1 years (five volumes per subject). In these tests, liver vessels in the intercostal and epigastric regions were targeted. The volumes were acquired as the subjects held their breaths to reduce vessel deformation due to respiration.

4. Results
4.1 Accuracy of 3D Ultrasound Calibration
The 3D ultrasound calibration was completed in approximately 20 minutes: 5 minutes for phantom preparation, 5 minutes for measurement, and 10 minutes for manual post-processing. An acquired volume of the fiducial markers and their estimated spheres are shown in Fig. 9. The mean SFE was 0.6 mm, and the mean FRE was 0.2 mm (Table 1). Using the accuracy assessment board, the TRE at each depth is shown in Table 2. The results show that the errors are quite stable and do not depend on position in the volume.

4.2 Artificial Blood Vessel Volume Fusion
Figure 10 shows the superimposed volumes transformed by the tracking data (a) and by the proposed method (b). Both surface representations and centerlines are shown. The proposed method required a total of less than 30 seconds for extraction of bifurcations (14 seconds: 7 seconds × 2 volumes), automatic registration (2 seconds), and transformed volume fusion (10 seconds). Although the results obtained using the tracking data have errors of a few millimeters, the results obtained by the proposed method had no gap. As shown in Table 3, the average distance between the shared bifurcations (error) was reduced from 2.4 mm using the tracking data to 0.5 mm using the proposed method. The numbers of true positives (correct bifurcations) were not different between two methods, but the numbers of false negatives (incorrect bifurcations) were significantly different (16.3 vs. 9.3). With the proposed method, the false negative bifurcations were not created during fusion processing but preexisted in the original volumes. Therefore, fusion processing could not reduce the error.

4.3 Volume Fusion of Human Livers
Highlights of the data of the transformed surface and fused volume of blood vessels in the human liver are shown in Fig. 11. The results suggest that it is possible to transform and fuse the volume in a qualitative manner. In the registration, approximately an hour was required for computation. Table 4 displays the mean distances between the shared bifurcations in the subjects. While the mean distance of shared bifurcations was 10.4 mm using the tracking data, the distance was reduced to 0.6 mm using the proposed method. The number of shared bifurcations found was 5.2 ± 1.3. The number of bifurcations in the fused volumes was also significantly reduced from 474 using the tracking data to 251 using the proposed method. Although it is not possible to determine whether these bifurcations are true or false, the number of false positive bifurcations should be reduced by correction of the transformation accomplished by the proposed method. These results confirm that the proposed method is capable of correctly fusing multiple ultrasound Doppler volumes.

5. Discussion
In this paper, we proposed a method for fusing ultrasound Doppler volumes to construct extensive and complete blood vessel network structures for navigation in microbubble delivery therapy.

In this study, we used Doppler volumes to acquire data on blood vessels easily without segmentation procedures. B-mode imaging is better than Doppler imaging in terms of volume resolution, but B-mode imaging requires segmentation of blood vessels. Several methods have been reported for vessel segmentation using 2D ultrasound. However, 3D ultrasound segmentation remains a research frontier, as 3D ultrasound using a matrix array transducer is a relatively recent technology.

The proposed method does not consider the deformation of blood vessels. However, the topology of the blood vessel network is maintained even when soft tissues are deformed. Therefore, topological information provides compensation for deformation.

In the current state, implementation of the proposed method requires considerable time to search for shared bifurcations; an
hour of computation is needed to determine the best transformation in the liver of human subjects. General-purpose computing on graphics processing units may reduce this time through parallel computation.

In the future, data of the blood vessel network will be applied to the navigation of microbubble delivery through path generation and to the detection of key bifurcations.

6. Conclusions

In the present study, we proposed methods for 3D ultrasound calibration and ultrasound Doppler volume fusion using point registration of shared bifurcations among volumes to acquire extensive and complete blood vessel network data. The proposed ultrasound calibration method is practical, simple and accurate, and the proposed volume fusion method can register volume positions by matching shared bifurcation. The validations conducted in this study confirm the feasibility of the proposed methods.

Table 3 Results of artificial vessel fusion.

<table>
<thead>
<tr>
<th></th>
<th>Error [mm]</th>
<th>Number of bifurcations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ground truth</td>
<td>TP: 7</td>
<td>FP: 0</td>
</tr>
<tr>
<td>Single volume (n = 4)</td>
<td>TP: 5.8 ± 1.3</td>
<td>FP: 6.8 ± 2.2</td>
</tr>
<tr>
<td>Tracking data (n = 7)</td>
<td>2.4 ± 1.3</td>
<td>TP: 6.7 ± 0.5</td>
</tr>
<tr>
<td></td>
<td>FP: 16.3 ± 8.2</td>
<td></td>
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<tr>
<td>Proposed method (n = 7)</td>
<td>0.5 ± 0.12</td>
<td>TP: 6.8 ± 0.4</td>
</tr>
<tr>
<td></td>
<td>FP: 9.3 ± 4.7</td>
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</tbody>
</table>

Table 4 Results of human liver fusion.

<table>
<thead>
<tr>
<th></th>
<th>Error [mm]</th>
<th>Number of bifurcations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tracking data</td>
<td>10.4 ± 5.5</td>
<td>474 ± 235</td>
</tr>
<tr>
<td>Proposed method</td>
<td>0.6 ± 0.3</td>
<td>251 ± 135</td>
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Fig. 10 Results of volume fusion for the artificial blood vessel.
Conflict of interest

We have no conflicts of interest relationship with any companies or commercial organizations based on the definition of Japanese Society of Medical and Biological Engineering.

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References


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