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Abstract. A registration method to fuse two-dimensional (2-D) echocardiography images with cardiac computed tomography (CT) volume is presented. The method consists of two major procedures: temporal and spatial registrations. In temporal registration, the echocardiography frames at similar cardiac phases as the CT volume were interpolated based on electrocardiogram signal information, and the noise of the echocardiography image was reduced using the speckle reducing anisotropic diffusion technique. For spatial registration, an intensity-based normalized mutual information method was applied with a pattern search optimization algorithm to produce an interpolated cardiac CT image. The proposed registration framework does not require optical tracking information. Dice coefficient and Hausdorff distance for the left atrium assessments were 0.87 ± 0.04 and 1.23 ± 0.32 mm, respectively; for left ventricle, they were 0.82 ± 0.07 and 1.14 ± 0.18 mm, respectively. There was no significant difference in the mitral valve annulus diameter measurement between the manually and automatically registered CT images. The transformation parameters showed small deviations (≤ 1.14 mm deviation in translation and $< 2^\circ$ deg for rotation) between manual and automatic registrations. The proposed method aids the physician in diagnosing mitral valve disease as well as provides surgical guidance during the treatment procedure. © 2017 Society of Photo-Optical Instrumentation Engineers (SPIE) [DOI: [10.1117/1.JMI.4.3.037001](https://doi.org/10.1117/1.JMI.4.3.037001)]

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1 Introduction

Multimodality imaging plays an integral role in enhancing a physician's capability to utilize medical imagery information to diagnose diseases.¹ Images acquired from multiple modalities could be realigned to a common coordinate system in postprocessing for surgical planning and guidance. Currently, cardiac surgery for mitral valve treatment is increasing. Mitral valve disease contributes to $\sim 10\%$ of all valve diseases diagnosed in Europe and remains prevalent in developing countries.^{2,3} The mitral valve is located between the left chambers of the heart, allowing unidirectional blood flow control between the left atrium and left ventricle.⁴ Several types of diseases or diseased conditions are known to reduce the performance of the mitral valve, including stenosis (narrowing of the valve), tissue prolapse (the flaps on the valve bulge), and regurgitation (blood leaks from the valve and flows backward into the left atrium).^{5,6} Treatment options include surgical repairing or replacement of the mitral valve,⁷ although both procedures have been associated with risk and morbidity, such as renal injury and stroke.^{8–10}

To date, two-dimensional (2-D) and three-dimensional (3-D) echocardiographies are the main preoperative imaging modalities used for assessing mitral valve pathology. These modalities provide reliable information on the degree of mitral valve regurgitation and stenosis, annular size, anterior or posterior leaflets involvement, chordal and papillary muscle structural integrity, the overall left ventricular size, and the left ventricular systolic

function.¹¹ Echocardiography can also be used as an intraoperative imaging modality for real-time surgical guidance as it does not utilize ionizing radiation and is low cost compared with other imaging modalities.¹² However, the image quality of echocardiography is inferior in comparison to other modalities such as computed tomography (CT) or MRI due to the presence of speckle noise and limited field of view.¹³ 2-D echocardiography provides only planar images, making it difficult to maintain both the surgical tool and the anatomical targets in the same imaging plane.¹⁴ Cardiac CT, by contrast, is commonly applied as a preoperative imaging tool. Despite the high radiation dose, the modality can help to detect mitral valve diseases and assess the severity of valvular dysfunction quantitatively.¹⁵ CT has also been found useful for identifying complications in patients who have undergone mitral valve surgery during follow-up examinations.¹⁶

Complementary anatomical and functional information fusion using images obtained from multiple imaging modalities could potentially improve the diagnostic accuracy of mitral valve dysfunction, facilitate preprocedural planning, and provide intraprocedural guidance during surgical procedures. Such fusion can be achieved by establishing a direct spatial correspondence between different modalities through image registration. However, fusion of ultrasound technology and CT for cardiac application is more complex compared with the kidney¹⁷ and liver¹⁸ due to the associated motions of the heart and thorax as well as the deformable nature of the heart. Limited literature exists^{14,19–21} concerning the feasibility of fusing a 2-D echocardiography and 3-D CT for guiding cardiac surgery.

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Many researchers proposed the use of an optical tracking system to track the position and orientation of the echocardiography transducer during the image registration process.^{14,19–21} An optical tracker, however, may not be available or integrated with existing ultrasound systems for routine clinical application. In addition, the cost associated with the optical tracking hardware and multiple software packages for its operation makes the tracker less cost effective for system integration. Fusion of 3-D echocardiography with volumetric data²¹ has also been studied previously. Similarly, the proposed multimodality fusion utilized the optical tracking system in their registration framework.

In this study, we proposed an intensity-based image registration technique to register the 2-D echocardiography images to the 3-D cardiac CT volume. Compared with the existing methods for registering 2-D planar echocardiography with cardiac CT images using optical tracking system, our technique consists of two major steps: temporal registration and spatial registration. Adding an optical tracking system not only adds the cost and requires experienced and trained users but also adds more equipment at the already busy scene of the operation theater. We have shown the applicability of this technique using echocardiography acquired without optical tracking information and applied it in the four chamber view in the imaging results for the purpose of fusing both structural and functional information of the mitral valves from these two modalities. Our approach to fuse both modalities closely follows our earlier work on application for aortic valve disease treatment and surgical guidance procedures.²² Quantitative and qualitative evaluations have been performed to investigate the performance of the proposed algorithm.

2 Methodology

2.1 Data Acquisition

Five patients with indicated mitral valve disease who had undergone scanning using both 2-D transthoracic echocardiography

and cardiac CT on the same day were recruited in this study. The 2-D transthoracic echocardiography was performed using the Phillips Medical Systems IE33 ultrasound system equipped with an S5-1 phased-array (1.0 to 3.0 MHz) transducer (Phillips Medical Systems). The standard views were obtained at 800×600 pixels, a resolution of 0.3×0.3 mm, and a frame rate of 30 to 100 Hz. The scans cover more than one cardiac cycle. The cardiac CT data of the same patients are collected after echocardiography examination on the same day. Retrospectively, gated cardiac CT scans were performed on patients using a 64-slice dual source CT scanner (Somatom Definition, Siemens Medical Solutions, Germany) with 120 kVp tube voltage, a tube current depending on patient size, 0.33 s gantry rotation time, and a pitch of 0.2 to 0.43, which was automatically adapted to the heart rate. The reconstruction of the raw cardiac CT data was performed at 40% to 70% of the *R–R* interval with a slice thickness of 0.75 mm, a matrix size of 512×512 , and a voxel length of $0.4 \times 0.4 \times 0.4$ mm at a single frame per cardiac cycle. All data were collected under a protocol approved by the Research Ethics Board of National Heart Institute, Kuala Lumpur, Malaysia.

2.2 Image Registration

The proposed method consists of two major steps: echocardiography image frame selection or temporal registration and spatial registration. The overall registration workflow proposed is shown in Fig. 1, and the details of each step are described in the following sections.

2.2.1 Temporal registration

Temporal registration was essential to align echocardiography and cardiac CT images in time. This is because both modalities produce images of different sampling latencies and temporal resolution.²⁰ The echocardiography data were acquired in a video recording format that depicts a pumping heart moving through systolic and diastolic phases during surgical navigation,

Fig. 1 Overall registration workflow.

whereas cardiac CT was captured during preoperative assessment at a single-time point, typically at the diastolic phase. Thus, correct selection of 2-D planar echocardiography images is critical for the success of spatial registration with the cardiac CT.

As the cardiac CT was reconstructed within 40% to 70% of the R - R interval, echocardiography image frames at the same phase can be extracted from the recording, with reference to the time stamp information available from electrocardiogram (ECG) gating signals that were acquired concurrently during echocardiography imaging. Compared with Huang et al. who used 3-D US images that were augmented with both ECG signals and spatial tracking information, our technique automatically detects the R peaks from the ECG signal based on the signal amplitude, and three frames located within 40% to 70% of the R - R interval were interpolated using a linear interpolation technique. These image frames were then registered spatially with the cardiac CT.

2.2.2 Noise reduction

To succeed in registration, a voxel similarity measure such as the mutual information function should be quasi-convex and contain a minimum number of local maxima. The inherent undesired property of an echocardiography image, i.e., speckle noise artifacts, impedes the above-mentioned condition by affecting the mutual information value.²³ Removing speckle noise, hence, is significant for improving the registration accuracy. Median filtering is often adopted to suppress noise, aiming to smooth the mutual information function for improved registration; however, this filtering undesirably blurs the boundaries of the anatomical structure. We, therefore, proposed the use of speckle reducing anisotropic diffusion (SRAD),²⁴ which is an approach based on both additive-noise-reduction's anisotropic diffusion²⁵ and multiplicative-noise-reduction's Lee and frost filters,^{26,27} for noise reduction. SRAD confers one main advantage over conventional filtering methods: it preserves and

enhances edges while suppressing the speckle noise. Despite being more computationally demanding, implementing SRAD remains feasible in the registration process since only a single selected echocardiography image is used throughout the entire registration process in our case.

2.2.3 Spatial registration

The spatial registration scheme employs a rigid 2-D to 3-D intensity-based registration, utilizing mutual information as the similarity metric and a pattern search algorithm as the underlying optimizer to perform spatial registration between echocardiography image frames and cardiac CT volume. To search for the best matching cardiac CT plane, the 2-D planar echocardiography image is spatially maneuvered within the vicinity of the cardiac CT volume. The search is initiated by placing the echocardiography image at the seed position, which is at the level of mitral valve location in the cardiac structure. This seed position was estimated and provided by the expert during preprocedural planning on cardiac CT volume with respect to 3-D axes of the patient's body.

A rigid spatial transformation consisting of 8-degrees of freedom to the 2-D planar echocardiography images was applied.²² This transformation includes 3-D translation, 3-D rotation, and 2-D scaling (i.e., along both dimensions of the planar image) as shown by Eqs. (1), (2), and (3), where u, v, w are the input image coordinates, u', v', w' are the transformed coordinates, α, β, γ are the rotation angle about the x, y, z axes, respectively, and " T " refers to the transformation

$$\begin{bmatrix} u' \\ v' \\ w' \end{bmatrix} = T \begin{bmatrix} u \\ v \\ w \end{bmatrix}, \quad (1)$$

$$T = \text{scaling}_{x,y} \times \text{rotation}_{x,y,z} \times \text{translation}_{x,y,z}, \quad (2)$$

$$T = \begin{bmatrix} sx & 0 & 0 & 0 \\ 0 & sy & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix} \times \begin{bmatrix} \cos \beta \cdot \cos \gamma & -\cos \beta \cdot \sin \gamma & -\sin \gamma & 0 \\ -\sin \alpha \cdot \sin \beta \cdot \cos \gamma + \cos \alpha \cdot \sin \gamma & \sin \alpha \cdot \sin \beta \cdot \sin \gamma + \cos \alpha \cdot \cos \gamma & -\sin \alpha \cdot \cos \beta & 0 \\ \cos \alpha \cdot \sin \beta \cdot \cos \gamma + \sin \alpha \cdot \sin \gamma & -\cos \alpha \cdot \sin \beta \cdot \sin \gamma + \sin \alpha \cdot \cos \gamma & \cos \alpha \cdot \cos \beta & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix} \times \begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ tx & ty & tz & 1 \end{bmatrix}. \quad (3)$$

A linear interpolation method was applied on the cardiac CT volume to sample the 2-D CT plane of the same size and spatial location as the echocardiography image. The best matching interpolated 2-D CT plane, and therefore the optimal alignment, is determined using normalized mutual information (NMI).²⁸ The mutual information metric $I(A, B)$ measures were defined by

$$I(A, B) = H(A) + H(B) - H(A, B), \quad (4)$$

$$I(A, B) = \sum_a \sum_b p_{AB}(a, b) \log \frac{p_{AB}(a, b)}{p_A(a)p_B(b)}, \quad (5)$$

where $H(A)$ and $H(B)$ are the Shannon–Wiener entropies of cardiac CT (image A) and echocardiography (image B), respectively, and $H(A, B)$ is the joint entropy of the two images.²⁸ The $H(A)$, $H(B)$, and $H(A, B)$ are defined as

$$H(A) = -\sum_a p_A(a) \log p_A(a), \quad (6)$$

$$H(B) = -\sum_b p_B(b) \log p_B(b), \quad (7)$$

$$H(A, B) = -\sum_a \sum_b p_{AB}(a, b) \log p_{AB}(a, b), \quad (8)$$

where $p_{AB}(a, b)$ is the joint probability of the two images and $p_A(a)$ and $p_B(b)$ are the marginal probabilities of image A and B, respectively, which can be estimated from the normalized joint histogram.

The registration task was carried out based on an iterative algorithm using a generalized pattern search algorithm to find the optimal spatial transformation parameters that maximize the NMI measure of overlapping image pixel intensities.²⁹ After optimal transformation was computed, it was applied to cardiac CT volume to create a matching 2-D CT planar image. The registration framework was implemented in MATLAB (vR2014a, Mathworks, Natick) on an Intel(R) Xeon (R) CPU E5-26200 at 2.00 GHz computer.

2.3 Validation of Registration Accuracy

To perform validation, the registration results of the proposed method were compared with the gold standard manual registration. Manual registration was performed by an expert whereby the best matching CT plane was selected through manual manipulation of the transformation parameters. The expert contoured the left atrium and left ventricle on four-chamber echocardiographic views and the CT planes obtained from the manual and automatic registrations. The left atrium and left ventricle are the two closest structures to the mitral valve and are affected by mitral valve disease.^{5,6} The Dice similarity coefficient (DSC) and Hausdorff distance (HD) were calculated from the segmented contours to assess registration accuracy. This comparison was essential for investigating whether the automatic-CT plane resulting from the proposed method can provide similar or equivalent registration accuracy to the gold standard manual registration CT (manual-CT).

The DSC and HD were calculated to assess registration accuracy in terms of overlap and distance errors. DSC measures the spatial overlap between two contoured regions of interest (ROI). This measure has been found to be sensitive to both location and size of the contoured ROI,³⁰ and the measures were defined by

$$\text{DSC} = \frac{1}{n} \sum_{j=1}^n \frac{2(R_A \cap R_{Bj})}{R_A + R_{Bj}}, \quad (9)$$

where R_A and R_B are the contoured ROI in two images, respectively. n is the number of echocardiography frames used in registration. DSC ranges from 0 to 1, indicating no overlap (DSC = 0) and complete congruence (DSC = 1) between two ROIs.

HD, by contrast, is a distance measure to estimate the distance between two ROIs by the spatial distance of their contour points. This measure is defined by

$$H(A, B) = \frac{1}{n} \sum_{j=1}^n \max[h(A, B_j), h(B_j, A)], \quad (10)$$

$$h(A, B) = \max_{a \in A} \min_{b \in B} \|a - b\|, \quad (11)$$

where A and B are two sets of contour points of two ROIs, respectively. In other words, HD computes the mutual proximity between two ROIs by indicating the maximal distance between one ROI and the other ROI.³¹

In addition, the diameter of the mitral valve annulus was measured from both automatic and manually registered CT planes and a Bland–Altman with 95% limit of agreement graph plotted to compare the agreement in diameter measurements obtained from the two different registration mechanisms. The Bland–Altman plot with 95% limit of agreement was used to describe the agreement between two quantitative measurements, the automatic registration method, and the gold standard manual registration. The 95% agreement limit allows for the estimation of the size of the possible sampling error.³² The 95% limit of agreement was calculated using the mean and the standard deviation of the differences between two measurements (mean difference $\pm$ 1.96 standard deviation of the difference).

In addition, the root-mean-square error (RMSE) was calculated to compare each of the transformation parameters between manual and automatic registrations. This measure is defined as

$$\text{RMSE} = \sqrt{\frac{1}{n} \sum_{i=1}^n (\|Tm_i - Ta_i\|)^2}, \quad (12)$$

where Tm is the transformation parameter (i.e., translation, rotation, or scaling) obtained from the expert's manual registration and Ta is the corresponding transformation parameter resulting from the proposed algorithm.

3 Results and Discussion

Figure 2 shows the results of registration on five patients. Row 1 shows frames of echocardiography images interpolated during the temporal registration process. Row 2 displays the gold standard manual-CT images selected by the expert, which is used for the validation of the automatic-CT images output by our proposed method (row 3). Based on the results, the automatic-CT images were found to resemble the gold standard manual-CT images with regards to the cardiac structure such as left atrium, left ventricle, mitral valve annulus, and leaflets.

The DSC and HD of the left atrium and left ventricle are tabulated in Table 1. The DSC values of the left atrium at $0.87(\pm 0.04)$ for echo-autoCT and $0.86(\pm 0.04)$ for echo-manualCT. The DSC value above 0.7 indicates that the contoured ROI in both types of images have considerable similarity in area size and spatial overlap.³³ HD was also computed between the two contoured ROIs, with the value for the echo-autoCT equal to $1.23(\pm 0.32)$ mm and the echo-manualCT equal to $1.24(\pm 0.29)$ mm, which equals a about 3 to 5 pixels offset in cardiac CT and echocardiography. This is considered acceptable in view of the much bigger field of view yielded by both imaging modalities. The performance of the proposed

Fig. 2 Registration results of five patients.

Table 1 Registration accuracy as measured using DSC and HD.

Structure	Measure	Echo-autoCT ^a (mean $\pm$ std)	Echo-manualCT ^b (mean $\pm$ std)
Left atrium	DSC	0.87 ± 0.04	0.86 ± 0.04
	HD (mm)	1.23 ± 0.32	1.24 ± 0.29
Left ventricle	DSC	0.82 ± 0.07	0.84 ± 0.06
	HD (mm)	1.14 ± 0.18	1.09 ± 0.21

^aEcho-autoCT: echocardiography-automatically registered CT.

^bEcho-manualCT: echocardiography-manually registered CT.

algorithm was found consistent for the left ventricular structure too.

The agreement between the automatic registration method and the gold standard manual registration was estimated by means of Bland–Altman plots. Using this graphical approach, the difference of two measurements against the mean of the same measurements was shown. This approach allows visualization of the extent to which the measurements differ from each other. Figure 3 of the Bland–Altman plot demonstrates a good agreement in the diameter measurement of mitral valve annulus between the automatically and manually registered CT planes. There is no significant bias for diameter measurement of the mitral valve annulus between both methods, with the limit of agreement being about -2.42 to 3.08 mm and the mean difference for diameter measurement being -0.33 ± 1.41 mm.

The quantitative error of transformation parameters are tabulated in Table 2. The RMSE for translation ranges from 0 to 1.14 mm, whereas the angular deviation is less than 2 deg. Error in scaling has been found to be minimal.

Cardiovascular imaging, for decades, plays an important role in ruling out various types of cardiac diseases, facilitating

Fig. 3 Difference of mitral valve diameter measurement between automatic and manual registration methods (black dotted line—95% limits of agreement, blue line—bias).

surgical planning, and providing invaluable guidance during intervention. The benefits brought about by integrating images from various modalities are paramount and could be realized using image registration methods. Image registration caters to the needs of physicians to understand more comprehensively both the structures and functions of the heart, which very often can only be achieved with multiple modalities, to make an optimal clinical decision. Modern technologies such as CT and MRI provide good quality 3-D tomographic images of the heart but are infeasible for guiding minimal invasively procedures for heart intervention as these modalities do not have real-time imaging capability and are too expensive to be utilized for large numbers of patients in an operational theater or catheterization laboratory. Echocardiography is a much cheaper and real-time imaging modality for surgical guidance. The 2-D intraoperative echocardiography images nevertheless are inherently speckly and can only be more easily interpreted if they are used in conjunction with preoperative CT or MRI data, which provide excellent image quality. In addition,

Table 2 RMSE of transformation parameters.

Patient #	Translation (mm)			Rotation (deg)			Scaling	
	Δtx	Δty	Δtz	$\Delta \alpha$	$\Delta \beta$	$\Delta \gamma$	Δsx	Δsy
1	0.02	0.27	0.01	0.24	0	0.53	0.01	0
2	0.14	0.28	0.42	1.89	0	0	0	0
3	0.22	0.04	0.02	0.03	0	0.18	0	0
4	0.42	1.13	0.78	0.47	0	0	0	0
5	0	0.07	0.06	0.03	0	0.24	0	0

Note: Δtx , Δty , and Δtz refer to RMSE for the translation, whereas $\Delta \alpha$, $\Delta \beta$, and $\Delta \gamma$ refer to RMSE for rotation along the three axes. Δsx and Δsy are RMSE of scaling along both dimensions of the planar image.

these modalities most often offer different structural and functional imaging features that are complementary to each other.

In this study, we have presented a registration framework for combining 3-D cardiac CT volumes with 2-D echocardiography frames. The applied alignment procedure is based on the maximization of the mutual information function, which stems from the probability and information theory, of two arbitrary datasets from the CT and echocardiography modalities. Our proposed method has shown the practicability in visualizing the anatomical structures such as the mitral valve and the left atrium in the absence of an optical tracking system compared with previous studies.^{14,19–21} The accuracy of our proposed method was evaluated against the gold standard manual registration. The expert's visual inspection and quantitative analysis divulges that the proposed registration method is able to align the images successfully and shows promise for clinical application.

Currently, we employed a rigid spatial transformation matrix in the registration process and assumed that the heart is a rigid body. Although the heart is deformable, the validation results have shown that sufficient accuracy could be achieved with simple rigid transformation for intraoperative surgical guidance. One notable limitation with the current proposed method is the computation time in which the average time to accomplish a single 2-D to 3-D registration took ~ 46 s. This nearly real-time algorithm may be further improved by adding the multiresolution or pyramid³⁰ scheme. Implementing the algorithm in a more efficient programming platform, such as Insight Segmentation and Registration Toolkit, may provide a higher image registration speed for real-time application. In addition, our method requires a manual seed placement at the rough position and orientation of the mitral valve plane during preoperative planning to initiate the search for actual intraoperative surgical guidance. Without prior knowledge of the anatomy of the cardiac structure, it is quite challenging to estimate the exact location of the mitral valve plane, which may jeopardize the accuracy of the final CT plane found through the optimization process. When a large displacement of a few centimeters is applied, the resulting interpolated CT plane may show a low degree of area similarity (DSC) and a huge shape difference (HD) to the echocardiography image. The robustness of the algorithm to large displacement, nevertheless, may be improved using a multiresolution scheme that hierarchically refines accuracy through coarse-to-fine registration³⁴ or using a multistart optimization scheme.³⁵

4 Conclusion

The fusion of echocardiography and cardiac CT plays an integral role in enhancing a physician's capability to utilize medical imagery information for cardiac surgery involving the mitral valve. We have presented a method to register 2-D echocardiography images with cardiac CT volume, without the additional use of an optical tracking system as in the published literature. The temporal registration allows an echocardiography image frame at a similar cardiac phase as that of the cardiac CT to be automatically chosen for spatial registration. The spatial registration method consists of an intensity-based registration algorithm, which utilizes NMI and a pattern search optimization algorithm, to produce an interpolated cardiac CT image that matches optimally with the echocardiography image. Even without any tracking technology, the qualitative and quantitative validation shows excellent accuracy for potential use in clinical diagnosis of mitral valve diseases and for surgical guidance. Application of the framework for real-time guidance of minimally invasive treatment of other cardiac diseases is also of interest and will be left for future work. In future work, reducing the computation time using a pyramid or multiresolution image registration scheme or a multistart optimization scheme will be investigated to increase the feasibility for clinical integration.

Disclosures

The authors have no potential conflicts of interest to disclose.

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