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Abstract. In order to utilize both computed tomography (CT) and echocardiography images of the heart for medical applications such as diagnosis and image guided intervention concurrently, non-rigid registration is an essential task. A challenging but important problem in image registration is evaluating the performance of a registration algorithm. The direct quantitative approach is to compare the deformation field solution with the ground truth transformation (at all or some landmark pixels). However, in clinical data, the ground truth is typically unknown. To deal with the absence of ground truth, some methods opted to estimate registration accuracy by using uncertainty measures as a surrogate for quantitative registration error. In this paper, we define the registration uncertainty and explore its use for diagnostic purposes. We use uncertainty estimation for improving accuracy of a hybrid registration which register a pre-operative CT to an intra-operative echocardiography images. In other words, uncertainty estimation is used to evaluate the registration algorithm performance which integrates intensity-based and feature-based methods. This registration can potentially be used to improve the diagnosis of cardiac disease by augmenting echocardiography images with high-resolution CT images and to facilitate intra-operative image fusion for minimally invasive cardio-thoracic surgical navigation. Here, we show how to determine the registration uncertainty, by using uncertainty quantification regarding to abnormal intensity and geometry distribution. The result indicates that registration uncertainty is a good predictor for the functional abnormality of subjects.

Keywords: Uncertainty. Multimodality Image Registration. Hybrid. Feature-based. Intensity-based. Echocardiography. Computed Tomography (CT).

adfa, p. 1, 2011.

1 Introduction

Echocardiography imaging is an attractive alternative to MRI and CT during surgery due to ease of use, its safety, minimal disruption of the procedure, comparatively low cost, and lack of compatibility problems between echocardiography imaging and standard operating theater equipment. However, due to inferior overall image quality of echocardiography images than MRI or CT images, clinicians often have problem in assessing target organs in the clinical applications. To overcome this limit of echocardiography imaging, there have been several efforts to display or register an echocardiography image with its corresponding high-quality CT (or MRI) image to provide clear information related to anatomy and particular target [1, 2, 3, and 4]. Some structure target are often nearly invisible in an echocardiography image, the corresponding CT image is useful for providing information to clinicians for diagnosis and planning of intervention. To obtain a CT image correctly aligned to an echocardiography image for the heart, non-rigid registration between CT and echocardiography images is essential [2].

Registering pre-operative CT scan to echocardiography image of the patient heart can assist the guidance of surgical process and instruments, during cardiac surgery [3]. Also it can provide image-guidance for procedures that involves both anatomical and functional imaging.

The present paper briefly reviews the two-level non-rigid registration algorithm between CT images and echocardiography of the heart, and then by using uncertainty function tries to improve the registration accuracy through considering local deformations, which cannot be compensated using a global registration algorithm. In the registration technique, segmentation result information and intensity value information of the ventricles, are used for registration procedure.

Uncertainty is inherently an important issue to all image analysis tasks. However, few common algorithms estimate a measure of uncertainty for the calculated results. Automatic error detection would be very valuable in the practical use of medical image analysis tools, as it could provide the clinicians with more confidence on whether or not to use a computer-generated analysis. Registration uncertainty is important information to convey to a surgeon when surgical decisions are taken based on registered image data. However, conventional non-rigid registration methods only provide the most likely deformation [7].

There is a level of uncertainty associated with registering images that have any differences. A confident registration with a measure of uncertainty is critical for many change detection applications such as medical diagnostics. Several notable papers have attempted to quantify uncertainty in image registration in order to compare results [8, 9].

In this paper, we describe a method for non-rigid registration of cardiac images and quantify the uncertainty of the estimated transformation. The registration method was validated on a clinical dataset with results comparable to previously published methods, but with the added benefit of also providing uncertainty estimates which may be important to take into account during cardiac surgery procedures. Improvements are demonstrated in accuracy and robustness over non-rigid registration between CT and echocardiography images and it is shown how to summarize this uncertainty in terms of uncertainty quantification and user interaction. We also emphasis that non-rigid registration results come with a level of uncertainty and conveying the uncertainty, and not only the most likely estimation, is clinically important.

Previous works in our lab towards the goal of Computer Assisted Medical Research has included the develop an automatic coronary arterial tree extraction in angiograms [11], cardiac ultrasound fusion system development [12], Wavelet enhancement for x-ray angiogram [13], CT angiography components categorization and coronary artery enhancement [14], a hybrid non-rigid registration method based on pre- and intra-operative cardiac images [8], and some surveys including review on segmentation approaches [15, 16], and review on registration of cardiac images [17].

In this paper, we are trying to quantify the uncertainty measurement in the hybrid registration method which is presented in [18] in details. This paper is organized as following; Section 2, refers to describe the hybrid registration procedure briefly; in Section 3, uncertainty definition and evaluation is explained; Section 4, registration uncertainty quantification is explored and finally in Section 5, some future directions are presented and the paper is concluded.

2 Hybrid Non-Rigid Registration

In this work, interested region in two different modality images are segmented by a level set model which is proposed in [19], in first modality -echocardiography-, and in the second modality -computed tomography- by k-means clustering technique [20], and then images are registered together with the two-level registration method presented in [18].

The extracted features or segmented contours are represented by two different function sets of images. An objective function which is described based on segmentation result defines the mapping between the segmented contours. The presented registration method uses two relatively separated discontinuity sets to represent the contour sets of the associated images to tackle the registration problem between these contour sets.

For the ambiguity problem of the correspondence, we apply the idea of consistent registration [5, 6] to simultaneously estimate the forward and reverse transformations and to constrain one transformation to be the inverse of the other one. In this case, the contour sets of images have equal influence on the registration. Thus, the registration technique is one-to-one in the way that it allows to determine one-to-one correspondences between the contour sets of the images.

Symmetric one-to-one contour matching is not only more sound in mathematical sense, but also very important in determining the one-to-one correspondence of the same anatomical structures in two different images. The ability to correlate echocardiography images with pre-operative dynamic CT images would provide the surgeon with complementary information captured in two different modalities, and greatly facilitate the interpretation of the images.

Registration and segmentation of the ventricular myocardium in the images are important steps to extract useful qualitative or quantitative information about myocardial intervention. The hybrid non-rigid registration algorithm uses intensity value information and segmentation result information through a level set based segmentation to register echocardiography and CT images.

Different similarity measures are considered based on the correlation of the intensity value information and segmentation result information between echocardiography and CT images, according to the image characteristics of the features, including ventricle endocardial and ventricle surfaces in two images.

To represent the similarity measure between echocardiography and CT images, two objective functions based on the segmentation result information and intensity value information are adopted. The registration technique conducts the segmentation-based and intensity-based registration procedures according to corresponding similarity measure.

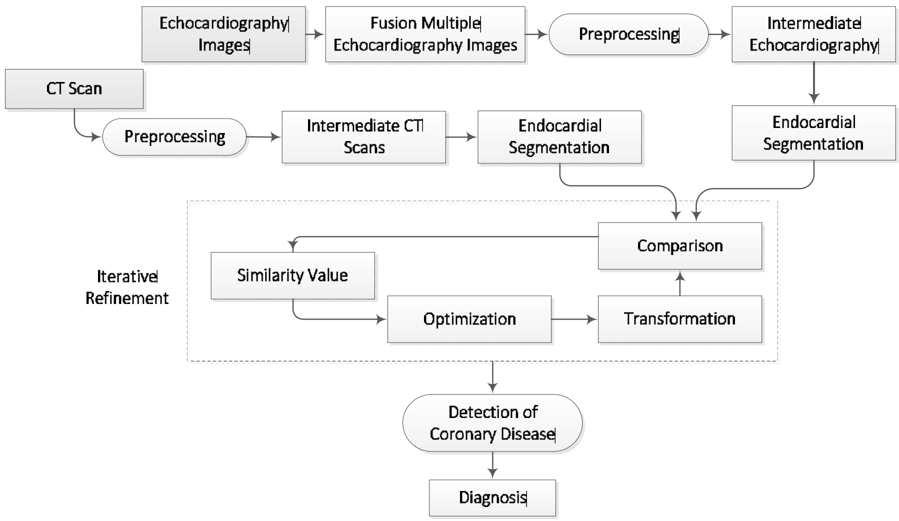

Fig. 1. Workflow for hybrid echocardiography-CT registration

The images have been preprocessed in order to increase the relationship between CT and echocardiography pixels. Image pre-processing is necessary to make the modalities as close as possible (interface enhancing in CT scans, filtering, and artefact and acoustic shadow removal and filtering in echocardiography images). The images have been preprocessed in order to increase the relationship between CT and echocardiography pixels.

The discussed non-rigid registration is less restrictive regarding the structure which is due to the faster implementation and inherently smooth nature of the basic functions. No search space or point to point mapping is needed either. It is possible to achieve smooth results and handle multiple point set models at the same time.

3 Uncertainty Definition and Evaluation

An important, but somehow neglected aspect of non-rigid registration is: how is it possible to quantify and visualize the registration uncertainty. The significance can be simply realized in the range of surgeries. Critical functional regions of the target are usually determined in the pre-operative domain. Current image guided navigation systems employ rigid registration to build the mapping between the intra- and pre-operative domains, but there is a move towards non-rigid registration recently, as we described in details in [18].

Regular registration techniques gives the most likely deformation and hence the most likely position of a functional region. However, non-rigid registration can behave randomly in the way that small changes of data parameters can produce completely different result.

In addition, metrics like resection of tissue and degraded intra-operative image quality can all contribute to increasing in the registration uncertainty. Thus, for a surgeon, the uncertainty in the estimated position of functional regions can be exactly as significant information as the most likely estimate of the position.

Registration uncertainty can be valuable information to portray to a surgeon/interventionist, especially when important clinical decisions are based on the registered data. In surgeries, target points are defined in the pre-procedural image and transformed into the intra-procedural image space to guide the surgeon during the procedures. It is important to understand that there is an uncertainty associated with the estimated transformation and consequently the transformed points.

In this paper, we define the registration uncertainty and explore its use for diagnostic purposes. We evaluated the registration accuracy via uncertainty estimation on images from 16 subjects in two cardiac phases, systolic and diastolic, acquired from UiTM hospital in Malaysia under supervision of cardiac surgeon.

Since, results indicate that the described registration system is capable of producing segmentation results with high robustness and high accuracy with minimal user interaction across all subject groups, high registration uncertainty will indicate functional abnormality of the subject. We show that registration uncertainties are good predictors for the functional abnormality of the subject.

Several challenges are common in inter-subject registration, which can cause the occurrence of local uncertainties of the transformations [21]:

- Missing one-to-one correspondences of anatomies across subjects
- Mismatch of structures due to local minima of the registration
- Untrustworthy image information due to acquisition noise and artefacts

No matter how robust a registration technique is, it is important to have the ability to alert the user if the uncertainty of the registration quality is high. High uncertainty can either be a sign of an unreliable registration result or of an abnormal cardiac anatomy. The integration of feature- and intensity-based registration has shown the ability to achieve both good robustness and accuracy [18].

Back to the important, but not fully explored topic in the domain of non-rigid registration; the question which mentioned at the beginning of the section; how is it possible to quantify and visualize the registration uncertainty? Since the hybrid registration combines information from two sources which they are intensity value and segmentation result information, this question can be further divided into uncertainty arising from the segmentation result [7, 24] and uncertainty arising from abnormal intensity, which is related to functional abnormality of the subject. The registration uncertainty which comes from intensity relates to abnormal intensity like ischemic cardiomyopathy, while registration uncertainty which comes from segmented region (geometry distribution) corresponds well to abnormal geometry like dilated cardiomyopathy.

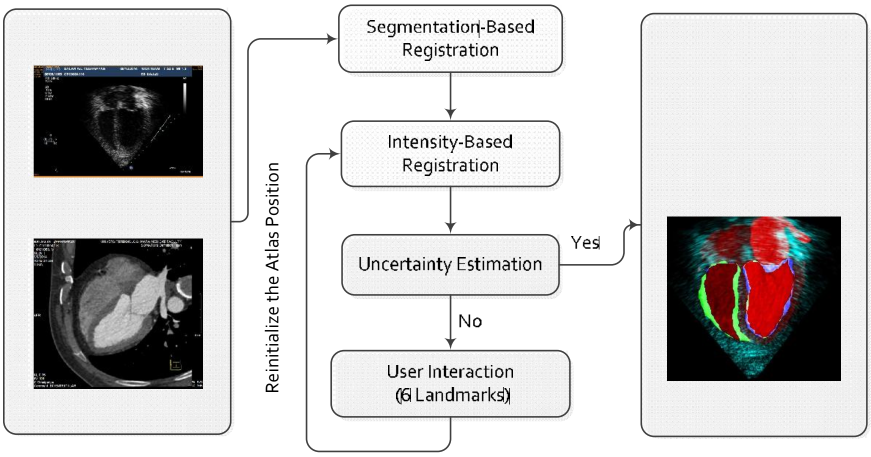

Fig. 2. Workflow of the uncertainty estimation framework

We also explore the potential of registration uncertainty in improving the robustness: If and only if the uncertainty of the registration is high, the system will ask the user to input additional landmarks to help better initialize the estimated transformation for registration. The landmarks include apex, center of mitral valve, center of left ventricle, center of right ventricle and two right ventricle insertion points (anterior and inferior insertion points of right ventricle) and center of basal plane.

4 Registration uncertainty

4.1 Uncertainty Definition

Given two images, I_{at} and I_{mo}, we can estimate a transformation T which maps image I_{mo} to I_{at}, so that a pixel of $I_{mo}(x)$ correspond to $I_{at}(T(x))$ and their intensity values should be similar. Using a probabilistic formulation for the image registration problem [7], the uncertainty of a transformation T at point x can be modeled by the following equation:

$$uc(T(x)|(I_{mo}(x), I_{at})) = 1 - \frac{p\Big((I_{mo}(x), I_{at})\Big|T(x)\Big)p(T(x))}{p((I_{mo}(x), I_{at}))} \quad (1)$$

We model the likelihood term $p((I_{mo}(x),\ I_{at})|T(x))$ as a normal distribution of the intensity difference between transformed I_{at} and I_{mo} estimated. Comparably, the prior of the transformation, $p(T(x))$, is modeled as a Rician distribution of the Jacobian determinant of the transformation [22]. The distribution is estimated based on the inversion technique proposed in [23]. The Rician distribution is a non-negative and asymmetric distribution which approximates the distribution of the Jacobian determinant well for a given transformation. Finally, $p(I_{mo}(x),\ I_{at})$ can be modelled as a constant term.

4.2 Uncertainty Quantification and User Interaction

For each pixel x_i in all images, its registration uncertainty can be evaluated and visualized using equation (1). We can further define the registration uncertainty of a given region L_j by averaging over the region. The quantification of uncertainty can be used to inform the user about how reliable the registration results are. Based on results from the uncertainty analysis, we can design a system that detects functional abnormality with high uncertainty. High uncertainty can either be a sign of an unreliable registration result (registration failure) as well as abnormal cardiac anatomy.

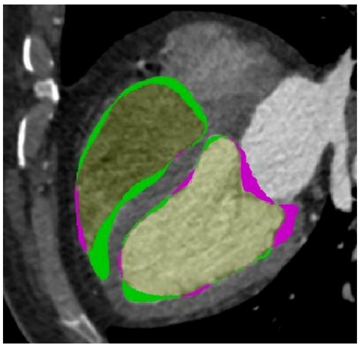

Fig. 3. LV and RV differences; difference between transformed LV and RV, and the intra-procedural CT is shown in green color, while difference between transformed LV and RV, and the pre-procedural echocardiography is shown in pink.

In the cases, we detect registration failure, the user is asked to define 6 landmarks (apex, center of left ventricle, anterior and inferior insertion points of right ventricle, center of right ventricle and center of basal plane). These landmarks are also defined in the atlas. By introducing knowledge about these additional 6 landmarks, the atlas-to-image registration can be initialized more accurately and all registrations performed correctly.

When the registration is considered successful, the uncertainty relates to abnormality of the patient's cardiac anatomy. This is possibly due to the fact that our segmentation algorithm using GCL is designed to segment pathological images well [19] and k-means clustering [20]. To examine if the uncertainty correlates to the abnormality of the patients, as mentioned in previous section, registration uncertainty which comes from intensity relates to abnormal intensity like ischemic cardiomyopathy; while registration uncertainty which comes from segmented region or geometry distribution corresponds to abnormal geometry like dilated cardiomyopathy.

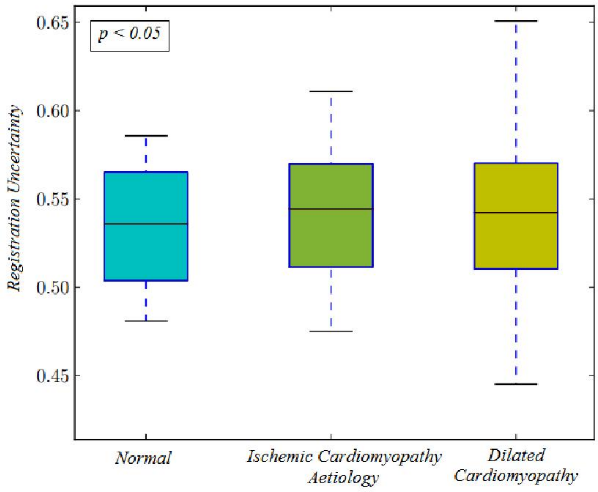

Fig. 4. This figure shows registration uncertainty

Figure 4 shows that registration uncertainty is a very good predictor for separating ischemic cardiomyopathy, dilated cardiomyopathy, and normal subjects.

The accuracy is significantly improved compared to previous registration methods by utilizing both pre- and intra-image information. We define a system that detects either registration failures or abnormality of the patient's cardiac anatomy using registration uncertainties.

5 Conclusion

Registration uncertainty is important information to convey to a user when automatic image analysis is performed. Uncertainty information may be used to provide additional diagnostic information to traditional analysis of cardiac function.

Cardiac pathology is not always easily detectable in images, but likely to be detected by registration uncertainty. Since, we can define uncertainty for every part of the cardiac anatomy, it is desirable to investigate if the relationship between uncertainty and abnormality could help to detect these pathologies automatically.

The registration uncertainty has the potential to convey information on our confidence in the resulting transformation. To form an uncertainty map describing the registration result, we calculate uncertainty of the transformation at every pixel.

While the particular registration uncertainty proposed in this paper as a preliminary outcome, it is believed, firstly, that in the future, with increasing computational power, more highly developed algorithms and better modeling, it will be practical to get dense information related to uncertainty of the estimated transformation, and secondly that it will be important to share that information with the surgeon in a purposeful and valid way.

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