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A Literature Survey of Ultrasound and Computed Tomography-Based Cardiac Image Registration

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Graphical abstract

Reference	Year	Method
Zhong, H. *et al.* [58]	2006	Virtual touch and Iterative closest point
Sun,Y. *et al.* [59]	2007	Normalized Cross Correlation
Huang, X. *et al.* [10]	2009	Mutual Information and Fiducial marker
Lang, P. *et al.* [61]	2011	Iterative closest point and Mutual information
Feng, L. *et al.* [62]	2012	Iterative closest point followed by Mutual information
Sandoval, Dillenseger [60]	2013	Intensity based similarity measure
Feng, L. *et al.* [63]	2013	Generation of the synthesis 4D cardiac CT images

Abstract

A literature survey of Ultrasound and Computed Tomography (CT) -based cardiac image registration is presented in this article. We aim to provide the reader with a preliminary discussion into the area of cardiac image registration, as well as to briefly describe the major contributions in the field and present collective and comprehensive knowledge as guidelines for beginners in this field to initiate their research. We also highlight the major challenges where CT and Ultrasound are the modalities concerned in fusion and registration tasks. Further, we found that a majority of research in medical image registration are suitably categorized based on these factors: anatomy, imaging modality and image registration methods. Our focus in the article is on Ultrasound-CT image registration of the heart, where numerous algorithms under this scope have been elaborated. Overall, multimodal cardiac image registration offers great benefit for image visualization systems during surgery. It facilitates accurate alignment of the patient's heart imagery acquired via different imaging sensors, without extensive user involvement and interception. Through registration, the combined anatomical and functional information from multiple modalities may be derived by the medical practitioner to aid in physiological understanding, disease monitoring, clinical treatment and diagnostic purposes.

Keywords: Computed tomography; multimodal; medical imaging; registration; literature survey; ultrasound

Abstrak

Artikel ini adalah satu kajian literatur yang membentangkan pendaftaran imej jantung dalam *Ultrasound* dan Tomografi terkomputasi. Artikel ini bertujuan untuk memperkenalkan dan menyediakan pembaca dengan perbincangan awal dalam bidang pendaftaran imej jantung, menerangkan sumbangan-sumbangan besar dalam bidang ini secara ringkas dan juga memberi pengetahuan kolektif dan komprehensif sebagai panduan untuk memulakan penyelidikan baru dalam bidang ini. Kami juga mengetengahkan cabaran utama di mana Tomografi terkomputasi dan *Ultrasound* adalah modaliti pengimejan yang terlibat dalam proses gabungan dan pendaftaran. Di samping itu, kami mendapati bahawa majoriti penyelidikan dalam pendaftaran imej perubatan dapat dikategorikan berdasarkan faktor anatomi, pengimejan modaliti dan kaedah pendaftaran imej. Fokus artikel ini adalah mengenai algoritma-algoritma yang digunakan dalam pendaftaran imej *Ultrasound*-Tomografi terkomputasi jantung. Secara keseluruhan, pendaftaran imej jantung dalam pelbagai modaliti pengimejan menawarkan banyak manfaat dalam sistem visualisasi imej semasa pembedahan. Ia memudahkan kerja-kerja penjajaran imej jantung pesakit yang diperolehi melalui pelbagai sensor pengimejan, tanpa penglibatan pengguna yang meluas dan pemintasan. Melalui pendaftaran, maklumat mengenali anatomi dan fungsi dari pelbagai modaliti yang diperolehi oleh pengamal perubatan dapat digabungkan untuk membantu dalam pemahaman fisiologi, pemantauan penyakit, rawatan klinikal dan tujuan diagnostik.

Kata kunci: Tomografi terkomputasi; pelbagai modality; pengimejan perubatan; pendaftaran; kajian literature; *ultrasound*

1.0 INTRODUCTION

Medical imaging is an integral part of modern healthcare. It continues to be used widely for diagnosis, treatment planning, disease monitoring, image-guided surgery and managing patient's historical documentation. The quantitative evaluation of medical images, using computer-aided imaging techniques, is able to help the medical practitioner in reaching an unbiased and objective decision within a short span of time [1, 2]. Numerous imaging modalities born from various sensors are available nowadays which include Computed Tomography (CT), Magnetic Resonance I However, it also exposes both patient and surgeon to harmful ionizing radiation, especially during long surgical periods. It is thus recommended that conventional CT be implemented pre-operatively for surgery planning, and practitioners resort to CTF only if highly necessary. Meanwhile, diagnostic Ultrasound is the most commonly used modality during surgery. It offers a practical alternative to CT due to its safety, low cost, ease of use, real-time capability, minimal procedural disruption, portability, and compatibility with standard operating room equipment [10]. maging (MRI), Positron Emission Tomography (PET), Ultrasound, and single-photon emission computerized tomography (SPECT). The images obtained however are usually raw in nature and require subsequent pre-processing, information extraction and data analysis in order for the potentially useful information to be benefitted by the medical practitioner. Different imaging modalities convey different advantageous information for clinical analysis and decision-making. Each modality therefore has its focus on different clinical domains and range of applicability [3]. For example, CT and MRI are mainly used to capture anatomical information of the organs, while PET and SPECT provide functional and metabolic information that highlight a tumor's activity [3]. Due to this, it is not feasible for a single imaging modality aforementioned to comprehensively derive all details required to conduct a proper diagnosis and treatment plan.

As an alternative, a more reliable clinical analysis and accurate decision making may be facilitated by a combination of information from different imaging modalities. This is the motivation of multimodal image registration, which offers improved and complementary information by establishing the correspondence between the information acquired from multiple imaging modalities [4]. Image registration is defined as a process of finding a transformation that spatially and geometrically aligns two or more images [5, 6]. In medicine, registration helps medical practitioners to merge important spatial and temporal information from different sources, thereby aiding in the planning and providing of detailed road maps which may lead to a successful treatment plan for the patient.

As the medical imaging technology advances, the role of medical imaging has expanded beyond just the visualization and inspection of anatomic structures [7]. Medical imaging tools and systems have also been developed for clinical use such as image-guided surgery. Registration of image data encompassing various stages of cardiac surgery for example–pre-operative, intra-operative and post-operative, is seen as essential for the diagnosis, treatment planning and monitoring of cardiovascular diseases [8].

This would seem an ideal solution, nevertheless, there remain a few challenges that hinder the progress of registration. The first is the spatial relationship that is unknown between existing pre-operative images and the physical patient in the operating room [9]. For instance, pre-operative CT images coupled with intra-operative Ultrasound images may assist the surgeon to identify the patient's cardio anatomical structure. Though the contrast in viewing size, angle and position between the respective modalities means that the exact spatial correspondence is unavailable. Secondly, challenges are also present through the limitations in operating certain imaging modalities. CT-based fluoroscopy (CTF) is a method developed that is capable of producing richly-detailed and moving images of the heart during surgery [10]. However, images generated via Ultrasound tend to have poor spatial resolution, coupled with high noise content, that they are often inadequate for cardiac surgery.

Table 1 Medical image registration classification proposed by Maintez *et al.* [13]

Fundamental criteria	Subdivision
Dimensionality	Spatial dimension (2D, 3D, 4D) Temporal series
Modalities involved	Monomodal Multimodal Modality to model
Interaction	Interactive Semi-automatic Automatic
Nature of Registration basis	*Extrinsic:* Invasive, Non-invasive *Intrinsic:* Landmark-based Segmentation-based Voxel property-based
Domain of Transformation	Local Global
Nature of Transformation	Rigid Affine Projective Curved
Subject	Intra-subject Inter-subject Atlas
Object	Head, brain Thorax, lungs, heart Abdomen Pelvis, spine
Optimization procedure	Parameters computed Parameters searched

Hence the goal of registering pre-operative CT and intra-operative Ultrasound images is to complement these features to produce better looking output images, which significantly boast real-time capability and are non-invasive in nature. To this end, multimodal image registration is an essential part in the medical imaging field.

A substantial amount of work has been devoted to medical image registration over the past few decades due to its potential clinical impact, which have produced a broad range of methodologies for various conditions, types of data, problems and application. Brown [11] first published a comprehensive survey of image registration techniques in 1992. Elsen *et al.* [12] have reviewed and classified the medical image registration algorithms by their dimensionality, domain and elasticity of the transformation, origin of image properties, tightness of property coupling, parameter determination and degree of interaction. More significantly, Maintz *et al.* [13] have introduced nine fundamental criteria based on certain characteristics that a registration algorithm may exhibit. They are summarized as in Table 1. It must be noted however that not all methods in literature can be classified into the categories above. Some methods are developed to register images for much more complex and wider range of applications, which may comprise a combination of several classifications.

A number of survey papers, review articles and books on medical image registration have been proposed and published over the years [14-20]. Though essentially, works specific to cardiac registration have been sorely lacking. Most studies tend to focus on other parts of the human anatomical structure such as the brain, lungs and abdomen, as opposed to the heart. To date, the work by Makela *et al.* [21] in 2002 remains the only notable review article pertaining cardiac image registration methods.

Registration of the heart is known to be a unique endeavor that possesses its own complications, notably deformation due to the cardiac and respiratory cycles, which may not be an issue in other parts of the anatomy. The study of multimodal cardiac registration therefore presents a novel and interesting outlook into a relatively new research area that can potentially benefit the medical industry in the future.

In this paper we aim to provide the reader with a preliminary discussion into the area of cardiac image registration, as well as to briefly describe the major contributions in the field and present collective and comprehensive knowledge as guidelines for beginners in this field to initiate their research. We have also highlighted the major challenges where CT and Ultrasound are the modalities involved in registration tasks. This paper starts with an introduction to multimodal medical image registration in Section 1. Section 2 describes the anatomical structure of the heart and the issues involved in its image acquisition, and in turn Section 3 presents the details of the imaging modalities of choice involved–namely CT and Ultrasound. Section 4 discusses the various methods that have been used in literature to perform cardiac image registration. Lastly, section 5 concludes the paper with a brief description of the future direction involving cardiac image registration that is on-going at the IJN-UTM Cardiovascular Engineering Centre.

■2.0 CHALLENGES IN CARDIAC-BASED IMAGE REGISTRATION

Numerous studies related to multimodal image registration of several essential human organs such as brain [22-27], lungs [28-33], kidney [34-37], liver [38-41] and pelvis [42, 43] have been conducted in literature. As mentioned previously, the topic of research particular to the heart though is not yet prevalent. This section describes the anatomy of the human heart and the image registration issues that exist due to its deformable characteristics.

The heart is a muscular organ the size of a closed fist; it functions as a circulating pump for the human body. It is a vital organ that continuously circulates blood throughout the whole body during a person's lifetime. Blood must be constantly pumped through the human blood vessels in order to supply oxygen and nutrients to the cell. The heart beats up to 100,000 times per day and pumps around 5 liters of blood each minute. The heart sits within the pericardial cavity, which is a fluid-filled anatomical region. The pericardium is a type of serous membrane that produces serous fluid to lubricate the heart and also serves to hold the heart in position. The heart wall is made of three layers: epicardium, myocardium and endocardium. The thickness of the wall varies in different parts of the heart. The atria are smaller, thinner, and feature less muscular walls than the ventricles. The ventricles have thicker myocardium compared to the atria as the ventricles are required to pump blood to the lungs and throughout the body. Meanwhile, the heart's left section contains more myocardium as it is responsible for pumping blood through the whole body; whereas the right side only pumps blood to the lungs. The heart contains four chambers: right atrium, left atrium, right ventricle and left ventricle [46].

Prior to cardiac-based image registration, the segmentation of images plays an important pre-processing step that enables the extraction of anatomical and contractile functional information of the heart. Segmentation of the epicardium and endocardium is essentially the most challenging part in the pre-processing step [44]. Segmentation of epicardium is more complex, as the image tends to display poor contrast and high fuzziness of the voxel intensities between the outer tissues and the heart. Second, segmentation of the endocardium too is not easy due to low visibility of the papillary muscles while local image features, such as intensity and gradient, have not shown real contours near the papillary muscles. Errors that tend to occur in the segmentation process will directly affect the performance and accuracy of the image registration algorithm in whole.

The immense complexities of the heart anatomy, its deformation and its non-rigidity characteristic have all made cardiac registration a particularly difficult process. The heart valvular plane moves between 9 to 14 millimeters towards the apex and the myocardical walls thicken approximately 10 to 15 mm during a cardiac cycle, from diastolic end to systolic end [45]. Further, the heart has much fewer fixed and accurate anatomical landmarks [21]. No common method has yet been able to perform multimodal registration of cardiac images automatically, as the cardiac images from various modalities are usually shown in differing and contrasting orientations, voxel intensities and fields of view [21]. For this reason, most cardiac registration methods tend to be implemented semi-automatically. The approach effectively requires anatomical knowledge from expert personnel as an additional system input, thereby restricting its operability and user-friendliness.

■3.0 IMAGING MODALITIES INVOLVED IN CARDIAC REGISTRATION

There are three imaging modalities that are most frequently used by medical practitioners in relation to heart disease: Computed Tomography (CT), Magnetic Resonance Imaging (MRI) and Ultrasound. In this paper, we have decided to focus the discussion on CT and Ultrasound as the registration modalities. It is already known that the objective of the registration process is to align the image data from two different imaging modalities, so as to obtain benefits and compensate weaknesses from both images. The choice of modalities therefore reflects real-world situations as exemplified in the previous section, in which high temporal resolution and real-time processing capability of Ultrasound is aligned and combined with high spatial resolution and better quality CT images. The combined information helps to guide the medical practitioner as it derives all details required to facilitate better analysis, treatment planning and diagnosis.

The advantages of CT-Ultrasound registration as opposed to CT-MRI or MRI-Ultrasound is notable. Scanning via MRI utilises magnetic fields and radio waves, which are known to be harmful, and computer aids to form images of the body structure. Due to these strong magnetic fields, implementation of MRI has been restricted from the operating room, as a number of implementation issues arise including restricted surgical access, incompatibility with conventional surgical instruments, and increased complexity of procedures [10]. MRI imaging can only therefore be implemented in the pre-operative stage of surgery. As shall be described later, a majority of these issues are found to be also prevalent within CT scans. The nature of MRI image acquisition is essentially similar to that of CT.

In contrast, Ultrasound imaging may be implemented intra-operatively with minimal disruption to the procedure and is fully compatible with standard operating room equipment. Real-time capabilities and non-invasive properties of Ultrasound imaging play a vital role in visualizing the heart and guiding the surgeon during surgery, as the Ultrasound image are enhanced by registering with the pre-operative CT cardiac images.

In terms of image features however, CT concentrates on hard structure such as bones and joints while MRI discerns soft tissues, much like Ultrasound. It is clear that each modality offers its own advantages whilst having several limitations. Based on all factors, an optimal approach would be to combine the best aspects of two modalities; that is, CT and Ultrasound.

3.1 Computed Tomography

CT is a highly accurate imaging system that has proven extremely beneficial in assisting radiologists to diagnose cardiovascular diseases. The term 'tomography' entails that a session of the CT scanning procedure displays the organs, bones and other tissues in a thin slice or cross-section series of two dimensional images. 2D CT slices may then be reconstructed and visualized in three dimensions, as shown in Figure 1 [47, 48] and Figure 2.

Table 2 Hounsfield units values with respective substances [49]

Substance	Hounsfield Units
Bone	400 to 1000
Soft tissue	40 to 80
Water	0
Fat	-60 to -100
Lung	-400 to 600
Air	-1000

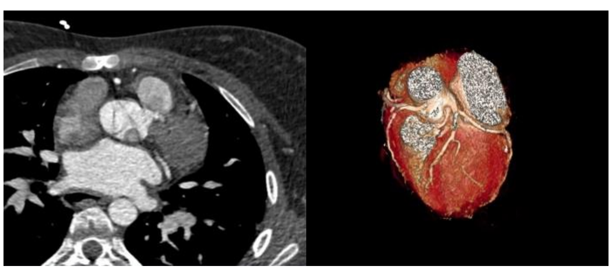

Figure 1 2D CT cross-sectional slice (left) and 3D CT image after reconstruction and rendering (right) of the heart [48]

The source of CT, the X-ray produces a narrow, fan-shaped beam used to irradiate a section of the patient's body. The range of thickness of the fan beam can be from 1 to 10 mm. The CT image is based on the absorption of X-rays as they pass through different parts of a patient's body. Depending on the amount absorbed in a particular tissue, such as muscle or lung, different amounts of X-ray will pass through and exit the body. The resultant X-rays interact with an X-ray receiver, thus providing a two dimensional projected image of the tissues within the patient's body. Thus, the formation of a CT image is based on the exponential attenuation of X-ray energy as it passes through the tissues.

There are two types of CT scans. First, a conventional CT scan is taken slice by slice and requires the patient to remain static and hold his breath during the scanning process to prevent blurring of the images. On the other hand, a spiral CT scan runs continuously in a spiral path as the X-ray tube rotates around the patient. It allows more image slices to be captured in a shorter period of time. Modern CT scanners use a high resolution matrix with either 256×256 or 512×512 pixels. Furthermore, CT number is defined as the values of each pixel stored in the CT image after reconstruction. It represents the attenuation value of the corresponding voxel intensity. The unit for the CT number is Hounsfield Unit (HU). A wide range of HU is used for different types of tissues as shown in Table 2 [49].

CT scanning possesses many advantages over other modalities, among them are high spatial resolution, shorter scan times and adaptability for a wider range of conditions. Conversely, its main drawback is its injection of the contrast dye in certain applications, which may cause an allergic reaction, as well as high dose of radiation exposed to the patient [50]. Real-time CT applications such as CT fluoroscopy also expose relatively high level of radiation to medical practitioners. For this reason, CT imaging is practiced preferably outside the operating theatre.

3.2 Ultrasound

Ultrasound is a diagnostic device used routinely to observe the patient's internal organs, by transmitting and receiving sound waves into the human body. An Ultrasound image is the result of the sound waves emitted from the Ultrasound probe, which are then reflected off body tissues before returning and are accumulated by the same probe. The Ultrasound probe applies the principle of piezoelectric effect to convert electricity into sound waves and vice versa.

The piezoelectric element is a type of artificial crystal that is commonly used in modern transducers, and is treated with high temperatures and strong electric fields to produce the piezoelectric property that is necessary to generate sound waves. The expansion and contraction of the piezoelectric element must be at 20000 times per second for it to produce the Ultrasound wave.

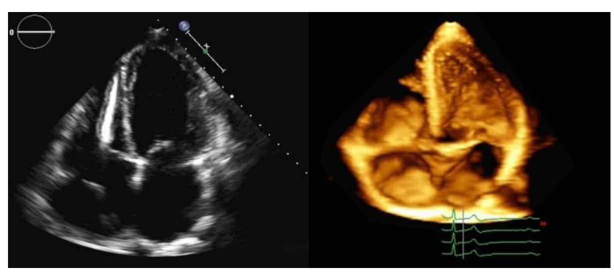

Figure 2 2D Ultrasound image (left) and 3D Ultrasound image (right) of apical four chamber view of the heart [51]

An Ultrasound transducer with many piezoelectric elements converts electrical pulses from the transmitter into Ultrasound beams. This beam propagates into the body, where echoes from interfaces between tissues with different impedances are reflected back to the transducer. The echoes received by the piezoelectric tend to deform the crystal, convert it into electrical signals and thereby producing a 2D Ultrasound image.

In extension, a 3D Ultrasound image can be obtained by acquiring the volume data and reconstructing the 2D Ultrasound images in different planes. There are four different approaches to this: mechanical scanners, free-hand techniques with position sensing, free-hand techniques without position sensing and 2D arrays [52]. 4D Ultrasound meanwhile is defined as a 3D Ultrasound image that is displayed in real-time, whereby time is the designated fourth dimension.

The limitation of Ultrasound image often relates to poor contrast, low resolution and low image quality. In addition, noise, echo effects and occlusion too are among the main artifacts that limit the quality of the Ultrasound image [53, 54, 55]. These artifacts may instigate errors that hinder the accuracy of image analysis tasks. Nevertheless, the modality is still routinely used for assessment and diagnosis of the heart due to its high temporal resolution, real-time capability, non-invasiveness, portability, low cost and possesses no danger of side effects to the patient.

3.3 Issues Pertaining Ultrasound-CT Registration

The correlation between Ultrasound and CT images is naturally rather poor [21, 36]. This is due to several factors: first, the image acquisition of Ultrasound is heavily operator-dependent. Appropriate skills are vital in acquiring image data, so as to avoid undesired results. Secondly, the field of view (FOV) of Ultrasound is limited; the user may only view certain sections of the organ at a time. CT scans meanwhile have a much more comprehensive FOV. Moreover, Ultrasound images are acquired off true axial, sagittal or coronal planes, while an image derived from a CT scan constitutes the cross-section of the organ. The distortion in angular planes further hampers the task of automatic correlation [21].

Several pre-processing steps such as image de-noising, image enhancement and image segmentation are therefore necessary in order to increase the degree of likelihood of both images and ensure the higher accuracy of the subsequent analyzing steps such as registration process. The choice of pre-processing methods is highly dependent on the type of application implemented and the properties of image data. Several commonly used medical image pre-processing methods are listed in Table 3.

4.0 MEDICAL IMAGE REGISTRATION METHODS

Image registration is the process of establishing the correspondence between images of the same scene. It maps the related position in one coordinate space to the corresponding position in another coordinate space. In other words, image registration is essentially a transformation procedure that aligns the images spatially and geometrically for similar or different subjects, acquired from similar or different modalities, at similar or different viewpoints and timelines [5, 6]. The generic image registration algorithm can be decomposed into four components [11]. First, feature space extracts the feature chosen to be used for mapping. Second, search space determines the degree of transformation that brings alignment between the reference and target images. The most common transformations include rigid, affine, projective, and curved [13]. This is followed by a similarity measure which estimates the similarity merit of the reference image and transformed target images. Lastly, the search strategy, also known as optimization step, decides how to compute the optimal transformation. The search process continues according to the strategy until a transformation which satisfies the similarity measure is found.

Table 3 Medical image pre-processing steps and their methods

Image Pre-processing	Techniques
Image de-noising	Median filter weighted median filter Wiener filter Morphological operation wavelet de-nosing
Image enhancement	Normalization Histogram equalization Contrast stretching
Image segmentation	Histogram-based Methods Statistical Model-based Methods Region-based Methods Graph-based Methods Deformable Model-based Methods Atlas-based Methods

Cardiac image registration algorithms can be divided into either extrinsic methods or intrinsic methods. Recent related studies in literature are summarized in Table 4. Extrinsic implies that the correspondence between the images is obtained from artificial objects that have been attached to the subject [16]. They are purposely designed to be visible and detectable by the modalities involved. Huang *et al*. [10] have proposed and demonstrated an intra-cardiac procedure to register 2D intra-cardiac Ultrasound images to 3D CT image of the heart phantom. They aim to present the complementary anatomical information of the heart phantom from both imaging modalities simultaneously by maximizing the mutual information metric. A spherical glass target was attached to the surface of the heart phantom as the fiducial marker to evaluate the registration accuracy by calculating the target registration error (TRE). The study gained positive results with 3.7mm of the resultant TRE on the heart phantom [10]. However, the extrinsic method of cardiac registration can only be utilized for testing and evaluating the registration algorithm. It is not possible to attach the fiducial marker on the surface of the human heart before pre-operative images are acquired, due to its invasive nature. Application of extrinsic methods is also limited to rigid registration as it does not include visual-based information related to the subject [56]. It thus cannot guarantee accurate results as the heart tends to deform along with the patient's body position, movement, and respiration and cardiac cycles [57].

On the other hand, intrinsic registration methods are based on inherent properties such as anatomical landmark points, geometric features or image intensity that are obtained directly from the patient using an imaging device. It can be classified into two basic categories: feature-based and intensity-based.

Zhong *et al*. [58] present a feature-based technique known as virtual touch used to collect the intra-operative surface points of the heart by using a 3D Ultrasound catheter. The iterative closest point (ICP) method is then implemented to register the surface points of the left atrium to the surface model derived from CT images. The method boasts fast, accurate and stable performance based on a static heart phantom experiment as it is able to extract high quality surface points more than 700 times faster than conventional methods at 1.2 mm TRE.

Meanwhile Sun *et al.* [59] propose an intensity-based method for registering 2D intra-cardiac Ultrasound images to pre-operative 3D CT images to help the physicians learn and perform complex electrophysiology ablation procedures. Due to the difference in voxel intensity of Ultrasound and CT images, the gated intra-cardiac Ultrasound image and its corresponding CT gradient magnitude slice are used to compute the similarity measure to optimize the registration parameter. The research utilises normalized cross-correlation (NCC) as the similarity measure, and best neighbour method in the optimization step. The research has been successful in animal testing and it does not require segmentation the Ultrasound images. However, user interactions are still required to key in the proper threshold value to produce the CT gradient magnitude data and provide the initial alignment before the intensity-based registration process is applied.

In [60], Sandoval and Dillenseger present a work to evaluate and compare the performance of eight intensity-based similarity measures namely mutual information (MI), normalized mutual information (NMI), entropy correlation coefficient (ECC), joint entropy (H), point similarity measure based on MI (PSMI), energy of histogram (E), correlation ratio (CoR) and Woods criterion (WC). The experiments were set up to register 2D intra-operative Ultrasound images and 3D pre-operative CT images of the left atrium and the pulmonary veins. In a rigid registration context, WC and MI obtain better performance compared to others. Though for elastic registration, NMI has higher efficient results than MI.

Furthermore, Lang *et al.* [61] have implemented and evaluated two different methods, feature-based iterative closest point (ICP) and intensity-based mutual information (MI) method to register a peri-operative CT image and intra-operative TEE image. The experiments were conducted on small preliminary data sets and results affirm the potential for these registration techniques to be implemented in real-time applications for minimally invasive cardiac interventions. In concurrence, Feng Li [62] from the same research group have developed a hybrid method to register intra-operative Ultrasound and pre-operative CT images. The method is divided into two stages. First, the ICP method is used to obtain the geometric transformation based on the anatomical features extracted from first frame of the Ultrasound and CT images. This transformation acts as the initial alignment for stage two. Secondly, the intensity-based mutual information technique is implemented to register Ultrasound images to the CT image Powell's optimization method is used to search the transformation parameters until the parameters that maximize the mutual information between two images are found. The transformation computed in this study is limited to rigid transformation with six parameters, three for translation over the X, Y and Z axes and three for rotation over roll, yaw and pitch. However, the segmentation of CT and Ultrasound images as well as the initialization using the ICP algorithm would have to be done manually prior to surgery [62].

Another work by Feng Li *et al.* [63] has introduced a method to generate synthesized 4D cardiac CT images using a static CT image and 4D ultrasound images. The deformation fields are generated by performing non-rigid registration between pre-operative 4D Ultrasound datasets. They are then used to deform the static CT into a series of dynamic CT images. The results were validated by comparing the synthesized CT images to the CT database which was pre-acquired from the patient. The results however suffered from inconsistency due to the different image acquisition protocols for CT and Ultrasound. During the CT scan, the patient heart rates are reduced by using β-blockers, while this does not apply during Ultrasound procedures. In addition, the patient is fully conscious during CT scans, while TEE scanning procedures dictates the patient to be under general anesthetic. The different approaches cause the patient's cardiac motion and heart rate to be different which can cause misalignment of intra-operative Ultrasound images and pre-operative CT images. Likewise, the FOV of the Ultrasound images may limit the features that are deformed in the synthetic CT images as the deformation fields of the synthetic CT images are derived from the Ultrasound images [63].

An observation of the trend of current literature suggests that the research direction has shifted from extrinsic to intrinsic-based methods. This may be due to several limitations posed by extrinsic approaches, including its invasive nature and lack of dynamic registration. Despite that, methods such as stereo-tactic frame and screw-mounted markers are still in clinical use on several organs as they possess reliable accuracy and are computationally efficient. In cardiac image registration however extrinsic methods do not guarantee superior results as the heart position tends to change along with the patient's body position, movement, respiration and cardiac cycle. Such an example of extrinsic methods towards the heart has been implemented in [10] that enables validation of the accuracy of cardiac rigid registration algorithm by attaching fiducial markers on a heart phantom.

Table 4 Cardiac image registration methods

Reference	Year	Method
Zhong, H. *et al*. [58]	2006	Virtual touch and Iterative closest point
Sun,Y. *et al*. [59]	2007	Normalized Cross Correlation
Huang, X. *et al*. [10]	2009	Mutual Information and Fiducial marker
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Intrinsic methods are categorized into either feature-based or voxel property-based methods. Feature-based approaches use salient, accurate and identifiable corresponding anatomical features in both registered images as an input. They are usually functionally important surfaces, curves and points that are located throughout the images. The mapping must align with the anatomical information to ensure that the registration is biologically and physiologically valid. Though since only several spatially accurate anatomical landmarks are available in a cardiac image, the task of localizing the corresponding anatomical landmarks remain a challenging one, especially in multimodal registration.

Voxel property-based methods exploit the full image content and match the intensity patterns in the images using statistical criteria. They measure the intensity similarity between the source and the target images in order to adjust the transformation until the similarity measure is maximized. Compared to feature-based methods, voxels have an important advantage in that it does not require *a priori* extraction of the registered features. In literature, a popular and particularly promising voxel property-based method named mutual information (MI) has been continuously researched. The method is a voxel similarity method which makes no assumptions on the relation between the registered images, hence rendering it suitable for multimodal registration. However, a known drawback of MI is that it does not hold spatial information presented in both registered images [65]. This may lead to mis-registration even when the MI measure has been maximized. Several researches have since proposed a hybrid framework which adapts and incorporates MI- and feature-based methods to overcome these limitations. Overall, it is of note that cardiac registration remains largely unexplored and much research can still be done within this field.

■5.0 CONCLUSION

Multimodal registration of cardiac images is seen as an essential preliminary step to fuse the heart's anatomical and functional information. Accurate registration of different imaging modalities provides useful evidence for clinicians and researchers to observe the human heart which is unavailable from a single modality. Since its inception, medical imaging technology continues to grow, as proven by the improved accuracy and resolution of current imaging modalities.

Nevertheless, each modality is subjected to its own advantages and disadvantages, thus leading to the idea of a multimodal imaging framework that can combine the best visual aspects from various sensors to provide clinically relevant information. A good image registration algorithm is thus critical as any inaccuracies shall be directly linked to poor results of multimodal image fusion [64]. The algorithm's processing speed must also be capable of processing real-time data as the output of registration would be continuously used to guide the clinician in any decision-making process during surgery.

On top of the above, medical knowledge is vital in designing a registration algorithm as it ensures medical relevance and accurate clinical outcome. The characteristics of cardiac are inherently complex, dynamic, non-rigid and deformable. The cardiac position tends to change with each movement involving body position, respiration and cardiac contraction [14, 46]. There are only several anatomical landmarks in cardiac images, which tend to be visualized and interpreted in numerous ways through different imaging modalities. Some landmarks are also prone to be less visible through certain modalities and even in some pathological cases, such as ischemia. The area of interest, type of modality and application are thus all inter-dependent and are all important information to be obtained prior to registration.

Cardiac image registration remains an open and challenging field since there is yet to be a standard procedure or a fully automatic method that exists to handle the various natures of clinical situations. A better understanding and expansion of both medical knowledge of the organ of interest as well as technical knowledge of image registration techniques would contribute to its development and widespread use.

5.1 Future Direction of Cardiac Registration

Standalone rigid image registration methods are inadequate to achieve correct compensation of cardiac movements and deformation. However, rigid registration can be legitimately implemented as an initialization step for further studies of dynamic and non-rigid registration. This has been the central aim of collaborative research efforts at the IJN-UTM Cardiovascular Engineering Centre in Universiti Teknologi Malaysia. Figure 3 presents the focus of the centre's research direction in cardiac imaging.

The overall goal is to facilitate surgery through higher quality real-time imagery of the heart. The patient undergoes CT scan prior to surgery where the images are stored in the hospital database. In intra-surgery, the Ultrasound probe is used by the surgeon on the patient. The resulting Ultrasound images are merged in real-time with the pre-existing CT dataset and the output are continuously displayed on the screen, thus giving an impression of dynamic and deformable 'fused' cardiac images containing salient features that can greatly assist in locating certain regions and critical decision-making.

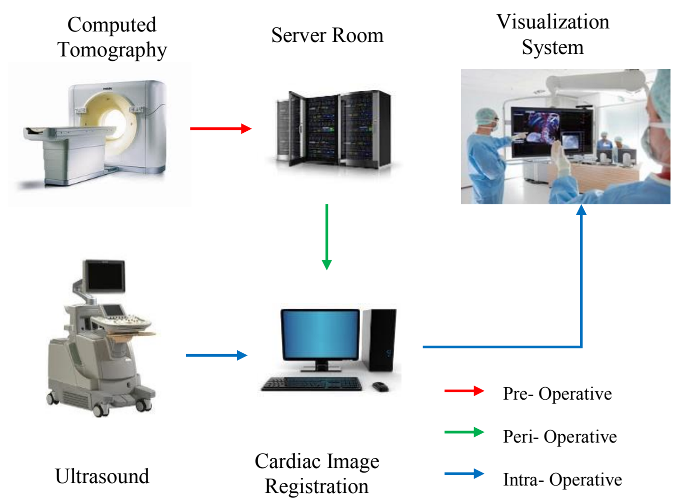

Figure 3 Our next research direction and framework, registration of intra-operative Ultrasound images and pre-operative CT images

In conclusion, this paper has discussed rigorously the study of the heart as well as cardiac image registration methods and the modalities they involve. As noted above, registration plays a decisive role in visualizing heart imagery during image-guided surgery, where it serves as a guide in making critical surgical decisions. Registration therefore requires a compromise between all aspects including accuracy, precision, robustness, reliability, computational speed, interactivity, user-friendliness, patient comfort and cost; that should also be easily integrated into a standard clinical workflow and is compatible with operating room protocol for surgeries.

It is hoped that strong progress in multimodal image registration and the field of medical imaging overall in the coming years shall contribute to more saving of lives and better healthcare for the society.

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