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MEDICAL IMAGING & VISUALIZATION

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COMPUTER INTEGRATED SYSTEM  
MEDICAL IMAGING &  
VISUALIZATION

Professor Dr. Rahmita Wirza O.K. Rahmat



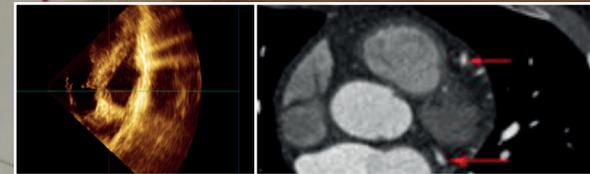
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**MEDICAL IMAGING &**  
**VISUALIZATION**



Professor Dr. Rahmita Wirza O.K. Rahmat

# COMPUTER INTEGRATED SYSTEM MEDICAL IMAGING & VISUALIZATION

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# Contents

Abstract	1
Introduction	3
Angiography Image Analysis and Diagnosis	8
Echocardiography Image Analysis and Diagnosis	34
3D Information Medical Visualization and Diagnosis	59
3D Multimodal Medical Images Registration for Visualization	73
3D Heart Surface Visualization	95
Conclusion	112
References	113
Biography	117
Acknowledgement	119
List of Inaugural Lecturers	121
Index	135



## **ABSTRACT**

The intent of this book's conception is to present research work using a user centered design approach. Due to space constraints, the story of the journey, included in this book is relatively brief. However we believe that it manages to adequately represent the story of the journey, from its humble beginnings in 2008 to the point where it visualizes future trends amongst both researchers and practitioners across the Computer Science and Medical disciplines.

This book aims not only to present a representative sampling of real-world collaboration between said disciplines but also to provide insights into the different aspects related to the use of real-world Computer Assisted Medical applications. Readers and potential clients should find the information particularly useful in analyzing the benefits of collaboration between these two fields, the products in and of their institutions.

The work discussed here is a compilation of the work of several PhD students under my supervision, who have since graduated and produced several publications either in journals or proceedings of conferences. As their work has been published, this book will be more focused on the research methodology based on medical technology used in their research. The research work presented in this book partially encompasses the work under the MOA for collaborative Research and Development in the field of Computer Assisted Surgery and Diagnostics pertaining to Thoracic and Cardiovascular Diseases between UPM, UKM and IJN, spanning five years beginning from 15 Feb 2013.



## INTRODUCTION

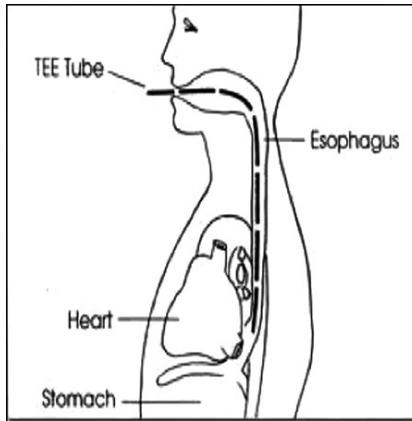
Coronary artery diseases are the main cause of deaths all over the world today. Heart diseases manifest as a result of major changes in life styles as well as unhealthy food habits. According to the coronary artery disease treatment guide from the website <http://my.clevelandclinic.org>, the heart is responsible for moving around 3000 gallons of blood in the body every day. The heart itself needs blood to do its job and to function properly. Cardiovascular imaging is used for the diagnosis of diseases of the heart itself and the coronary arteries. There has been a variety of cardiovascular imaging techniques developed in this field and a growth in their clinical use over the last few years. The goal of cardiac imaging is to diagnose major disorders that might occur in the heart or its arteries. Currently, one of the most commonly used imaging technologies for coronary arteries is angiocardiology or angiography. Imaging modalities that are common in cardiac abnormalities are Angiography, Echocardiography and Computed Tomography Angiography (CTA).

Angiogram, otherwise known as catheter angiography, is a procedure performed to diagnose narrowing, blocked, dilated or abnormal arteries. This minimally invasive test uses X-rays to expose different parts of the body, such as the heart, brain, abdomen, kidney, legs, etc. It can be performed using contrast dye materials and be used especially with coronary arteries. The catheter is a thin plastic tube that is inserted into one of the main arteries in the body, through the thigh or arm, and guided to the area to be explored. The dye is then injected and images are captured, showing details of that specific area. Most commonly, angiograms are used to diagnose coronary artery diseases of blockages and other abnormalities. A catheter is inserted through the groin or sometimes the arm to reach the arteries of the heart and imaging is then started using a

dose of X-ray radiation. After the test, the contrast material should be eliminated from the body by giving the patient some fluids to expel the contrast material through the kidney and urine. It is helpful for physicians and has many advantages as well as some disadvantages. The advantages are that it is an accurate test to the level that it may eliminate the need for surgery, allows real-time diagnosis and treatment, gives very clear images and the catheter insertion makes it possible for cardiologists to combine diagnosis and treatment in a single procedure. The method also provides a high degree of accuracy that cannot be found in other non-invasive procedures.

There are two types of echocardiography imaging techniques - the non-invasive dynamic or freehand imaging method and Transesophageal Echocardiography (TEE). The freehand imaging method is normally used for paediatric and young patients with small body surface areas (BSA), where the heart size and the distance between the probe and the heart are small. The advantages of this method are comfort, risk free and it enables the operator to modify and guide the acquisition of images from different angles. However, there are many limitations with this method, especially for adult patients with a thick chest and patients with heart enlargement. In this method, the distance between the probe and the heart, the shadow of the chest bone, fat, air (in the lungs) and motion of the probe during the acquisition are all factors that may affect the image quality. On the other hand, the Transesophageal Echocardiography (TEE) imaging method overcomes all the limitations of the freehand method since a cardiologist can insert the probe through the esophagus to be placed near the heart, which will give clearer images compared to the freehand method, as illustrated in Figure 1. A TEE test lasts around 15 minutes and it is able to give better information about the heart during surgery, according to

the website of the American Heart Association (<http://www.heart.org/HEARTORG/>). The only limitation of the TEE method is that it cannot be used with patients who have difficulty in breathing or who have an infection in the esophagus.



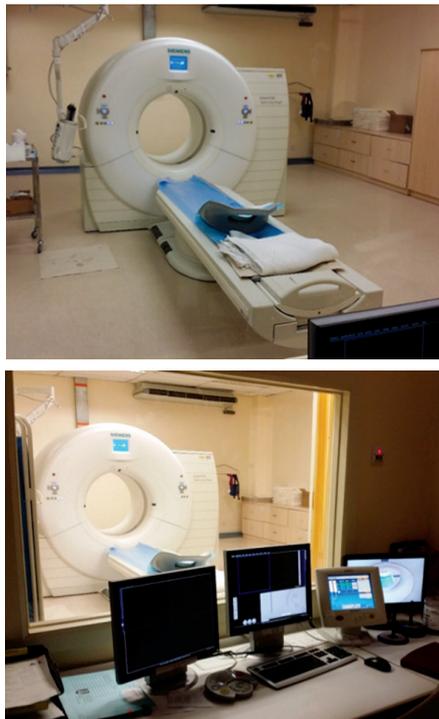
**Figure 1** Transesophageal echocardiography, the probe is inserted inside esophagus

For Computerized Tomography Angiography (CT Angiography), generally the CT scan is a form of X-ray which utilizes a computer system to generate cross-sectional images of the human body. In this technique, a 3D image of a component can be reconstructed from a series of 2D X-rays.

The modern progress of CT scan devices signifies a promising future with regard to CT imaging utilized in coronary artery disease diagnosis. The speed benefits of 64-slice CT scans allow its use for cardiac imaging. Further, dual source CT scanners together with dual X-ray tubes and also dual array of 64-slice detectors were introduced by Siemens in 2005. This technique permits better temporal resolution by obtaining a complete CT slice in one fourth

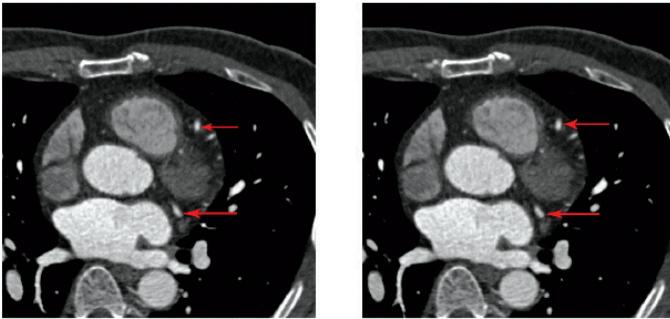
of the rotation and reduces motion blurring at high heart rates. Using the advancement in sub second rotation speeds coupled with multi-slice CT, higher resolution and higher speed CT scans can be acquired at the same time. It allows for the utilization of this technique for cardiovascular imaging.

The CT Angiography is a type of medical exam that mixes a CT scan with the injection of a specific dye, referred to as a contrast material, to generate images of vessels in specific parts of the body. For this purpose, the contrast material is often injected into a vein in the hand or arm. Figure2, illustrates a typical CT Angiography suite setup.



**Figure 2** A typical CT Angiography suite setup ( UiTMMC Sungai Buloh branch)

When CT Angiography is done, a series of images will be created, which can be observed as an axial view of the different cardiac components, such as the cardiac chambers, aorta, heart muscles and coronary arteries. This modality allows for 3D reconstruction of the coronary arteries and also to find out whether a plaque build-up has narrowed the patient's vessels. Figure 3 shows some CT Angiography slices from one subject of the dataset.



**Figure 3** Two sequential CT Angiography slices from one subject. Red arrows point to the coronary arteries (courtesy of UiTM medical center, Malaysia)

The research work discussed in this book, revolves around analysis of medical images and the assistance it provides to medical practitioners. As each of these studies has been published in various papers, the discussions are focussed more on the research methods and approaches used for each of the research works. The major references are not included in this book as they have already been referred to in the unpublished thesis for each work and related articles that have been published.

## **ANGIOGRAPHY IMAGE ANALYSIS AND DIAGNOSIS**

Stenosis is a narrowing of the inner surface of the coronary artery. When a stenosis is identified, a procedure called Percutaneous Coronary Intervention (PCI) may be prescribed. The basic idea of PCI is to navigate a guide-wire with a small inflatable balloon and a stent (which is wrapped around the balloon) and place the balloon at the narrowed section of the coronary artery. Once the balloon is positioned in the stenosed region of the vessel, it is inflated causing the stent to expand and press against the coronary wall. Then the balloon and guide wire are removed while the expanded stent can be considered as a permanent implant. The stent acts like a scaffold, keeping the coronary lumen open and allowing normal blood flow to occur through the coronary artery. This procedure helps many patients avoid emergency heart bypass surgery and/or heart attacks.

For navigating a guide wire through the patient's vascular system, X-ray fluoroscopy imaging is used to observe the balloon, stent and the stenosed artery walls. Since the vessels are mostly radio-transparent, a contrast agent is injected and diffused through the arteries to visualize the vascular structure and determine the target area for stent placement. Although, the stent placement is an interventional procedure associated with some potential risks major procedural complications, such as vessel wall dissection or perforation, are uncommon. Nevertheless, one of the likely risks of this type of treatment is inaccurate placement of the stent (so-called geographic miss) which could have serious consequences. By more precisely determining the optimal location for stent positioning, practitioners can avoid the cost of multiple stents and the potential complications of the geographic miss.

Among the different imaging technologies, intravascular ultrasound (IVUS) is recognized as the gold standard for validation of medical device placement procedures. IVUS is able to provide real-time high resolution images of vessel wall cross-sections and helps to minimize geographic miss by stenting normal-to-normal and covering all of the stenosed area. Unfortunately, this requires significant time, increases the cost of treatment and is inconsistent with the normal workflow of a PCI procedure.

Based on comprehensive literature review, we surveyed different solutions for developing an assistant system for therapeutic device positioning. The solutions include stent boosting, road mapping and 2D to 3D registration techniques that have gained significant interest among clinicians over the past years. Some of these methods are proved to be efficient in providing visual assistance to cardiologists, such as, enhancement of image quality and visualizing the position of the stent in relation to the target vessel segment in a 3D reconstructed model of the coronary arteries. Nevertheless, among previous research studies, the problem of providing real-time quantitative analysis for verification of the stent placement task in 2D single view image sequences has not been sufficiently addressed. Correct guide-wire navigation and selection of a proper device are keys to determine the success of the procedure and patient's safety. In relation to this, there are some complexities that make accurate device positioning a challenging task:

- Limitations associated with two dimensional angiogram images such as low signal to noise ratio, vessel foreshortening and out-of-plane magnification.
- Complex motion of the projected arteries in angiogram sequences.
- Difficult morphologies of the arteries, such as bifurcation and complex geometry lesions.

One effective solution is to design real-time algorithms which contribute to the development of an assistant system for accurate navigation and localization of the therapeutic device. It could prove absolutely beneficial in reducing the time of interventional procedure which leads to less radiation exposure and less amount of contrast material injected into the patient's body. It could also improve the accuracy of device placement which would enhance the success rate of the procedure. This motivated us to propose a set of computational algorithms for fast and accurate quantification of coronary lesions as well as localization and tracking of stents in angiogram image sequences.

What is of interest is to develop a set of computational algorithms for automatic verification of image-guided stent placement in cardiovascular interventions. The specifications for a computer assisted stent positioning system are very demanding. Consultation with medical experts to determine the specifications for a computer assisted stent positioning system has been done. Based on the experts' advice, in the context of clinical applications, and a comprehensive literature review, the system proposed is expected to meet the following requirements:

- Automatic and accurate extraction of vessel centerlines as well as quantification of multiple coronary lesions in a coronary angiogram;
- Robust and automatic localisation and tracking of a stent in fluoroscopic image sequences;
- The system should not require additional equipment; and
- The system should not require any alteration to the standard flow of the clinical procedure.

The first requirement deals with fast and accurate seed point detection and centerline extraction from noisy coronary angiograms. Although many efficient algorithms have been proposed to address this challenge few are suitable for the automatic and real-time image analysis tasks needed as per the first requirement. Additionally, most of these algorithms suffer from incomplete results due to inappropriate selection of the initial points. The conventional seed point selection algorithms either rely merely on signal-to-noise ratio analysis, which results in a large number of false traces, or impose a set of strict geometrical validation rules that lead to more false negatives and require more computation time.

In the literature of centerline extraction, some methods suffer from inaccuracy caused by calculating the vessel direction merely based on the geometry of parallel edges of the arteries and neglecting inherent intensity and contrast variations between two corresponding edge points at the same coronary segment. Furthermore, some other methods are reported to have difficulties in coping with situations such as sudden changes in path-line orientation and small vessel diameters, vessel overlaps and image degradation.

The ideas behind the development of a device positioning assistant system emerged from different categories of solutions:

- Digital Stent Enhancement (DSE) methods
- Dynamic Road Mapping and Virtual Arterial Maps (VAM)
- Real-time tracking of interventional devices followed by 2D to 3D registration

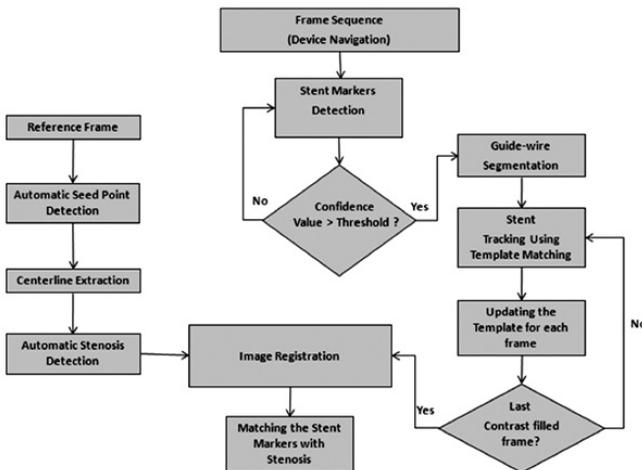
Since the last decade, a new image processing technique called Digital Stent Enhancement (DSE) has been proposed to provide an enhanced image of the stent during the stent placement procedure.

Some of the DSE methods have proved to be efficient in the enhancement of image quality and in providing visual assistance to the cardiologists. Nevertheless, they neither produce detailed quantitative analysis reports for the target lesions nor offer any assistance for the guide wire navigation procedure.

The second category of solutions are focused on assisting cardiologists with a two dimensional synthetic coronary arterial tree called the Dynamic Roadmap, to simultaneously visualize the position of the stent and the target coronary segment during the guide wire navigation procedure. This solution is helpful for cardiologists to avoid blind guide-wire navigation and to be able to constantly view the path without contrast material injection. However, in practice, irregular motions and arrhythmias of the heart cause most of the road mapping techniques to be out of phase. This issue accompanies most road mapping methods since the frames of the roadmap sequence are replayed consecutively without any prior knowledge about the exact phase of the next cardiac cycle, which should be considered for accurate correction of roadmap motions.

The methods involved in the third category emphasize on real time monitoring of the guide wire tip and therapeutic device in a fluoroscopic sequence and automatic registration to a reconstructed 3D model of the artery. This solution seems to be flawless with an ideal output. Nevertheless, among a few existing research works, the problem of rapid device localization without complete guide-wire segmentation has not been sufficiently addressed. Moreover, most of the proposed solutions either require acquisition of ECG-gated frames to synchronize the frames captured in different stages of the navigation procedure or reconstruction of a 3D model from multiple view projections. This necessitates additional equipment and modifications to the normal configuration of clinical environments.

The foundation of the framework builds upon three main phases: the diagnostic phase, navigation phase and registration phase as shown in Figure 4. The first stream corresponds with the diagnostic phase which aims at providing information about the dimensions of the target coronary lesion to be treated during the interventional procedure. It includes the acquisition of a reference frame, which serves as input for the subsequent steps, namely, automatic seed point detection, vessel centerline feature extraction and automatic stenosis detection. The second stream is responsible for handling the navigation phase. It consists of stent marker detection and stent tracking algorithms to verify the stent positioning task, through analyzing the navigation frame sequence. The final output is provided by the registration process which is responsible for estimating the position of the stent with respect to the target coronary lesion. The process consists of two stages: registration of the reference frame with contrast filled frames and registration of the current live frame with contrast filled frames.



**Figure 4** The research framework for this part of solution

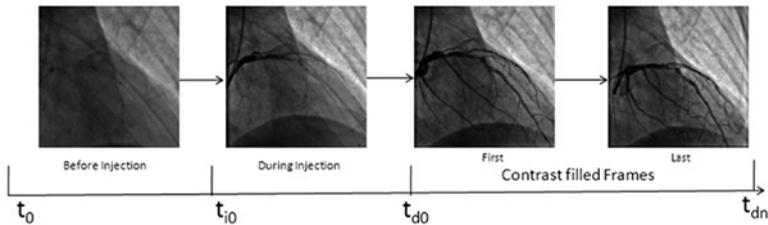
## Diagnostic Phase

At this stage the necessary information is prepared for guide-wire navigation. In fact, in order to accurately measure the dimensions of the coronary lesion, an image with optimal imaging conditions called the *Reference Frame* (usually acquired at the end-diastolic phase of the cardiac cycle) is identified and the area of the target lesion is selected by the medical expert. Specifically, the centerline extraction is performed for the whole coronary arterial tree where the starting point and ending point of the centerline segment corresponding to the lesion area is selected by the user and accurate dimensions of the lesion and optimal position for device deployment are estimated by the system.

Large amounts of contrast material is harmful to the patient, thus the coronary arterial tree is not visible in most of the frames acquired during the navigation phase. To avoid blind navigation, the last frame of the sequence, in which the arterial tree is filled with the contrast agent, called the *contrast filled frame*, is also acquired prior to the navigation phase. Figure 5 shows an example of the frame sequence, showing different intervals of the contrast injection process. The contrast filled frame can be used for mediatory correspondence between the reference frame and the current live frame. It is similar to the reference frame in terms of image content since they are acquired not too far apart in terms of timing. It is also similar to the live frame in terms of geometry and projection view.

The aim of the stent positioning system is to establish a spatial alignment between the current live frame and the reference frame using the contrast filled frame as a mediator. However, large differences in the content of the current live frame and last contrast filled frame acquired at different cardiac cycles may lead to significant miss-registration. To resolve this problem, the physician

records the last injection frame and the successive frames within a complete cardiac cycle. The recorded frames are then analyzed by the system to extract the centerlines of the vessel trees in all the recorded frames. The centerline images are then used as fiducial features for registration.



**Figure 5** The timing diagram of a contrast injection sequence

A three-dimensional model of the vasculature is also reconstructed at this stage. It is then possible to display the guide-wire in three dimensional (3-D) images. However, the motivation of this part of the research was mainly to develop fast and accurate algorithms for approximating the stent position and estimating the dimensions of the target coronary lesion from monoplane 2-D images. Further, it is assumed that the optimal fluoroscopic projection view (C-arm orientation) is selected for navigation, in which the local foreshortening is minimized. Since the vessels are mostly longitudinal, 2D anatomical landmarks are sufficient for guide-wire navigation and verification of the device positioning procedure.

## Centerline Feature Extraction

As stated earlier, the solution proposed is based on fully automatic and real-time analysis of angiogram images and making a spatial alignment between the location of the coronary lesion and the

position of the stent in live fluoroscopic sequences. This requires consistent features to be used for image registration.

Among several features that can be extracted from the vascular images, centerline features are of greatest interest due to the following reasons:

- Vessel centerlines and diameter information can be used to describe the geometric and shape characteristics of the vessels;
- The vessel motions can be estimated by the guide-wire motions; and
- Both centerlines and guide-wires can be represented by 1-D curves which are suitable for feature-based registration.

Thus, a centerline extraction method is required to accurately extract the vessel centerline for the whole coronary artery within a limited period of time. The following sections explain the methods used for automatic seed point detection and centerline extraction.

### *Automatic Seed Point Detection*

Automatic centerline extraction requires automatic definition of the starting points for the centerline extraction algorithm. This step involved collecting candidate seed points and verifying them to obtain a set of valid seed points which serve as starting points for the centerline extraction algorithm. The novelty of this solution for seed point detection is that, in contrast with previous methods it does not require verification of the existence of two parallel edges by searching along many quantized directions around each seed point. Also, it avoids *large angular quantization* errors associated with kernel-based methods. Instead, the discussed method utilizes both geometric and contrast-based information to verify similarities along the opposite vessel borders. This results in significant improvement in processing time and accuracy. The algorithm is also capable of increasing the number of true positives and decreasing

the number of false negatives by adjusting the angular tolerance and neighborhood size parameters.

### *Vessel Centerline Extraction*

There were major problems associated with previous methods employed for real-time and fully automatic centerline extraction. They suffered from inaccuracies caused by calculating the vessel direction merely based on the geometry of the parallel edges of the arteries. Another problem was lack of robustness due to neglecting the inherent intensity and contrast variations between two corresponding edge points of the same coronary segment. To overcome these problems, an improved algorithm for centerline extraction has been created, which is based on an exploratory tracing approach. The selection of this approach is based on a comprehensive study of the suitability and adoptability of different vessel segmentation techniques. It also incorporates a combination of geometric and intensity-based estimation of vessel direction, a vessel scanning mechanism which uses continuous vessel resemblance values with dynamic size profile and a self-adaptive method to estimate the look-ahead distance for linear extrapolation. The proposed centerline extraction algorithm is able to delineate the centerlines of all vessel segments without requiring low level pixel processing over the whole image. It is also fully automatic and does not require any human interaction in all parts of the detection process.

### **Device Navigation Phase**

The proposed navigation phase involved identification of the stent markers and tracking of the identified stent. In the first stage, the stent markers were detected by localizing the stent marker-balls in the first few frames using the point tracking approach. In the

marker detection process, several candidate clusters of pixels were selected. Then, for each cluster, a representative pixel was chosen and a confidence value assigned to it. Next, for every pair of pixels, combinations of two individual confidence values were calculated. On every successive frame the consistency of translation was examined for every pair from the last frame and the confidence value of the subsequent pairs re-calculated accordingly. The identification process was accomplished when one or more pairs obtained a confidence value higher than a specified threshold. In the second phase, the marker pairs identified in the previous frame were detected in the current frame using the template matching technique, correlation surface analysis and a criterion of motion consistency. In most related marker-ball localization methods, the estimation of the stent motion is based on estimation of the apparent motion of the marker-balls. However, in this discussed method, after the markers are identified, a piece of the guide-wire supporting the markers is also segmented. This improves the performance of the tracking algorithm to robustly track the stent in live frames during the guide-wire navigation procedure. The tracking approach consists of adaptive correlation tracking, region of interest processing and verification of motion consistency.

## **Image Registration Phase**

As mentioned before, this research effort does not aim to cover the registration phase. It is left to future research to address the problems involved in the image registration task. However, a procedure is suggested and the adoptability of existing registration methods is explained. The image registration phase faces two challenging problems: 1) registration between the target coronary lesion in the reference frame and corresponding region on a vessel segment in the last contrast filled frame; 2) translation of the stent markers

detected in the current live frame to the corresponding vessel in the last contrast filled frame. To address the first problem, since the arterial tree is included in the content of both images, a non-rigid registration algorithm can be applied to obtain a pixel-based correspondence between the vessel segments. The second problem deals with the matching of the detected stent in the current live frame with the stenosed vessel segment in the last contrast filled frame. This problem is similar to the problem of matching open 2-D curves. The researcher proposes the use of one-dimensional parameterization of the vessel centerlines (in the last contrast filled frame) and the segmented guide-wire (extracted in the navigation phase) in applying a 2-D curve matching algorithm, in which the segmented guide-wire is considered as the first input curve to be aligned with some part of the extracted centerline of the second input curve. This parameterization allows effective registration of the stent without requiring ECG gated frame for synchronization.

## **Implementation**

In this study, the discussed methods as well as closely related existing methods were implemented in MATLAB 2010. Moreover, a complete application was developed to create a synthetic data set of synthesized coronary vessels in VB.NET 2008. The implemented methods are as follow:

- Pixel-based vessel enhancement and vessel extraction methods including Top-Hat transform for background removal, morphological filtering, homomorphic filter, hysteresis thresholding, fuzzy clustering and Eigen-values of Hessian matrix.
- Thinning algorithm for skeletonization of completely segmented vessels.

- Seed point detection algorithms including directional kernel-based algorithm and clustering-based approach.
- Centerline extraction algorithm.
- A vessel generating tool for creating a synthetic vessel data set base
- Image registration methods including an intensity-based registration approach and a feature-based registration algorithm.
- Stent marker-ball detection method
- Stent detection and tracking algorithm

## **Data Collection and Dataset Preparation**

Medical imaging for coronary diagnosis comprises of several image modalities, such as, Conventional Coronary Angiography (CCA), Computed Tomography Angiography (CTA), Magnetic Resonance Angiography (MRA), Intravascular Ultrasound (IVUS) and many others, that are used to provide 2-D or 3-D visualization of the coronary arteries. The CCA is one of the commonly used imaging techniques for diagnosis and treatment of coronary artery disease. Despite its significance and the abundance of clinical data acquired in daily clinical examinations worldwide, very few publicly available standard datasets can be found for CCA. Recently, a comprehensive source of validated data for research purposes was established by the medical image analysis communities, called the *Midas Platform* (available at <http://www.midasplatform.org>). It includes reference datasets created for coronary CTA and MRA with corresponding reference standard centerlines, a set of evaluation measures and an online tool for comparison of CTA centerline extraction techniques. However, these datasets are composed of 3D images and are unsuitable for validating the proposed algorithms. Another source

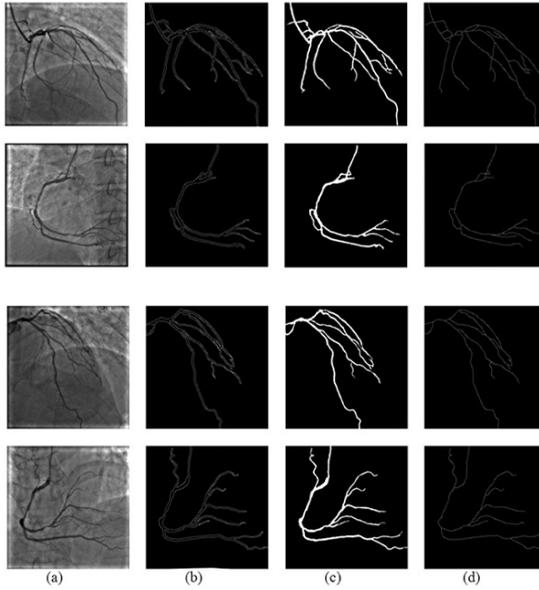
of medical image datasets is from the website “<http://pubimage.hcuge.ch:8080>”. The dataset called GRUSELAMBIX includes 14 angiographic sequences in DICOM file format. Although the image modality is compatible with the discussed case, there are only a few image sequences for pre and post balloon angioplasty of a stenosis in the right coronary artery.

## **Clinical Dataset**

To validate the said algorithms in the seed point detection and centerline extraction steps, an image database of routinely acquired coronary angiograms was collected, with anonymous patient information, from the UKM Medical Center. It comprised a large number of angiogram images (315 angiograms) with a wide variety of vessels, with different types of coronary lesions (types A, B and C in AHA classification) and different geometries of vessel segments. The selected images had spatial resolution  $512 \times 512$  and 8-bit quantization, acquired by a “GE-Innova 2100-IQ” C-arm system. This dataset was preprocessed and the vessel centerlines were manually annotated to obtain reference standard centerline images. Additionally, for the stent localization and tracking step, a large set of X-ray angiographic sequences covering one or several cardiac cycles during the stent placement procedure was compiled. This dataset included 264 clinical sequences illustrating more than 6000 marker-ball pairs obtained from PCI examinations for stent placement for 32 anonymous patients. The sequences included a wide range of stent lengths and diverse range of guide-wire positions and curvature. To prepare the dataset, the position of each marker-ball in each image was manually determined by marking a point inside the marker-ball, but not necessarily at the center of the marker-ball since this location is unknown.

Further, the locations of some points on the guide-wire supporting the marker-balls were marked in a subset of the collected images to validate the guide-wire segmentation algorithm. This dataset was used for parameter tuning for the proposed algorithms and in estimating typical parameters and characteristics of the marker-balls, such as, shape, size and motion, as well as, the guide-wire curvature. It also provided a ground truth for validation of the marker-ball detection and tracking algorithms.

**Approximating the Ground Truth from Manually Traced Images**  
To obtain a set of reliable centerline images as ground truth data, a modified version of the ground truth estimation method was employed. In the first step, the boundaries of the arterial tree in each angiogram were manually traced 5 times by the same person at different times, ignoring small arteries of less than three (3) pixels wide. This resulted in five corresponding edge images for each image in the dataset. Then, the images in a correspondence set were superimposed on each other such that the pixel value in the resulting image was a function of the number of overlapping pixels. This yielded average images with unavoidable discontinuities. To remove the holes and discontinuities, a morphological closing operator with a  $3 \times 3$  square identity matrix was used as the structuring element. In the next step, the boundary images were filled (with white color) to obtain binary images which illustrated the silhouette of the coronary arterial tree. Finally, an accurate skeletonization algorithm was used to estimate the location of the true centerline points. Nevertheless, the resulting centerline images were manually modified where needed. A set of angiograms and their corresponding ground truth images are shown in Figure 6.



**Figure 6** Four angiogram images and their corresponding feature images. (a) Original angiogram; (b) Average boundary image; (c) Silhouette image; and (d) Centerline image.

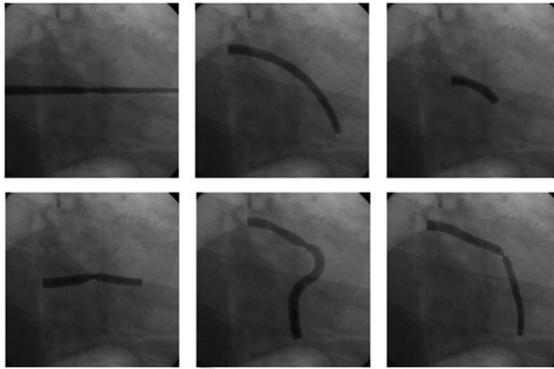
## Synthetic Dataset

In most of the works in the literature of centerline extraction and stenosis quantification, the validation methodology is based on the assessment of specialists or phantoms with known dimensions. In the first methodology, however, there exists a large inter-observer variability as well as a lack of objective criteria for visual assessment of coronary lesions. On the other hand, in most cases, due to variability in the configuration of the imaging systems, the phantom-based evaluation method does not deliver reliable standard results. A more objective method is to use a synthetic image dataset to compare estimated results with *a priori* data, i.e. synthesized images of vessels with known geometry, centerline and lesion dimensions.

In this research project, in order to analyze the performance of the centerline extraction algorithm under various geometries of the vessel segment, different vessel contrast and different values of signal-to-noise ratio, a method for generating a synthetic vessel dataset was adopted. As shown, the method is able to provide an objective way of comparing different centerline extraction algorithms. Nevertheless, the original method was modified to generate a wider range of geometric features, such as, symmetric and asymmetric lesions, radial dilation of the vessels and multiple stenoses in a single segment. Figure 7 illustrates sample vessel images in the synthetic dataset. The dataset comprised the following image groups:

- 19 vessels with zero curvature, zero taper or medium taper value with stenosis;
- 23 knee-type vessels, no stenosis;
- 9 vessels with curvature, with stenosis;
- 9 multiple segment vessels, with stenosis;
- 13 multiple segment vessels with multiple stenosis, zero taper; and
- 13 multiple segment vessels with multiple stenosis, medium taper.

For each image group, four sub-groups were generated by adding white Gaussian noise with different variance values to each original image, resulting in 344 synthetic images. The method used to generate synthesized vessels models the coronary angiogram image based on the 2-D geometrical representation of the vessel's projection using four parameters: vessel taper, percent stenosis, and centerline curvature and curve length. A complete description of the vessel generator tool will be provided later.



**Figure 7** Sample vessel images from synthetic dataset, including vessels with different values of taper, curvature, percent stenosis and number of stenosis

## Experimental Design

Based on the research sub-problems, the experiments were divided into the following categories: 1) experiment for tuning the different parameters used; 2) experiments for validating the algorithms; and 3) experiments for evaluating the performance of the algorithms in comparison to well-known existing methods. Before evaluating the performance of the algorithms, it is necessary to identify the conditions under which the optimal performance of a given algorithm can be obtained. In the first category, a set of experiments were designed for tuning the parameters of the said algorithms. For comparative performance evaluation, the optimal parameter values were also used for the existing methods, based on the parameter settings described in the corresponding publication.

In the second category, the functionality of the algorithm was compared with the ideal situation. That is, for a given set of parameter values, the results produced by the algorithm were compared to the ground truth. In these experiments, for each discussed method, a set of ground truth images was prepared, the algorithm was then

introduced as the experimental treatment followed by a posttest measurement which determined how well the algorithm was able to perform its expected function. The measurement was defined based on a set of predefined quality metrics for each individual algorithm.

The third category consists of experiments in which the performance of the algorithm was compared with that of well-known methods that are closely related to the proposed methods. That is, for a given set of parameter values, the results produced by the algorithm were compared to that of a particular related work. The design used for these experiments is *within-subjects design*, in which two or more methods are applied to the same image dataset or ground truth images and the performance of each method observed. In all experiments the initial parameters were chosen to provide similar conditions for the algorithms being tested. For instance, in the experiments to evaluate the performance of the seed point detection algorithms, the same number of grid lines and neighborhood size were chosen to generate an equal number of initial candidate points for both algorithms. The experiments are summarized in Table 1.

## **Experiments for Parameter Tuning**

The algorithms for seed point detection, centerline extraction and stent marker detection and tracking required a large number of parameters to be set before the other experiments were performed. In order to obtain optimal values for the parameters, a set of experiments were defined in which different values of a given parameter were examined against some pre-defined constraints of the algorithm, such as, computational time, performance or lower and upper bounds defined for other parameters. Tables 2 – 4 depict the set of parameters for which optimal values must be set for the algorithms.

**Table 1** The experiments conducted for evaluation of the proposed methods

The Method	Opponent Related Works	Dataset	Dependent Variable	Performance Metrics: Equation and Reference
Seed Point Detection Algorithm	1- Directional Kernel-based Approach 2- Clustering-Based Approach	Clinical Images	Preciseness and Completeness	Precision : $P = \frac{TP}{TP + FP}$ Recall: $R = \frac{TP}{TP + FN}$ F-Value: $F = \frac{2 \times R \times P}{R + P}$
Centerline Extraction Algorithm	1-Geometric Vessel Tracing 2- Directional Kernel-based Tracing Approach 3- Combination of Geometric and Eigen-values of Hessian Matrix	Clinical Images	Accuracy	Consistency With Respect To the Ground Truth: $\alpha_{pq} = \frac{ P_q }{ P } \times 100\%$ $\alpha_{qp} = \frac{ Q_p }{ Q } \times 100\%$
			Accuracy	Discrepancy With Respect To the Ground Truth: $\mu = \frac{1}{2 P_q } \sum_{p \in P_q} \ p - C_q(p)\  + \frac{1}{2 Q_p } \sum_{q \in Q_p} \ q - C_p(q)\ $
			Robustness	Orientation error: $O_{MSE} = \sqrt{\left(\frac{1}{N}\right) \sum_{i=1}^N O_i^2}$
		Synthetic Images	Robustness	Normalized Global Distance Error: $d_{NORM} = \sqrt{\left(\frac{1}{N}\right) \sum_{i=1}^N \frac{d^2}{r_i^2}}$

The Method	Opponent Related Works	Dataset	Dependent Variable	Performance Metrics: Equation and Reference
Marker-Ball Detection and Tracking Algorithm	1- The Marker-Ball Detection and Tracking Algorithm	Clinical Sequences	Accuracy	Percentage of True Positives, False Positives and False Negatives Per Image Sequence
				$\text{Precision} = \frac{\text{number of correct correspondences}}{\text{number of established correspondences}}$
			Accuracy	$\text{Recall} = \frac{\text{number of correct correspondences}}{\text{number of actual correspondences}}$

**Table 2** List of parameters to be set for the seed point detection algorithm

<b>The Algorithm</b>	<b>Parameter</b>	<b>Symbol</b>	<b>Value(s)</b>
Seed Point Detection	Number of Grid Lines	$N$	8,10,12,14,16
	Angular Tolerance	$\varphi$	27.5-45 degrees
	Neighborhood Verification Distance	$d$	1, 2, 3, ... ,
	Contrast Sensitivity Threshold	$\tau$	[0 , 3]

**Table 3** List of parameters to be set for the centerline extraction algorithm.

<b>The Algorithm</b>	<b>Parameter</b>	<b>Symbol</b>	<b>Value(s)</b>
Centerline Extraction	Weighting Factor for detection of overlapping vessels	$\beta$	1.5
	Proportionality constant for search window	$K_w$	2
	Proportionality constant for look-ahead distance	$K_d$	2
	Threshold for percent dynamic range	$\gamma_t$	0.5%

**Table 4** List of parameters to be set for the Stent Marker-Ball Detection Algorithm

The Algorithm	Parameter	Symbol	Value(s)
Stent Marker-Ball Detection	Laplacian Kernel Scale	$h$	2-10
	Filtering Threshold	$T_r$	10%
Stent Marker-Ball Tracking	Template Size	$S_i$	20-50

### Performance evaluation for the Seed Point Detection Algorithm

As mentioned earlier, the main requirement for the seed point detection algorithm is that it should be able to deliver a set of points that are located on or close to the centerline of the coronary arteries visible in the image. Thus, to validate the proposed seed point detection algorithm, it is necessary to use *a priori* data for centerline locations, i.e. ground truth images.

Two experiments were conducted for comparative performance evaluation. In the first experiment, the performance of the proposed seed point detection algorithm was compared to existing approaches in terms of the ability of the methods in balancing between the completeness and the preciseness of the seed point detection process. The following metrics were measured in this experiment:

- **Precision** which reflects the preciseness of the algorithm.
- **Recall** which reflects the completeness of the algorithm.
- **F-Value** which reflects the balance between the precision and recall.

The second experiment was conducted to evaluate the efficiency of the algorithms participating in the first experiment, in terms of computational time as *input size* (i.e. number of candidate points) increased. The following metric was used to measure the efficiency of the algorithms:

$$P_t = \frac{\text{number of correctly detected points}}{\text{total number of candidate points}} \times \text{computational time}^{-1} \quad (2.1)$$

However, since the number of candidate points was kept equal for all algorithms, the above metric can be simplified as:

$$P_t = \frac{\text{number of correctly detected points}}{\text{computational time}} \quad (2.2)$$

## Performance evaluation for the Centerline Extraction Algorithm

For the centerline extraction algorithm, the validation process includes validating the accuracy and robustness of the proposed algorithm. Therefore, for a given angiogram image, the validation process includes quantitative measurements for comparing manual traces and the centerlines produced by the proposed algorithm by estimating their similarity against the ground truth. It should be noted that in addition to the ground truth images, which are established based on manually traced angiogram images, synthetic ground truths can also be used to measure the ability of the centerline extraction algorithm to tolerate certain types of image variations, e.g. complex curvatures and different levels of additive noise.

For comparative performance evaluation, four experiments were conducted on the said centerline extraction method and three existing tracing methods. These experiments were designed to evaluate the accuracy and robustness of the algorithms based on the following criteria:

### ***Evaluating the accuracy***

Accuracy is evaluated by measuring the similarity between the tracing results produced by the algorithms and the ground truth skeleton images. The similarity is defined based on the following metrics:

- ***Consistency*** which reflects the average error of the corresponding traces in the algorithms' output with respect to the ground truth with a distance.
- ***Discrepancy*** which reflects the percentage of inliers between the algorithms' output with respect to the ground truth with a distance.

The above metrics were measured for each image in the *clinical dataset* and their averages calculated over all traces at each distance value.

### ***Evaluating the robustness***

Robustness is evaluated in terms of the ability of the algorithm to regenerate the trace in complex vessel geometries, such as different curvatures, different lumen diameters and different tapering values, as well as complex imaging conditions such as low signal-to-noise ratio. This is performed by measuring the error estimation metrics between the extracted centerline and the reference centerline in each image group in the *synthetic dataset* and taking the average over all images in each group of the dataset. As mentioned before, the synthetic dataset comprised different vessel types (or vessel classes), each of which represents a specific group of geometric parameters. Therefore, the behavior of each algorithm could be examined for different classes of vessels. The error estimation metrics are as follow:

- ***Normalized Global Distance Error*** which is the average distance error between each point in the reference centerline and its corresponding point on the estimated centerline. The corresponding point is defined as the intersection between the profile, which is a line perpendicular to the reference centerline at a given point on the reference centerline and the extracted centerline.
- ***Global Orientation Performance Measure*** which is the difference between the tangents calculated at two corresponding points on the reference centerline and the extracted centerline.

## **Performance Evaluation for Stent Marker-Ball Detection and Tracking Algorithm**

The problem of validating the stent marker-ball detection and tracking algorithm can be divided into the following sub-problems:

- Measuring the ability of the detection algorithm to localize the marker-balls in complex image content such as different imaging artifacts.
- Measuring the ability of the tracking algorithm to generate correct point trajectories in complex respiratory and cardiac motions and guide-wire deformations.

The quantitative measurements in the first sub-problem require ground truth images in which the position of the stent markers in the clinical image sequences are marked by an operator. Then, the detection performance is measured by comparing the position of the detected marker-balls relative to the position of actual marker-balls in every image in the dataset. The following were measured to determine the performance of the proposed algorithm:

- **True Positives:** the number of detected markers that were at an acceptable distance from the ground truth;
- **False Negatives:** the number of actual markers that were mistakenly rejected by the detection algorithm;
- **False Positives:** the number of false regions that were mistakenly considered as actual markers; and
- **True Negatives:** the number of false regions that were correctly rejected by the algorithm.

For the second sub-problem, since the proposed algorithm is based on the point tracking approach, the performance was measured based on object correspondences by calculating the *precision* and *recall* standard measurement. For further details on this part of the research please refer to Boroujeni *et.al* (2010a, 2010b), Boroujeni *et. al* (2011), Boroujeni *et. al* (2012) and Boroujeni (2012). This work was copyrighted under the title “Automated System for identification and Quantification of Lesions in Coronary Arteriograms” on 29<sup>th</sup> July 2013. This project won a Silver Medal at the Malaysia Technology Expo 2012, with the title “Automated System for Identification and Quantification of Lesions in Coronary Arteriograms”

## ECHOCARDIOGRAPHY IMAGE ANALYSIS AND DIAGNOSIS

The complexity and criticality of heart disease diagnosis and treatment have attracted the attention of researchers to develop approaches that can handle accurate clinical assessments. One of these complexities is measuring the right ventricle (RV) stroke volume from Three Dimensional Echocardiography (3DE) images. The RV has a particularly complex geometry and accurate stroke

volume measurement requires full coverage of the RV cavity. Studies have been undertaken to measure the RV stroke volume but these studies were based on geometrical assumptions or intensive manual interactions. Different cardiac imaging techniques have been developed to help specialists in their regular clinical work and in the operating theatre, to assist in diagnosis, monitoring of the treatment and to ensure the success of a cardiac intervention as far as possible. Echocardiography is one of these cardiac imaging techniques and it is considered as the most effective imaging technique as it is minimally invasive, quick and cheap. Real time 3D Echocardiography (RT3DE) is the most recent innovation of the echo imaging system. This innovation provides potential for improving the image quality and 3D visualization of the entire cardiac chambers. Numerical measurements are an important indicator in any clinical report since they can assist in assessing the normality or abnormality of the structure and function of the ventricles. Therefore, this innovation is utilized to provide a numerical measurement. Even though the current technique succeeds in measuring the left ventricle (LV) function and volume, it cannot provide accurate measurements of the right ventricle (RV) function and volume. Echocardiography is a key tool and the most widely clinically used imaging technique for assessment and evaluation of cardiac structure and function. It helps with detecting different heart diseases, by visualising the structure of the heart ventricles, and measuring their dimensions, masses and assessing the wall motion velocity and its up-normality. In addition to the heart structure, echocardiography is capable of assessing normal and abnormal blood flow using a Colour Doppler, which enables the visualisation of the blood motion and diagnoses ventricle shunting and valve abnormality.

Before developing the new three-dimensional echocardiography (3DE) technology, the twodimensional echocardiography (2DE) technology was used as a key tool to assess the LV volume, function and structure. However, the assessment and calculation formula were based on assumptions, which refer to inaccurate results from the 2DE. Real Time Three-Dimensional Echocardiography (RT3DE) provides a fully sampled matrix-array transducer, which consists of thousands of piezoelectric elements, and each of them transmits and receives ultrasound signals. The RT3DE overcomes some of the limitations of the previous 2D technique and gives better quality images in 2D and 3D. RT3DE has three imaging modes. Firstly, a Wide-Angle Mode or full volume mode, acquiring a 3D image from only one shot for one full cardiac cycle. This mode is used for a specific structure such as the aortic root and mitral valve. It does not require respiratory gating.

RT3DE also enables the assessment of the normality or abnormality of blood using Colour Doppler imaging, which can be undertaken using the full volume or narrow angle mode. The echocardiography imaging system consists of the following parts:

- A specifically designed probe which is registered with the machine to perform the imaging process;
- Special software designed to view, analyse and perform measurements; and
- A workstation to save and process the data that is transferred from the imaging system.

Since Computer Aided (or assisted) Diagnosis systems (CAD) are becoming increasingly affordable, such systems are being incorporated into routine clinical practice. The segmentation of an anatomy structure is the most important function of the assessment

and diagnoses process. However, segmenting a complex geometry and function, such as the RV cavity, is still a challenge. Accurate segmentation affects the assessment and diagnoses results.

New algorithms are thus needed to overcome the problems of complex geometry organs and analysis functions in medical applications. In this work we propose a method for semi-automatic segmentation and stroke volume measurement of the RV cavity in echocardiographic images. The proposed methodology is based on a novel method of analyses for the complex geometrical structure and complex function of the RV. The volume of the anatomical structure of the RV is measured by the segmentation of the actual structure of the cavity, with automatic detection of the End-diastolic (ED) and End-Systolic (ES) functions. The proposed methodology includes an automatic seeded region growing (ASRG) segmentation algorithm for the cavity region in 2D images, based on a priori region of interest (ROI) knowledge, and the computed resolution of the (X7-2t) transducer used in the TEE imaging process. The ventricle function is also determined automatically based on mathematical modelling to compute the cavity stroke volume. Finally, the contours of the segmented region are extracted to generate the R3 point. 3D modelling for the segmented cavity is performed in two stages, by orientation of the point cloud by close surface reconstruction in order to accurately delineate the required object.

In this work an algorithm is presented in detail, including the evaluation of the accuracy of the volume measurements which is based on accurate quantitative segmentation and by human experts. The results show that an organ with a complex geometry and function such as a RV cavity can be measured accurately using the discussed method.

The discussed method requires minimal user-initialization to determine the ROI and its execution requires only a few seconds

for one time. Comparisons with currently available software for LV volume and function assessment and 3D modelling to validate the merit of the proposed work are also provided.

The goal of this part of the research is to measure the cavity stroke volume to assist specialists and practitioners to determine any abnormality of the RV. Numerical measurements are an important indicator in the clinical assessment of the normality or abnormality of the structure and function of heart ventricles. However, the 3DE imaging technique gives good imaging quality in addition to the features of 3D imaging which provide the full structure of the ventricle cavity. Measuring the RV volume is big challenge because of the complexity of its geometry.

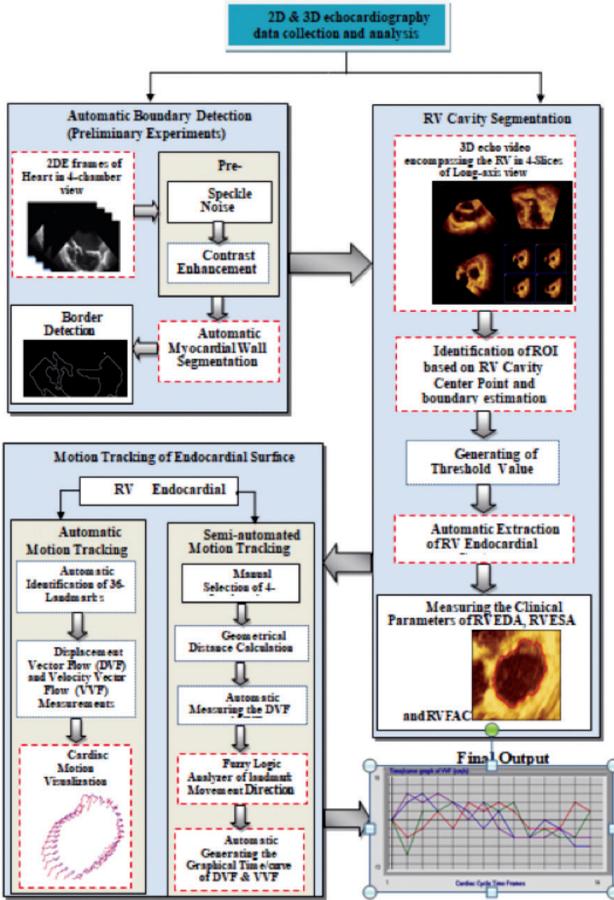
This work presents a ventricle stroke volume measurement by segmenting the RV from 3DE images using an improved fast single seed point region growing segmentation method for the intracardial cavity of the ventricle. An automatic approach in the determination of the seed point is used, a novel method performed for the automatic detection of the ED and ES frames from one cardiac cycle video is introduced and the stroke volume is computed based on the intracardial structure of the right ventricle.

The chosen framework indicates a schematic view of the solution, which is to introduce a robust algorithm for motion tracking and analysis of RV endocardial surfaces. The suggested methodology primarily focuses on quantitative approaches to measure some clinical parameters for assessing the RV function. As shown in Figure 8, the overall framework comprises three main phases: (i) Automatic boundary detection; (ii) RV cavity segmentation; and (iii) motion tracking of the endocardial surface. The processing stages within each phase are considered as research contributions and are highlighted using dashed lines. Dotted lines on the other hand highlight stages that correspond to improvement of existing

methods. Accordingly, preliminary experiments of automatic boundary detection for heart wall motion in 2D echocardiography images were carried out in the first phase. In the second phase, an automated approach for RV cavity segmentation was created, which comprises four main processing steps, namely, (i) automatic region of interest identification, (ii) contrast enhancement, (iii) automatic threshold generation, and (iv) endocardial contour extraction. The purpose of the third and final phase is to detect and track the cardiac motion of the RV endocardial surface automatically and semi-automatically. Both methods include velocity motion tracking and analysis for the candidate landmarks throughout the 4-slices. The displacement vector flow (DVF) and velocity vector flow (VVF) are measured to generate the time/curve graph.

## **Data Acquisition and Preparation**

In this research, echocardiography images were obtained, with permission, from the Malaysian National Heart Institute (IJN). These images were acquired using the 'iE33 Philips' medical machine with 3D QLAB software, under the supervision of a Consultant cardiac anaesthesiologist. Two types of echocardiography images are used: (i) Two-dimensional echocardiography (2DE) and (ii) Three-dimensional echocardiography (3DE).



**Figure 8** The research framework showing the three phases of the solution. The steps highlighted in red dashed lines correspond to the research contributions

The 2DE data set acquisition and preparation phase consisted of three major steps: (i) a matrix array transducer of TEE probe connected to a capable echocardiography system to be used on a

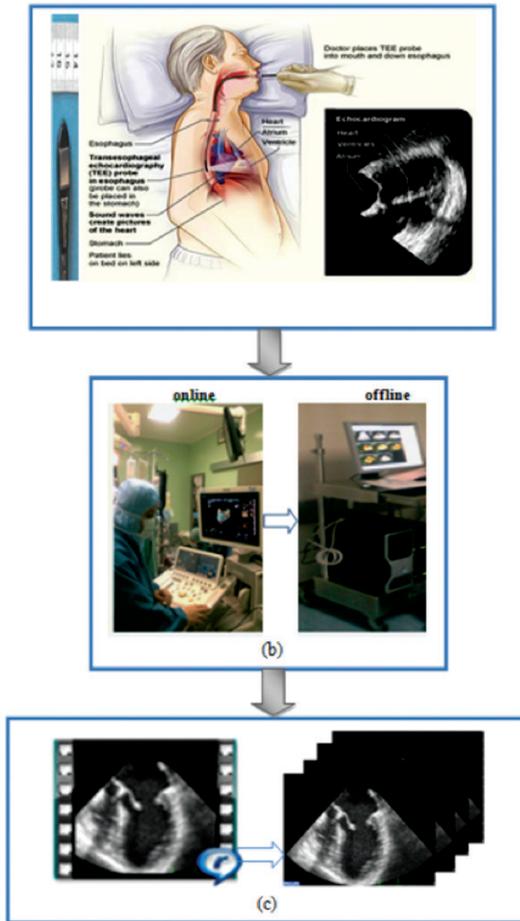
normal subject; (ii) all acquired data was transferred from the ‘on-line’ medical system directly to the ‘off-line’ workstation by running the QLAB software; and finally, (iii) each 2DE video was broken down into its constituent frames according to the frame rate. Each of the frames was saved in the Windows BMP format. The steps in 2DE image data collection and analysis in this research are shown in Figure 9. The datasets were divided into two groups: the first group consisted of original 2DE videos with a complete cardiac cycle that belonged to different patients, saved in AVI format. The second group was used for comparison and performance validation, and it contained resultant ground truth datasets with complete borders, derived from a specific ‘plug-in function’ in the QLAB software based on the same original 2DE videos.

### **3D Echocardiography Dataset**

The developments in real time 3D echocardiography imaging have provided new insights into RV images that encompass all portions of its asymmetric shape. Conventionally, RV echocardiographic data acquisition is very challenging due to its anterior position, complex geometry and morphology with prominent trabeculations. Therefore, four stages of dataset collection and preparation were required: firstly, a matrix array X2-7t transducer (TEE) was used to acquire a live 3D full volume dataset encompassing the RV. In the second stage, all the acquired 3D datasets were transferred from the online medical system directly to an ‘Xcelera’ server or to the offline workstation by running the QLAB software. In the third stage, the 3D RV full volume dataset was viewed as orthogonal slices using the ‘MPR’ mode (multi-planar reconstruction) and 3D Quantification (3DQ) Plug-in. Then, 4-slices from the 3D full volume, encompassing RV in long-axis view based on the RV inflow-outflow view, were identified using the ‘2x2 iSlices’

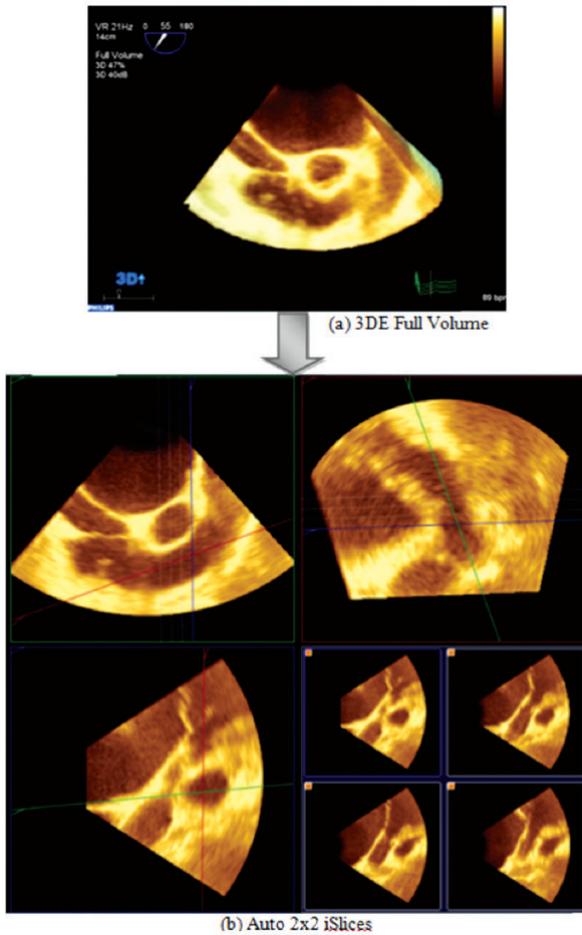
Plug-in, as shown in Figure 9. Finally, these 4-slices were stored individually as AVI videos with complete cardiac cycles. Each slice was converted to a fixed number of frames ( $F_1, F_2, F_3, \dots, F_n$ ) according to the frame rate, where each frame was represented as a BMP image.

Some duplicate frames were generated due to the stitching process in the 3D full volume reconstruction through the complete cardiac cycle. Automatic detection of these duplicate frames is important and highly desirable in dataset preparation, to reduce the time-consuming tasks of image processing and analysis. An automatic method capable of detecting duplicate frames was therefore developed. All the detected frames were saved as target images in a dedicated folder and serially re-numbered. In one example, a 15 x 15 pixel block of two-consecutive frames was identified and the pixel intensity for each was saved in individual 1D-lists. Then, a block-matching algorithm was applied and the Coefficient Correlation Similarity (CCS) of pixels intensities within two blocks was compared. The processing stages of 3D echocardiography dataset preparation are illustrated in Figures 10- 11.

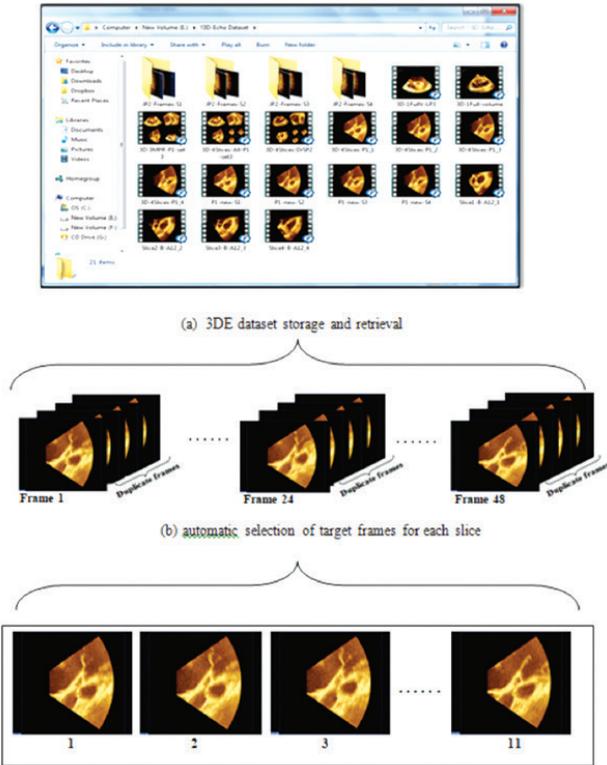


**Figure 9** The steps of 2D echocardiography dataset collection and analysis: step 1: 2DE dataset acquisition (a) ; step 2: dataset transformation (b); and step3: 2DE images preparation (c).

(Image in (a) adopted from: "National Heart, Lung and Blood Institute", 2012)



**Figure 10** The processing steps of 3D echocardiography dataset collection including 3DE full volume acquisition (a) and 4-slices encompassing the RV in long-axis view using MPR mode in 3D QLAB software (b)

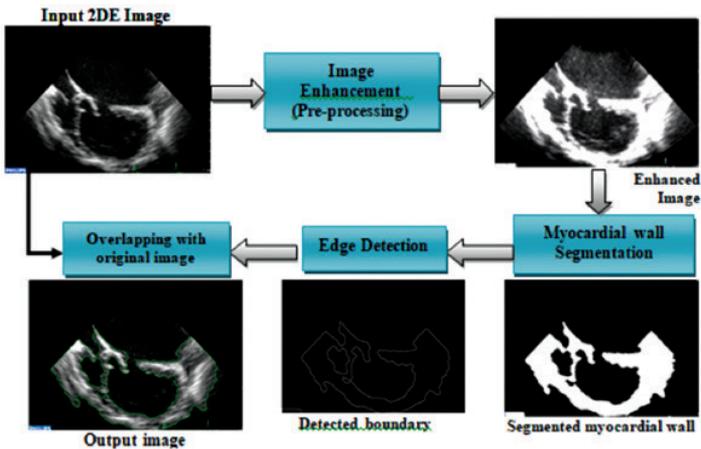


**Figure 11** The processing steps of 3D echocardiography dataset preparation including: 3DE dataset storage and retrieval (a), conversion of each 3DE video into a number of frames and automatic selection of target frames with motion (b) and storage of all target frames of each slice with new re-numbering in individual folders (c)

## Automatic Boundary Detection

One challenge most researchers face is how to speed up clinical decisions and reduce human error in accurately estimating the boundaries of heart wall movements. A tool that can automatically do this can be very useful for qualitatively and quantitatively assessing many cardiovascular diseases. An efficient and accurate

method of automatic boundary detection for wall motion from echocardiographic images has become of major research interest, which essentially requires several methods of image processing and analysis. Specifically, there are three main stages. First, pre-processing is performed where it involves image contrast enhancement and speckle-noise reduction techniques. Second, image segmentation is performed through an improved method of global thresholding. This stage segments the myocardial wall from the background, automatically implementing segmentation based on the mean value of pixel intensities (as a threshold) for all frames. In order to improve the segmentation results, two common morphological operators, ‘erosion’ and ‘dilation’, were used for smoothing the myocardial wall image. The third stage applies the Robert’s operator for edge detection in order to indicate the final segmentation results. All the stages of the method for automatic boundary detection applied on a 2DE image are presented in Figure 12.



**Figure 12** An example of the implementation stages of automatic boundary detection with sample of resulting image in each stage

## **RV Cavity Segmentation**

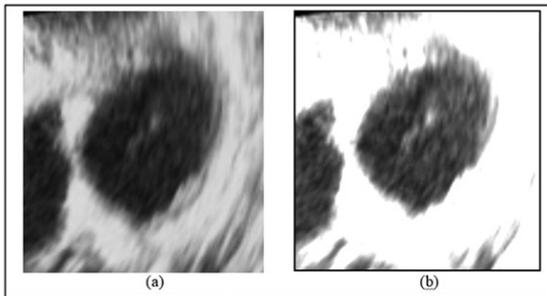
The main objective of segmentation in echocardiography is to separate or divide the image into distinct regions. The anatomical complexity and geometrically asymmetric shape of the RV make segmentation a difficult task. An automated approach for RV cavity segmentation with minimal user interaction is thus introduced, which comprises four processing phases.

### ***Phase I: Region of Interest Identification***

Identification of the region of interest (ROI), which in this case is the RV cavity, is basically performed by identifying and extracting the RV region from its background. This is done for all frames of the 3D echocardiography video clip. A new method was introduced, which consists of two procedures. First, the initial RV cavity centre point RVCCP () was manually marked by an expert in the first frame, i.e. end-diastolic, and considered as a reference centre point. The initial is hence defined as the closest region around the RV cavity in a rectangular acoustic window of size  $M \times N$ . The reference point and were used in the next procedure of cavity boundary estimation. In order to successfully identify the next ROI in all successive frames, an automated technique for cavity boundary estimation based on the RVCCP and the geometrical distance calculation (GDC) algorithm is proposed. Moreover, to determine the corresponding RVCCP in the remaining frames, the mean values of the x, y coordinates were considered as reference centre points for the extracted current ROI.

### *Phase II: Pre-processing*

Image pre-processing is one of the fundamental issues in the field of medical image analysis. Two processing tasks were performed for speckle noise reduction and contrast enhancement on the gray-scale of the images. Averaging smoothing was firstly carried out to remove the speckle noise in the echocardiography images using the linear mean filter. The main aim of contrast enhancement is to improve the quality and appearance of an image for visual interpretation and analysis and to gain a better understanding of the imagery. Towards this aim, the second task of pre-processing performed image contrast enhancement was by highlighting the features of interest, i.e. the RV myocardial wall tissue. In this research, the percentage linear stretch contrast method was improved by generating a contrast factor automatically. The contrast factor is capable of controlling the contrast adjustment percentage of image intensity values. More specifically, the contrast factor was proposed to highlight the RV myocardial wall tissue and darken the RV cavity region by manipulating the image brightness. An example of the contrast enhancement task on the gray-scale image of the extracted ROI is shown in Figure 13.



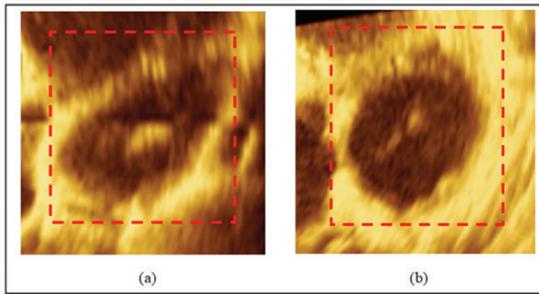
**Figure 13** An example of the extracted ROI image in gray-scale (a) and contrast enhanced image after application of the improved method of percentage linear stretch (b)

The ROI did not contain the proper contrast with the background, hence necessitating this step for solving this problem that poses a challenge in cardiac structure of RV echocardiographic images with thin walls and heavy trabeculation. Obtaining accurate results of automatic extraction for RV endocardial contour in the complete cardiac cycle greatly depends on the efficiency of the results obtained from the contrast enhancement step.

### *Phase III: Cavity Segmentation*

The cardiac structure of RV echocardiographic images is very complex. For example, the cavity area includes papillary muscles, which are attached to the tricuspid valve and are responsible for valve movement and the trabecular tissue. Two examples of the RV cavity region with complex anatomical structure are shown in Figure 14. These types of anatomical complexities make automatic segmentation of the RV cavity in a complete cardiac cycle a difficult task. It is not easy to segment one region from another due to the overlap and low contrast that exists between structures. An improved algorithm was implemented to segment the RV cavity from the myocardial wall. Two image processing procedures were used for this purpose, namely, intensity threshold generation and cavity surface smoothing. The contribution is that the threshold value is generated automatically and the same calculations are used for all frames. It was performed by improving the existing technique of global thresholding segmentation. A comparison was done between each pixel's intensity and the threshold value to segment the enhanced image into two regions (i.e. binary image). The black pixels correspond to the ROI, i.e. RV cavity, whereas the white pixels correspond to the background, i.e. myocardial wall tissue. In the context of improving the segmentation results for RV cavities in all frames, two common morphological operators were applied,

namely erosion and dilation on the resultant binary- threshold image for two reasons. First, to fill up the gaps between muscles that may appear within the cavity area, due to the anatomical problems of speckle noise or artefacts that were not previously eliminated by pre-processing. The second reason was for improving the RV cavity shape by smoothing the inner surface border, i.e. the endocardium wall.



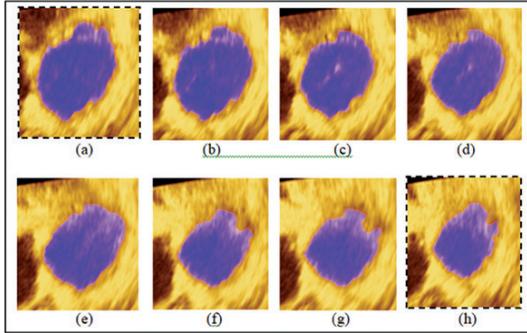
**Figure 14** Two examples of RV cavity region with complex anatomical structure, including large papillary muscles (a) and trabeculated wall (b)

#### *Phase IV: Endocardial Contour Extraction*

In this phase, an algorithm for automatic extraction of the RV endocardial contour through the complete cardiac cycle was introduced. As mentioned earlier, the anatomical complexity and asymmetrical shape of the RV make contour detection a difficult task. The main goal of the said algorithm is to detect and extract the RV endocardial contour in 4-slices from the 3D echocardiography full volume dataset. The algorithm can be applied on the resultant binary-threshold image by combining the improved method of radial search and shape-based contour detection. Its contribution is to partition the RV cavity area into four parts (P1, P2, P3, P4)

according to the asymmetric shape-based area. Accordingly, eight geometrical distances are calculated for the current RV cavity from the center point to determine the maximum value  $D_{\max}$  of each distance individually in each part. Then, the inner contour for the RV cavity area is detected by the radial search based on  $D_{\max}$  and the circular scan. Finally, the RV endocardial contour is extracted from the background. Automatic detection and extraction of RV endocardial contours in the complete cardiac cycle is the main contribution of this method which could be a very important stage in the field of diagnosis and decision making.

One of the conventional parameters often used for quantification of the performance of the RV function is the right ventricular fractional area changes (RVFAC). This clinical parameter is expressed as a percentage change in the RV cavity area from the end-diastolic (ED) to end-systolic (ES) phases. Moreover, the accuracy of the RVFAC measurements is largely dependent on the accurate results of the RV cavity segmentation, based on the extracted RV endocardial contour. An example of the final results for the segmented RV cavities from ED to ES by applying the said algorithm is presented in Figure 15. The frames highlighted by black dashed lines are the maximum and minimum area of the RV cavity that are considered as the RV end-daistolic area (RVEDA) and RV end-systolic area (RVESA), respectively.



**Figure 15** Examples of the segmented RV cavity through a cardiac cycle based on the extracted endocardial contours from ED(a) to ES(h) frames highlighted in black dashed lines

### *Motion tracking of endocardial surface*

In echocardiography imaging, an essential requirement for endocardium wall motion estimation is contour extraction over a complete cardiac cycle. The main objective is to detect and track the motion velocity of the RV endocardial surface within a complete cardiac cycle in 4-slices from the 3D echocardiography dataset. Towards this objective, automatic and semi-automatic methods are being introduced.

### *Automatic Motion Tracking*

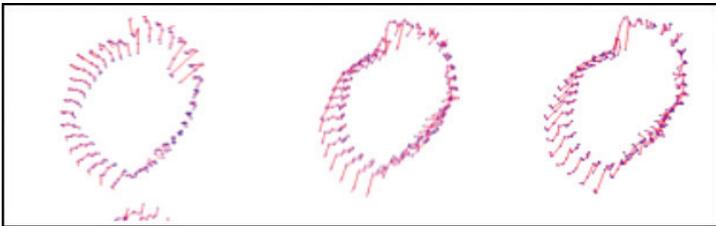
An automatic method proposed in this project is to track and analyze the RV endocardial surface motion in 36-landmarks that cover the whole endocardial surface. The results obtained from the previous phase of the RV endocardial contour extraction were used as input images for the cardiac motion tracking and analysis processes. This method consists of three main processing stages as detailed below:

**Stage 1:** Automatic identification of the 36 candidate landmarks using the radial search method based on clockwise circular scanning.

**Stage 2:** Computation of the displacement vector flow (DVF) and velocity vector flow (VVF) according to the movement distances of each landmark. The movement distance is calculated using the Euclidian distance formula for pair-contours in each two-consecutive frames.

**Stage 3:** For cardiac motion visualization, the x- and y- velocity maps, including the direction and magnitude, have been presented in two parts; from ED-to-ES (i.e. systole phase) and from ES-to-ED (i.e. diastole phase), respectively.

An example of cardiac motion visualization for RV endocardial surface in 4-slices based on the VVF measurements is presented in Figure 16. The main advantage of this method is that the velocity motion of the RV endocardial surface will be automatically tracked through the 36-landmarks.



**Figure 16** An example of cardiac motion visualization for RV endocardial motion tracking based on the VVF measurements from ED-to-ES in each slice

### *Semi-automatic motion tracking*

A semi-automatic method was introduced for motion tracking and analysis of the RV endocardial surface in 4-Landmarks through 4-slices of the long-axis view from the 3D echocardiography images. The main aim was to detect and track the 4-landmarks that had been manually selected by the specialist from the first frame in each slice. These anatomical landmarks indicate the four parts of

the RV endocardial wall. Specifically, these are the ‘Left-lateral’, ‘Right-lateral’, ‘Inferior’ and ‘Anterior’ walls. The framework of the method is based on the five main processing stages as follow: Stage 1:ROI extraction of RV cavity based on centre point identification.

**Stage 2:** Automatic detection and tracking of the 4-landmark locations based on the geometrical distance calculation (GDC) algorithm.

**Stage 3:** Measuring the DVF and VVF values in pixels and then converting the measurements into millimetres and centimetres, respectively.

**Stage 4:** Analysing the movement direction of each landmark using Fuzzy logic analyser technique and automatically updating the displacement and velocity values.

**Stage 5:** Automatic generation of the Time/curve graph for DVF and VVF measurements.

The advantage of this semi-automatic method is that it gives the user an alternative in case there is a need to track the motion of the RV endocardial wall in only four specific segments by manually selecting the 4 target landmarks on the first frame for each slice. One limitation is that it did not show perfect results for motion tracking of the RV endocardial surface in some cases, especially when there exists heavy trabeculation of the RV endocardial wall tissue.

## **Implementation**

In this research, the overall implementation was done using Visual Basic. An application was also developed for storing and retrieving the data sets of 2D and 3D echocardiography videos and images. The following are explanations on the methods implemented for this research.

### ***Implementation of Methods***

- i. The myocardial wall detection method was implemented and compared with the existing function provided by QLAB.
- ii. The method of ROI (RV cavity) identification based on cavity center point was implemented.
- iii. The automatic algorithm for RV endocardial contour extraction was implemented and compared with the specialist's manual annotations.
- iv. The method for cardiac motion tracking and visualization of the endocardial surface was implemented.
- v. The Fuzzy logic analyzer (FLA) was implemented to analyze the movement direction of candidate landmarks. The DVF and VVF measurements were updated according to the FLA results to support the Time/curve graph generation for each.

### **Performance Evaluation**

For performance evaluation the results produced by the methods and algorithms proposed were compared to the ground truth ((i.e. the results produced either by the specialist or using QLAB software). For qualitative evaluation, the results of each experiment in this research were visually validated by experts (i.e. clinical cardiologist and cardiac technicians). In addition, known performance metrics were used for quantitative evaluation, as summarized in Table 5.

### **Clinical Measurements**

The importance of the RV systolic function has been recognized in many cardiovascular diseases and cardiac surgery in the recent decade. In most investigated literatures, many clinical parameters have been developed to assess the RV function only in 2D echocardiography.

**Table 5** The experiments conducted for performance evaluation of the proposed methods and algorithms

Proposed Methods and Algorithms	Dataset	Dependent Variable	Performance Metrics
Boundary detection algorithm	2DE images in 4-chamber view	Accuracy	$FOM = \frac{1}{\max\{N_I, N_A\}} \sum_{k=1}^{N_A} \frac{1}{1 + \alpha d^2(k)}$
RV cavity segmentation approach	3DE dataset encompassing RV in long-axis view	Accuracy	$DSC(R_M, R_A) = \frac{2(R_M \cap R_A)}{R_M + R_A}$ $PTP = \frac{\text{Area}(\Omega_A \cap \Omega_B)}{\text{Area}(\Omega_A)} \%$ $PPP = \frac{\text{Area}(\Omega_A) - \text{Area}(\Omega_A \cap \Omega_B)}{\text{Area}(\Omega_B)} \%$
Endocardial contour extraction algorithm	3DE dataset encompassing RV in long-axis view	Robustness	$RMSD = \sqrt{\frac{1}{N} \sum_{i=1}^N \text{distance}(C_i, \hat{C}_i)}$
motion tracking method (Displacement measurement)	2DE dataset in 2-chamber view	Accuracy	Mann-Witney test

The experiments in this research work focussed on how the proposed methods and algorithms are able to perform clinical measurements of accurate quantification analysis for the RV function in 3D echocardiography. The most important clinical parameters measured are listed below:

1. RV cavity area ( $\text{cm}^2$ ): the total number of pixels within the segmented RV cavity which was then converted to centimetres ( $\text{cm}^2$ ).
2. RV EDA ( $\text{cm}^2$ ): the maximum area of the RV cavity through a complete cardiac cycle which is considered as the end-diastolic area.
3. RV ESA ( $\text{cm}^2$ ): the minimum area of the RV cavity through a complete cardiac cycle which is considered as the end-systolic area.
4. RV FAC (%): the change percentage of the RV cavity area from end-diastolic to end-systolic.
5. RV endocardial perimeter (mm): the total pixels in the extracted contour of the RV endocardial which was then converted to millimeters (mm).
6. Displacement (mm): the maximum value of movement distance for each candidate landmark on the RV endocardial surface through a complete cardiac cycle, i.e. the measure defining how far the end-cardial wall segment moves from an initial point.
7. Velocity (cm/sec): the amount of motion normalized to time for each candidate landmark on the RV endocardial surface. It is computed by dividing the movement distance over the time required, i.e. it is used to describe how fast the endocardial wall segment moves in a particular direction.

The first five measurements were produced through implementation of the approach for RV cavity segmentation and individually saved in a profile. Further, the displacement and velocity measurements were obtained through implementation of the algorithm for endocardial surface motion tracking supported with Time/curve graph visualization and saved in a specific profile.

For further detailed explanation please refer to Dawood *et. al* (2011), Dawood *et. al* (2014), Dawood (2014) and Dawood *et. al* (2015). This work has been filed for patent with title and filing numbers: (i) "A Method for Motion Tracking of Ventricular Endocardial Surface", PI2014701755 and (ii) "Automatic Segmentation for Right Ventricular (RV) based on Endocardial Contour Extraction in Echocardiography Image Sequences", PI2012700891, and has been copyrighted with the title "Automatic Boundary Detection of Wall Motion in Two-Dimensional Echocardiography Images" on 8<sup>th</sup> Feb 2012. This project won a Silver Medal at the International Invention, Innovation & Technology Exhibition (ITEX) 2012 with the title "Semi-automated Tracking of Mitral Anular Displacement". This project also won a Silver Medal in the Malaysia Technology Expo (MTE) 2012 with the title "Automatic Boundary Detection of Wall Motion in Two-dimensional Echocardiography". For further clarification on similar work for 2D echocardiography, please refer to Hussein Z.R. *et. al* (2010a), Hussen Z.R. *et. al* (2010b) and Hussein Z.R. *et. al* (2011).

## **3D INFORMATION MEDICAL VISUALIZATION AND DIAGNOSIS**

In medicine, visualization can be considered important to provide a more comprehensive picture. However the visualization challenge in medicine is the accuracy of the information that you want shown and how to analyze images from medical imaging tools. There are several reasons for involving visualization in medicine. Among them is the objective of looking into overall abnormalities, reducing human error in diagnosing illness and helping young doctors to analyze patients' illnesses.

Measuring ventricle volume is an important parameter for heart function assessment and medical decisions. However, even with the development of improved medical techniques, an accurate Right Ventricular (RV) stroke volume measurement is still challenging. In this research, we proposed a semi-automatic method to measure the RV stroke volume, where this method comprises two stages. The first stage is data generation (imaging), data collection and data simplification. This step is to satisfy maximum covering of the cavity structure (inflow, outflow and middle). The second stage also consists of a sequence of steps proposed to satisfy measurement of the real stroke volume and 3D modelling of the cavity structure. This is illustrated in Figure 17.

In accord with the problem statement of this research and consideration of the data characteristics to be used a mixed methodology (qualitative and quantitative) was proposed. The experimental research was designed specifically for each objective and the outcomes were validated qualitatively by expert cardiologists, using Likert's ranking questionnaires to assess the accuracy of the computed stroke volume and the reconstructed model. Quantitative validation was also conducted, using regression agreement and residual distribution, to assess the accuracy of the

computed stroke volume of the RV in comparison to the stroke volume of the LV for each case (patient) in the data set. This validation was conducted based on the medical fact that “RV stroke volume balanced the LV stroke volume with percentage”.

The dataset used in this research was obtained using a Philips QLAB system workstation. TEE imaging was used for acquiring the image of the RV cavity which is a dataset for cardiovascular patients. The optimum 3D full volume moving images, which is also known as 4D echocardiography, were used as input for this research. The optimum 3D full volume image is one that shows the complete structure of the RV cavity. This work encompasses a complete application that can be used by surgeons and cardiologists (specialists) for diagnosing RV abnormalities.

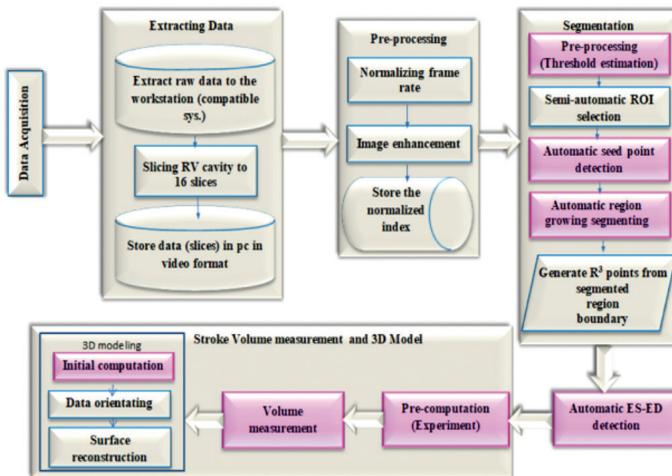


Figure 17 Research Methodology

## Data Collection

In this part of the research, a realtime three dimensional transesophageal echocardiography (3D-TEE) imaging method was used to acquire images of heart ventricles. 3D-TEE can be defined as on-line acquisition of a full volume heart structure using a 3D ultrasound matrix array probe which is passed into the esophagus of the patient. It is a non-invasive imaging technique which gives high quality data, and it is relatively inexpensive.

The acquisition process was performed using Philips iE33 with X7-2t matrix array transducer, as shown in Figure 18. Mid esophageal RV inflow outflow imaging view was used, to satisfy full covering of the complex structure of the RV cavity. Currently the RV stroke volume measurement introduced is based on a multiplanar view.

The imaging involves a sequence duration of four or seven cardiac cycles, using the mid esophageal RV inflow outflow to build a three dimensional full volume with breath holding each time.

The data for each patient was saved in a Philips echocardiography machine in four dimension (4D) DICOM format (Digital Imaging and Communications), in the hard disk of the acquiring machine. However, this data format is compatible only with the Xcelera-Philips software which cannot be used on a normal personal computer (PC). Thus, the raw data was transferred to a workstation installed with the Xcelera-Philips software. As shown in Figure 19, the software is designed for reading, off-line manipulation and analysing raw data in DICOM format from the iE33 Philips. The moving 3DE data can also be saved in standard formats, such as 2D image (JPEG) format or 2D video (AVI) format by the Xcelera software, which can be processed by the PC.

This project was developed under a memorandum of agreement (MOA) between the National Heart Institute, Malaysia (IJN),

University Putra Malaysia (UPM) and the National University of Malaysia (UKM), and the data was obtained from IJN with the permission of the Research Department, IJN.

***Preparation for Transesophageal Echocardiographic Imaging***

TEE may be used either in a clinic for diagnostic purposes, or in an operating theatre during surgery (non-cardiac surgery), for patients with known cardiac disease, to assess the cardiac status. Alternatively, it may be used during surgical intervention to evaluate the effects of the operation on the heart, such as “bypass surgery” or “valve replacement” or “valve repair”. As illustrated in Figure 20, the TEE procedure can be accomplished by passing a special probe through the mouth of the patient into the esophagus, directly behind the heart. In some cases the probe may be advanced into the stomach for an additional view of the heart. A small mouth guard is placed in the patient’s mouth to protect the tube from any accidental bites.



**Figure 18** Philips RT3DE machine, (b) TEE matrix array transducer (X7-2T)



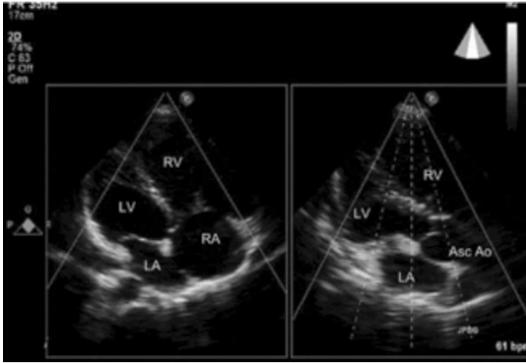
**Figure 19** Transferring raw data from the Philips machine to the workstation using a data cable



**Figure 21** Probe inserted through the mouth of the patient into the esophagus. Image taken from website <http://www.uofmmedicalcenter.org/healthlibrary/Article/82071>

### ***Full Volume TEE of RV (3D Acquisition)***

Four to seven wedges are acquired over four to seven consecutive ECG-gated cardiac cycles as this data acquisition method requires ECG gating. However, obtaining the gated data set is challenging especially for patients with arrhythmia and respiratory difficulties. The procedure of RT3DE imaging is performed by using a mid-esophageal RV inflow outflow view. Four to seven cardiac cycles are used to obtain a good image with high resolution from a narrow imaging angle, as illustrated in Figure 21. These four or seven imaged cardiac cycles are stitched together by the imaging machine. However, this process may cause a complication of overlapping at the imaged regions (tissues), which is called the stitching effect problem.



**Figure 21** Full volume acquisition using four narrow angles through four cardiac cycles.

### **Pre-Processing**

The purpose of pre-processing is to obtain the data from the machine and build a data set with the best view and setting that can be used to illustrate the right ventricle anatomy accurately. The gain, slicing orientation and slice thickness all have a strong influence on the

final results. Two stages of pre-processing were implemented in this work. Data simplification was employed in the first stage of pre-processing to overcome the difficulty of extracting the raw data by converting it to a standard format (AVI). Then frame normalization was performed to reduce the data size for a substantial reduction of the required computational time.

### *Data simplification*

The procedure for raw data extraction from the imaging machine is an important step. The raw data was saved in the acquiring machine in DICOM format as mentioned earlier. Dealing with data in the 4D DICOM format of iE33 Philips was not feasible because a reader compatible with this machine is required. The only data viewer that is able to read iE33-Philips DICOM data is the Xcelera Philips software available in a computer workstation. Therefore, the first step of pre-processing was converting the data format from 3D DICOM format to video format. This was done by transferring the data from the hard disk of the acquiring machine iE33-Philips to the hard disk of a Philips-workstation using a data cable. The inflow outflow view gives full coverage of the RV cavity. It is quite difficult to get the full cavity structure from the 4D-DICOM data as in the original design of the iE33 Philips machine the extraction of raw data as a 3D cloud of points is not allowed, as illustrated in Figure 22.

Faced with the above-mentioned challenge the work was started with slicing the RV cavity images into slices along the distance from the pulmonary valve (PV) to the tricuspid valve (TV). Off-line cavity extraction of the RV was performed on the long axis view to get the best coverage of the convoluted anatomy of the RV. The RV was cut into 16 slices by the Xcelera DICOM reader to cover the RV structure details that would lead to accurate results. The QLAB

Xcelera DICOM reader provides an iSlice facility which is able to slice ventricles into four, nine and sixteen slices, as illustrated in Figure 23.

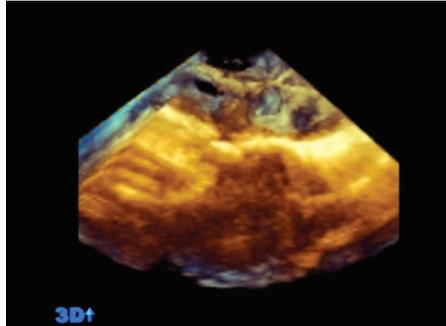
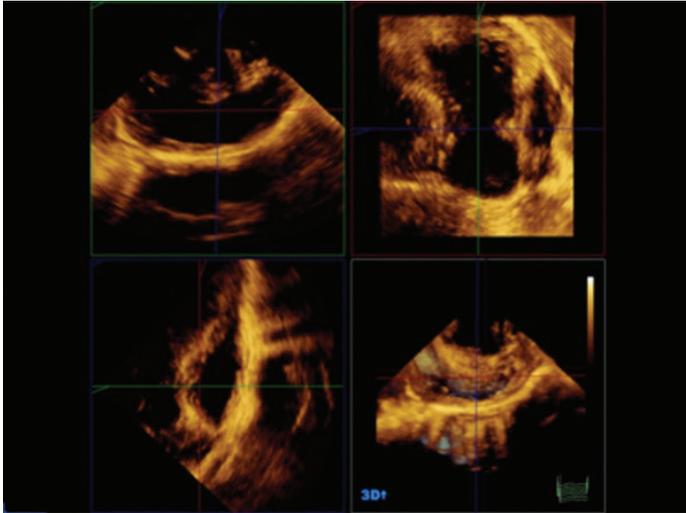


Figure 22 Full Volume Image of the RV.



Figure 23 Slicing options in the QLAB system.

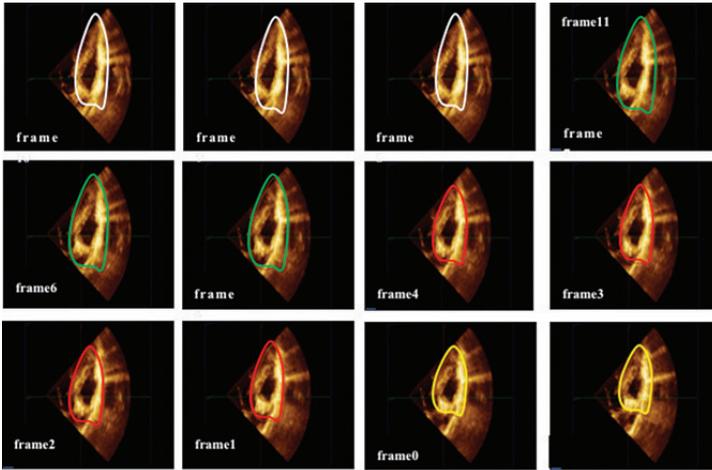
The software that was used in this research was designed originally for the LV cavity. The rotation and manipulation should be done on the slicing plane in order to achieve a good RV slicing process. The inflow-outflow view was chosen for slicing and the view rotated perpendicular to the cavity, as illustrated in Figure 24.



**Figure 24** Slicing direction, rotated perpendicular to the cavity

### *Frame Normalization*

Frame processing is one pre-processing approach that may be used to reduce processing time and storage cost (size of the dataset). Further, it also helps in motion tracking of the target and may also be used in feature extraction. In this study, the output of the data simplification process was 16 videos for 16 slices of the long axis view of the RV. The frame rate of each of these videos is 100 frames per second and the duration is one cardiac cycle. This characteristic leads to two limitations. First, the non-homogeneous frequent duplication in consecutive frames, as shown in Figure 25, such that there are no changes in the cavity region (no motion) in sequence frames 1, 2 and 3, and for the sequence frames 3,4 and 5, and as shown in Table 6. The second is that the number of frames in one cardiac cycle will differ from one patient to another, according to their cardiac cycle duration.



**Figure 25** Example of RV cavity motion according to the frame rate

**Table 6** Sample of Normalizing Process for one patient in the data set

Frame indicator	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Normalized Frames	1	5	9	13	17	21	25	29	33	37	41	43	47	51	55	59	63

To overcome these limitations, the RV wall motion is traced using an automatic normalizing method for the frames by choosing only the sequence of frames that have changes in the wall. A template matching technique was used for this as outlined in the following steps:

1. Convert the image format from colour image (RGB) to bi-level using the well-known Otsu thresholding method.
2. To reduce the computation cost, a window of empirical size of 200x200 pixels is used to crop the centre region of the image.

3. Next, match each two sequenced images ( $f_i$  and  $f_{i+1}$ ) using template matching to track the motion of the cavity.
4. Save the position of each frame that does not match the features of the preceding frame (i.e. if  $f_i \neq f_{i+1}$ ) in an array to generate a normalized frame sequence.

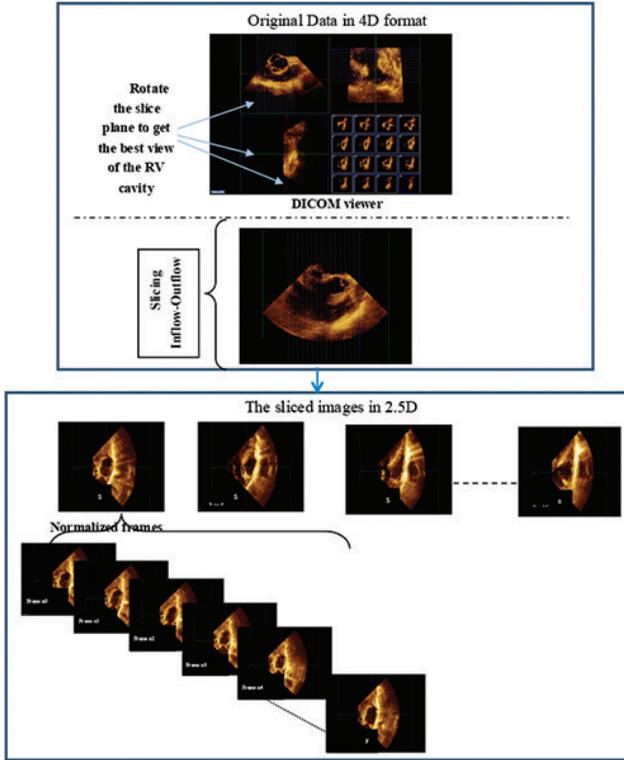
This process was used to normalise the video frames for the data sets of 13 patients, where the number of frames for the video of one cardiac cycle differed from one patient to another. Further, the numbers of the normalized frames differed from one patient to another, as shown in Table 7. For the current data set used in this thesis, the total number of the frames was ( $l=1016$  frames), and the total number of normalized frames was ( $g=305$  frames). This pre-process reduced the time of computation and data size by 70 %, based on Equation 1.

**Table 7** The number of frames in the echocardiographic video for one cardiac cycle, for each patient in the data set.

Patient No.	1	2	3	4	5	6	7	8	9	10	11	12
Frames in original video	69	69	79	115	68	46	94	74	107	75	87	72
Normalized frame	23	25	21	33	17	14	25	25	33	20	23	23

$$R\% = \frac{l - g}{l} \times 100 \quad (1)$$

where  $g$  is the number of frames resulting from the normalizing process, and  $l$  is the number of frames in the original video. The generated normalized sequence of frames was used as an indicator in all the subsequent processing steps of the discussed method.



**Figure 24** Process of extracting data from the moving 3D DICOM images

### *Segmenting the RV Cavity*

The process of segmenting the RV cavity from the moving images was to highlight only the RV cavity and omit the background of the image. This process was the start of the next steps of the discussed method. The purpose of this process was to focus on the complicated anatomy of the RV in the 3D echo images and segment it. The segmented region was estimated so as to measure the full volume of the cavity, and to build a 3D model of the RV. There have been many previous approaches to extract the RV cavity from 2D and 3D

ultrasound images. Those approaches adopted a manual interaction correction method for the RV segmentation. Since there was a lack of automation in those approaches, in this research a semi-automatic method for RV segmentation of the 3D echo images is presented. The RV cavity was partitioned into slices and the partitioned slices were the input for the discussed method. The output would be the segmented RV cavity from 16 slices. Region growing technique was deployed to segment each slice. This technique works automatically by detecting a seed point and then segmenting the Region of Interest (ROI) independently, utilizing pre-knowledge of the region feature. This method can give an accurate extraction of the RV cavity. The results were validated qualitatively by medical specialists and experts and benchmarked with other available segmentation methods and the currently available commercial technique using the A-QLAB system.

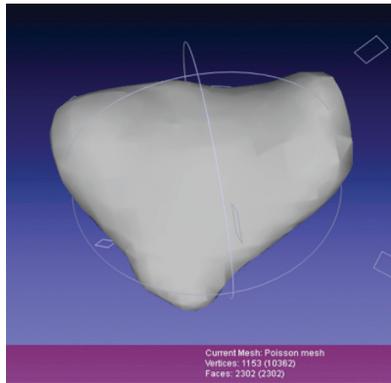
### **Automatic Detection of the End-Diastolic and End-Systolic Frames**

Ventricle stroke is the blood quantity stroked from the ventricle during the cardiac cycle. Measuring the stroke volume is computed by determining the difference between the ventricle cavity volume at the End-Diastolic (ED) and End-Systolic (ES) stages of the cardiac cycle. Based on this fact, the first part of the stroke volume computation process was to determine the ED and ES frames in the echocardiography video. An automatic method was introduced to determine the ED and ES stages by tracking the area of the fractional part of the cavity through one cardiac cycle. The input for this process was the indicator of the normalized frames and the segmented region of the RV cavity in frames of three slices.

## Stroke Volume Computation

The Stroke volume computation process was built based on disk summation principles. This process uses the segmented region of the cavity from the 16 slices at the ED and ES stages. Then the volume of the segmented cavity in each slice was computed by measuring the area of the segmented region multiplied by the slice thickness, which was determined from the distance between slices. The resultant volume of this computation was in pixel units. To convert the measurement unit to millilitre units requires knowledge of ultrasound probe resolution parameters. In establishing the parameters, an experiment was conducted to find the 3D ultrasound probe resolution, without depending on the physical parameters of the ultrasound probe. The ultrasound parameters that can be used to measure the resolution using the standard formula were not available in the current 3D ultrasound probe. This experiment was to simplify the method of measuring the ultrasound probe resolution.

Then the boundary of the segmented cavity was used for 3D illustration of the RV structure. The point sets were oriented in the first stage and then the 3D model reconstructed using Poisson surface reconstruction (refer to Figure 27). The importance of this process is to assist clinical experts by visualizing the 3D model. This step used the (x, y) axis of the boundary points of the segmented cavity for each slice, and the z dimension from the position of each slice in the Inflow-Outflow view. For further details please refer to Rahmat *et. al* (2013), Abboud *et. al* (2014a), Abboud *et. al* (2014b) and Anas A. Aboud (2014). This work has been patented under the title “A Method for Determining Right Ventricle Stroke Volume” with filing numbers PI2012001329 and US Patent 20,150,078,638. This project won a Silver medal at the Malaysia Technology Expo (MTE), in 2013 with the title “3D Heart Anatomy”.



**Figure 28** Poisson surface reconstructed for the RV cavity from orientated points. The MESHLAB viewer is used to view the surface

## 3D MULTIMODAL MEDICAL IMAGES REGISTRATION FOR VISUALIZATION

Coronary artery imaging techniques have played a significant role in research associated with coronary artery disease diagnosis and treatment. A variety of medical imaging techniques have been utilized over the years. Among these techniques, X-ray Angiography and CT Angiography were found to be the best for specialists (cardiologists and cardiac surgeons) for coronary artery disease diagnosis and treatment. Despite the increased usage of X-ray Angiography and CT Angiography nowadays some important information cannot be derived using each of these modalities alone, even by experienced specialists. From the technical stand point, there are several complexities which make precise 3D stenosis positioning a complicated task:

- Limitations associated with the output of X-ray Angiography (angiogram), such as 2D information. However, it is still possible to detect all types of stenosis lesions in coronary arteries from this modality.

- Limitations associated with the output of CT Angiography, such as the inability to visualize all types of stenosis lesions in coronary arteries. However, the output of CT Angiography is 3D and also includes information about other cardiac components.

These limitations were confirmed by expert cardiologists and surgeons who participated in the validation stage of the results to detect stenosis locations in the 2D coronary X-ray Angiography and 3D CT Angiography. This was the motivation to create a set of computational algorithms for 3D multimodal stenosis reconstruction using X-ray Angiography and CT Angiography.

Different modalities hold different information to assist physicians in making decisions. Previously, these images were viewed in-separate or adjacent windows, and fused together mentally. Even though medical image registration and image fusion have been successfully implemented for other organs, such as the brain and lungs, medical image registration and fusion for the heart present different challenges: (i) since the heart is beating, fusion requires synchronization with the rhythm of the heart for different phases and (ii) the heart is a non-solid organ, and thus acquired images give a vague impression.

Precise computer-assisted coronary artery analysis is consequential in diagnosis and treatment by cardiologists and cardiac surgeons. As explained previously, X-ray Angiography and CT Angiography are the best modalities to visualize coronary arteries and CAD diagnosis. Individually, these modalities provide valuable information, but they do not represent the complete information about coronary arteries. Thus, it is important for specialists (cardiologists or cardiac surgeons) to combine informative data from both modalities. Indeed, specialists believe that access to some extra information about stenosis points in coronary arteries extracted from angiograms, such as the 3D position and their

relative localization with respect to the corresponding coronary artery from CT Angiography, as an important aid in CAD diagnosis and treatment. There are few hybrid devices, like SPECT/CT, PET/CT, PET/MRI and MRI/PET, which give combined informative data. To the best of our knowledge, there are no hybrid devices available for combining the results of X-ray Angiography and CT Angiography devices. Moreover, these devices are very expensive and none of them provide the 3D position of stenosis lesion of the coronary arteries. These two modalities are currently available in most hospitals. One way to further aid the specialists is by setting up the connection between stenosis points from an X-ray Angiography along with their 3D positions on the coronary arteries from CT Angiography. This will provide them a 3D informative model showing the stenosis and coronary arteries information from both modalities. With this aim, it is highly necessary that firstly the coronary arteries be segmented, labeled and also their control points be extracted precisely from both modalities, and then an appropriate registration be computed based on these results. The main aim of this research project was to assist medical specialists in diagnosis and treatment by providing them with information showing the relationship between the CT Angiography and X-ray Angiography. With this aim the stenosis lesion positions were 3D reconstructed through CT Angiography and X-ray Angiography images' registration.

## **Research Framework**

As shown in Figure 28 the research framework consisted of three main phases. The first phase corresponded with the new method for coronary artery segmentation and labeling in X-ray Angiography. The second was coronary artery segmentation and labelling in CT

Angiography while the last phase was feature-based registration of coronary arteries in CT Angiography and X-ray Angiography.

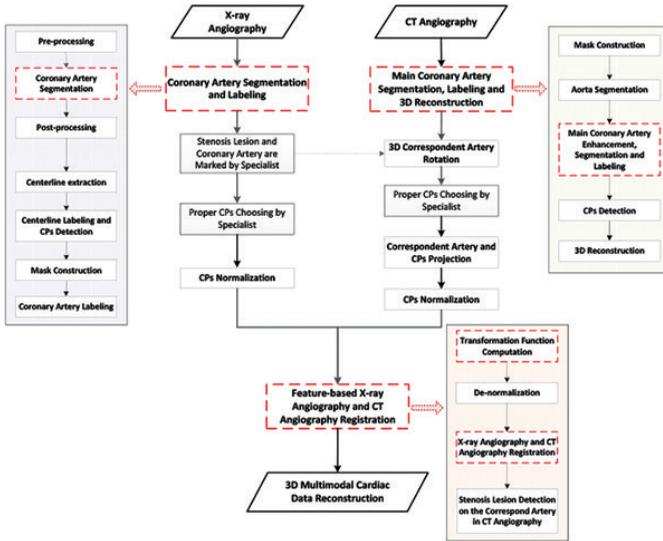


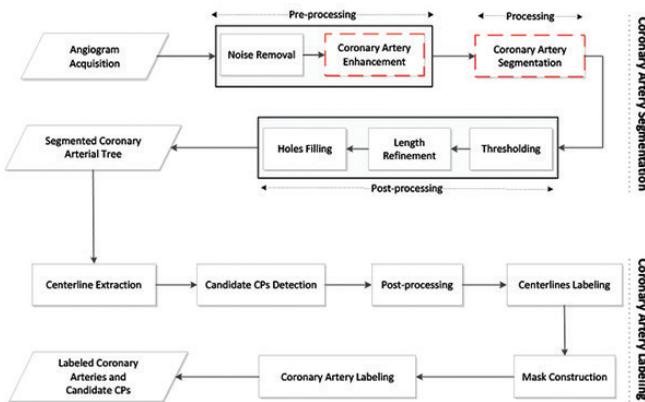
Figure 28 The research framework showing the three main phases of the research problem

## A New Method for Coronary Artery Segmentation and Labeling X-ray Angiography

In this phase, a new method for coronary artery segmentation and labeling from angiograms was created. The use of X-ray Angiography images by specialists is increasing, even though the images generally have a poor signal to noise ratio. The increasing use of coronary X-ray Angiography by specialists is due to its ability in handling diagnosis and treatment procedures online in real-time. At this stage, the tasks of coronary artery segmentation and labeling were separated into two sequential sub-phases. Generally, coronary artery segmentation from 2D angiograms is a process of separation of the blood arteries from the background. The input for this part

is a chosen frame, called the optimal frame, from the angiogram series, and the output will be networks of vessels in binary format image. Coronary artery labeling from 2D angiograms is a process of labeling coronary arteries and keeping them separate. Coronary artery labeling makes it possible to access each artery from the whole coronary arterial tree. The input for this part is a segmented coronary arterial tree, and the output will be labeled coronary arteries and the candidate control points. Candidate control points will be used later in the registration phase.

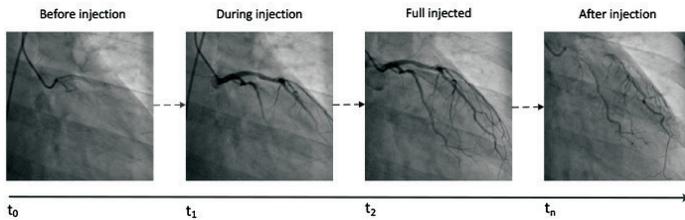
As illustrated in Figure 29, the following steps were defined for coronary artery segmentation: Angiogram acquisition, preprocessing (includes noise removal and enhancing coronary arteries), processing (includes coronary artery segmentation) and post-processing (includes thresholding, arteries' length refinement and filling the holes). The steps defined for coronary artery labelling are: Centerline extraction, candidate control points detection, post-processing, centerline labeling, mask construction and coronary artery labeling.



**Figure 29** The proposed framework for coronary artery segmentation and labeling X-ray Angiography

## Angiogram Acquisition

In the first stage, different angiograms from several angles were examined by a specialist (cardiologist or cardiac surgeon) to find the best view from which stenosis can be visualized and detected. Then an optimal frame was selected in a sequence of frames. A frame with optimal imaging condition in a series of angiograms usually means the acquired frame at the end-diastolic phase of the cardiac cycle. Since a large amount of contrast material is harmful for the patient and the coronary arterial tree is not visible in most of the frames, the angiogram can be considered as optimal when the arterial tree is filled with the contrast agent, called full injected. Figure 30 illustrates an example of a sequence of frames showing different intervals of the contrast injection process. This angiogram will be analyzed in the next stages of the discussed method for coronary artery segmentation.



**Figure 30** A timing diagram of the sequence of contrast injection

### *Angiogram Pre-processing*

Two main steps are defined here for pre-processing: noise removal and coronary artery enhancement. As has been mentioned before, X-ray Angiography images still suffer from a large amount of noise. The aim of the noise removal process is to eliminate all the noises while keeping the quality of images. The aim is to retain the arteries and particularly sub-arteries in angiograms. Using

traditional algorithms for this aim, such as smoothing methods include mean or median filters, will lead to some parts of coronary arteries disappearing, especially in thinner and sub arteries. Another technique for removing noise is by converting images into the transform domain such as wavelets and then comparing the transform coefficients with a threshold, which was the method used in this research.

In the next step, the coronary arteries were enhanced. Traditional methods were not applicable here because they enhance and sharpen not only the arteries, but also the background of the angiogram which leads to increased noise in whole image and also the appearance of some artifacts in the segmentation stage. Thus a new method was introduced for coronary artery enhancing by focusing only on the large angiogram features, which encompass the coronary arteries.

### *Angiogram Processing*

At this stage, a new method for coronary artery segmentation from angiograms was proposed. The input for this stage was the output from the angiogram pre-processing. After segmentation in this part the coronary arteries were segmented from the background in an angiogram. Post-processing was applied on the output to improve the quality of the results in the next stage.

### *Angiogram Post-processing*

In this stage, the final coronary arterial tree was extracted by thresholding followed by length refinement and then the filling holes methods. The length refinement and filling holes methods are needed because the outputs from the previous stages still have some noise, called residual noise, which comes from another organs (such as ribs, diaphragm and so on). We called this stage the angiogram post-processing in the discussed method.

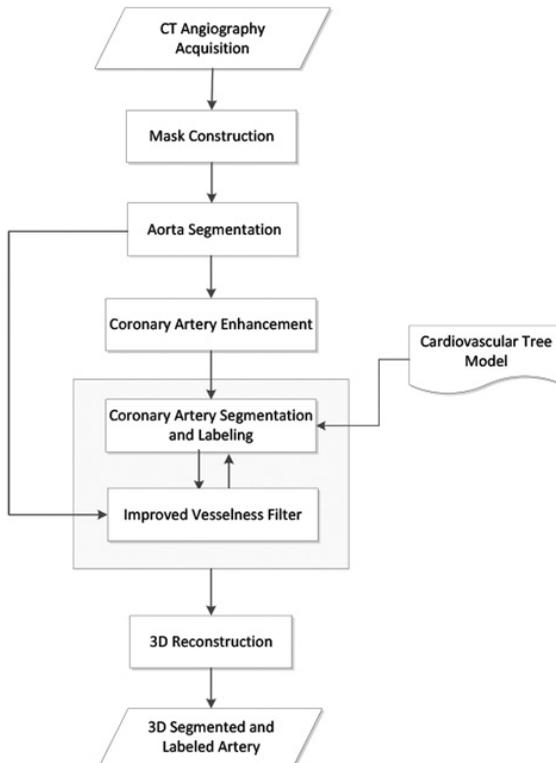
## **Coronary Artery Labeling**

As mentioned previously, the input for this sub-phase was the segmented coronary arteries. After coronary artery segmentation, firstly the centerlines and candidate control points should be detected for each artery. Then some post-processing steps were applied, including removing short terminal arteries and refining the branch points. Subsequently, centerlines were detached and labeled. Finally, the coronary arteries were labelled by constructing a proper mask.

### ***Main Coronary Artery Segmentation, Labeling and 3D Reconstruction from CT Angiography***

In this phase, a new method was introduced for main coronary artery segmentation, labeling and 3D reconstruction from CT Angiography. Precise computer-assisted coronary artery analysis in CT Angiography slices is very consequential in later diagnosis and treatment by cardiologists and cardiac surgeons. Coronary artery segmentation and 3D reconstruction should thus be done precisely because some other processes, such as registration with other images from different modalities, will be done based on these results. However, there are many problems in coronary artery segmentation from CT Angiography slices. Firstly, coronary arteries are shown as small parts, semi-circle or tubular shapes in each slice. Therefore, tracking them via slices is not a straightforward process. Secondly, artifacts which come from other body organs in the CT Angiography images, such as the backbone, ribs, cardiac chambers and other components, should be removed in the final segmented image.

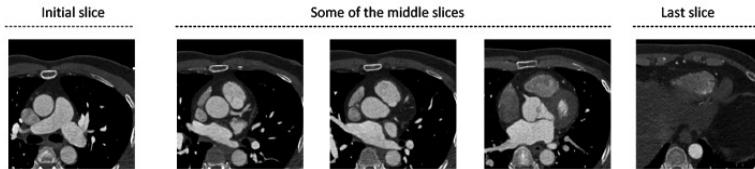
In the discussed method segmentation and labeling are done in the same phase. In addition, it is possible to visualize every artery separately as well as the whole coronary arterial tree. As illustrated in Figure 31, the steps for this method are: CT Angiography acquisition, mask construction, aorta segmentation, coronary artery enhancement, coronary artery segmentation and labeling and finally, 3D reconstruction.



**Figure 31** The proposed framework for coronary artery segmentation, labeling and 3D reconstruction from CT Angiography

## CT Angiography Acquisition

The second image for registration is the CT Angiography which should be acquired from the same patient. The CT Angiography modality is used to visualize cardiac components, especially coronary arteries and includes 3D information. Since in this research the optimal angiogram was chosen from the end-diastolic phase of the cardiac cycle, the best diastolic phase of CT Angiography was also acquired in order to reduce misregistration. Each CT Angiography dataset includes about 400 raw slices. The raw slices of CT Angiography were analyzed in the next phases in this research for main coronary artery segmentation, labeling and 3D reconstruction. Figure 32 illustrates an initial slice, some of the middle slices and a last slice of a CT Angiography.



**Figure 32** Some slices of the best diastolic CT Angiography.

### *Mask Construction*

In mask construction, an appropriate mask is constructed for each slice to specify the border of the heart clearly. Firstly the CT Angiography slices were classified anatomically. Normally, every CT Angiography slice is decomposed into main components, such as: pulmonary tissues, pulmonary vessels, aorta, diaphragm, pericardium, myocardium, aorta, bones, ventricles, hepatica tissues and (contrasted/uncontrasted) coronary arteries. Since the most important component in this research is the coronary artery, the

slices were categorized as it has the most probably coronary arteries through various other heart components.

### *Aorta Segmentation*

In this stage, the aorta is segmented into initial axial slices and the results saved in a 3D matrix, to be used in the 3D reconstruction stage.

### *Coronary Artery Enhancement*

Prior to coronary artery segmentation, a special filter was applied to measure the vesselness components in each slice. The aim of this stage was to enhance the coronary arteries in the CT Angiography slices as tubular shaped objects, to improve the segmentation results in the next stage. We thus proposed an improved vesselness response filter in this stage to enhance the coronary arteries in the CT Angiography slices.

### *Coronary Artery Segmentation and Labeling*

As mentioned earlier, there are many components in each CT Angiography slice that should be removed to achieve a better view of just the coronary arteries. For this, we proposed a new method, called Intersection Tracking, for tracking the coronary arteries through 2D slices, from ostium to the end. The discussed method works based on the fact that each coronary artery has continuous pixels through slices from the start to the end point. The improved vesselness filter proposed in this step also removes artifacts in the output. Moreover, at this stage the main coronary arteries are labeled as four types: LM, LCX, LAD and RCA. Another output of this stage is the candidate control points, which will be used in the registration phase.

### **3D RECONSTRUCTION**

In the previous stage of the discussed method, all coronary arteries were segmented as cross sections of each slice and kept in different 3D matrices. That means that for all parts of the coronary arteries, such as the LM, LAD, LCX and RCA, correspondent 3D matrices  $M_{LM}$ ,  $M_{LAD}$ ,  $M_{LCX}$  and  $M_{RCA}$  were respectively constructed, which preserved each pixel of the corresponding artery in the 3D coordinate domain. In this stage, the OPENGL library in the VC++ program was applied to the previous stage results to make 3D reconstruction and visualization of all parts of the coronary arteries. Using this method it was possible to visualize all coronary arteries together with the aorta or to show them separately.

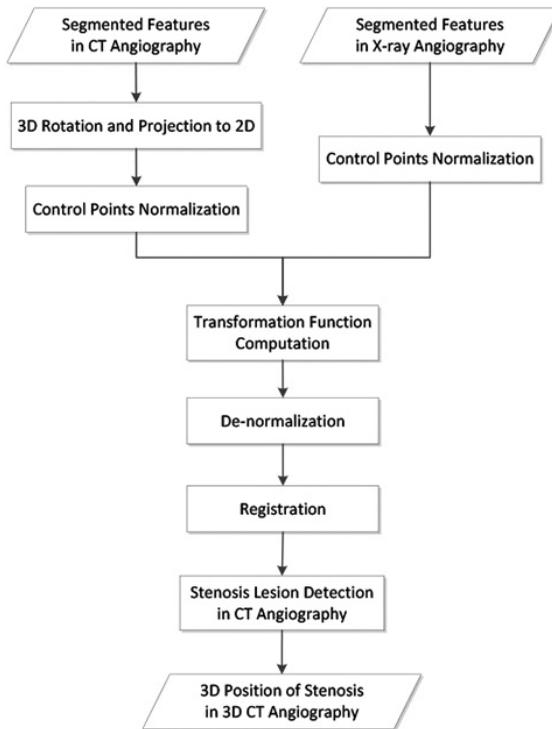
### **Feature-based Coronary Artery Registration from X-ray Angiography and CT Angiography**

In this phase, a new method was created for coronary artery registration in X-ray Angiography and CT Angiography. There is no previous work on coronary artery registration from X-ray Angiography and CT Angiography modalities to create a 3D reconstruction of stenosis points. Precise coronary artery registration and segmentation of 3D positions of stenosis lesions is very important for cardiologists and cardiac surgeons because most of their decisions in diagnosis and treatment, for example cardiac bypass surgery, will be made based on these results. Therefore, in this phase a proper transformation function was computed to register the coronary arteries in both the X-ray Angiography and CT Angiography modalities. After registration, the 3D positions of stenosis lesions were calculated.

As illustrated in Figure 33, the steps for solving this problem were: 3D rotation and also projection to 2D for segmented features

from CT Angiography, control points normalization in modalities, transformation function computation, de-normalization, registration and finally stenosis lesion detection in the CT Angiography.

In the discussed method, registration and 3D reconstruction were done based on the segmented features from the previous phases. These features include chosen coronary arteries in both modalities, chosen control points in both modalities and position of the stenosis lesion on the coronary artery in the angiogram.



**Figure 33** The proposed framework for coronary artery registration in X-ray Angiography and CT Angiography.

### ***3D Rotation and Projection to 2D***

As mentioned earlier, different angiograms from several angles were examined by a specialist (cardiologist or cardiac surgeon) to find the best view, in which stenosis can be visualized and detected clearly. Then, the specific coronary artery (which has stenosis on it) and its control points were segmented and labeled from the selected angiogram, using the method mentioned in the first and second phase of the proposed solution. Further, the position of the stenosis point was marked by the specialist on the coronary artery segmented from the angiogram. Subsequently the correspondent artery and their candidate control points were segmented from the CT Angiography, using the algorithm proposed in the second phase of the research framework.

As mentioned earlier, this phase started with rotating and 2D projection of the correspondent coronary artery and its control points in CT Angiography to achieve the same angle as the selected angiogram. This was to increase the accuracy of the registration results in the subsequent stages of this phase. Since the CT Angiography results were preserved as 3D points in one of the 3D matrices,  $M_{LM}$ ,  $M_{LAD}$ ,  $M_{LCX}$  or  $M_{RCA}$  (based on which one was detected as having the stenosis), it was possible to rotate the artery so that it was in the same angle as that in the selected angiogram. The output of the rotation was saved in the new matrix with new  $(x', y', z')$  Cartesian coordinates (3D). Then, the rotated CT Angiography was projected from the  $(x', y', z')$  Cartesian coordinates (3D) to the plane (2D). The same rotation and also projection were done for the control points in the selected coronary artery from the CT Angiography.

### ***Control Points Normalization***

In the next stage of this phase, the control points from both modalities were normalized to improve the accuracy of the results. This stage was carried out before computing the transformation function. Control points normalization provides a second advantage in increasing the accuracy of the results, in that a transformation function that incorporates a preliminary normalization step will be invariant with respect to irrelevant choices of scale and coordinate origin. This is because normalization will undo the effects of coordinate changes.

Normalization comprises of translating and scaling the coordinates in both images from the X-ray Angiography and CT Angiography. To this end, firstly the control points' coordinates inside every image were separately translated in order to bring the centroid towards the origin. Then it was scaled so that the Root Mean Squared (RMS) distance from the origin was equivalent to the square root of two.

### ***Transformation Function Computation***

After normalization, the geometrical transformation function  $T$  was computed using the normalized control points. In this stage, a proper transformation matrix was applied to find the best transformation function. To this end, all transformation types were evaluated to find the best one.

### ***De-normalization***

In this stage, proper correction had to be carried out to bring the (normalized) transformation function  $T$  to the original coordinate system. The new transformation function is called.

### ***Coronary Artery Registration***

After de-normalization, image registration was carried out by applying the transformation function . Cardiac image registration is really more complicated in comparison with that for other body organs (such as brain images registration), particularly due to the nonrigid and also combined movements of the heart and thorax. Furthermore, in comparison with other organs, such as the brain, the heart demonstrates much less precise anatomical landmarks. Furthermore, cardiac images, such as the X-ray Angiography, generally have lower quality and image resolution compared to the images of other organs. In this stage, both arteries were registered and displayed on the same plane using the transformation function, which was obtained in the previous stages.

### ***Stenosis Lesion Detection and 3D Position Detection***

After registration, both coronary arteries were shown on a same plane. In this stage, the stenosis point from the angiogram was located on the correspondent artery in the CT Angiography. After locating the stenosis point on the correspondent artery in the CT Angiography, back projection was done for 3D reconstruction. The final result of this part was the specific coronary artery including the located stenosis, which can be displayed in the original 3D space ( $x'$ ,  $y'$ ,  $z'$ ) Cartesian coordinates.

## **Implementation**

The discussed methods were implemented using MATLAB R2014a and VC++ 2008. Closely related existing methods are also implemented in MATLAB R2014a. The methods implemented specifically for this research comprised:

- The framework for automatic coronary artery segmentation from X-ray Angiography images and comparison with existing methods.
- The method for main coronary artery labeling and candidate control points detection from X-ray Angiography images.
- The algorithm for main coronary artery segmentation, labeling and candidate control points detection from CT Angiography and comparison with the existing method.
- The discussed method for feature-Based CT Angiography and X-ray Angiography registration.
- 3D multimodal cardiac reconstruction.

## **Dataset Preparation**

In this step, X-ray Angiography and CT Angiography datasets for each phase of the work were prepared. As mentioned in Chapter 1, medical imaging for coronary diagnosis comprises several image modalities, such as, X-ray Angiography, Computed Tomography Angiography, Magnetic Resonance Angiography, Intravascular Ultrasound (IVUS) and many others, that are used to provide 2D or 3D visualization of the coronary arteries. Among these modalities, X-ray Angiography and CT Angiography are the best ones which are commonly used for diagnosis and treatment of coronary artery diseases (CAD). Despite their significance and the abundance of clinical data acquired in daily clinical examinations worldwide, very few publicly available standard datasets can be found for each of these modalities. Indeed, there is no comprehensive source of validated datasets for cardiac imaging modalities, especially for X-ray Angiography and CT Angiography. The author was thus motivated to collect appropriate and comprehensive datasets from available clinical sources for different and also same patients.

### *Clinical Datasets of X-ray Angiography Images*

To validate our proposed algorithms in the coronary artery segmentation, labeling and registration phases, image databases of routinely acquired coronary angiograms and CT Angiography were collected from UiTMMC Sungai Buloh branch. This consisted of a large number of X-ray Angiography and CT Angiography images with a wide variety of vessels, with different types of coronary lesions and different geometries of vessel segments.

The X-ray Angiography dataset included 9600 angiograms of 20 patients acquired from eight angles for each patient, which were obtained using a standard C-arm PHILIPS X-ray Angiography system. These images have spatial resolution  $512 \times 512$  and 24-bit quantization in grayscale BMP format. We randomly selected 60 X-ray injected frames of these angiograms (30 LCA and 30 RCA) from this database as the dataset for this part of the research, where the coronary arterial tree was filled with the contrast agent and manually created the ground truth for each. All the ground truth images were validated by the expert cardiac surgeon, cardiologist and radiologist.

### *Clinical Dataset of CT Angiography*

The CT Angiography dataset included images of 16 patients acquired using a standard SIEMENS 3D CT Angiography system in best diastole. These images have spatial resolution  $512 \times 512$  in the horizontal plane and about 450 slices of 0.75mm for the z axis. The corresponding ground truths were created from the slices. All ground truth images were validated for accuracy by the expert cardiac surgeon, cardiologist and radiologist. The distribution of this data was allowed through a written agreement from the specialist and all patient identification was removed from the images to preserve confidentiality.

### ***Clinical Dataset of X-ray Angiography and CT Angiography for Same Patients***

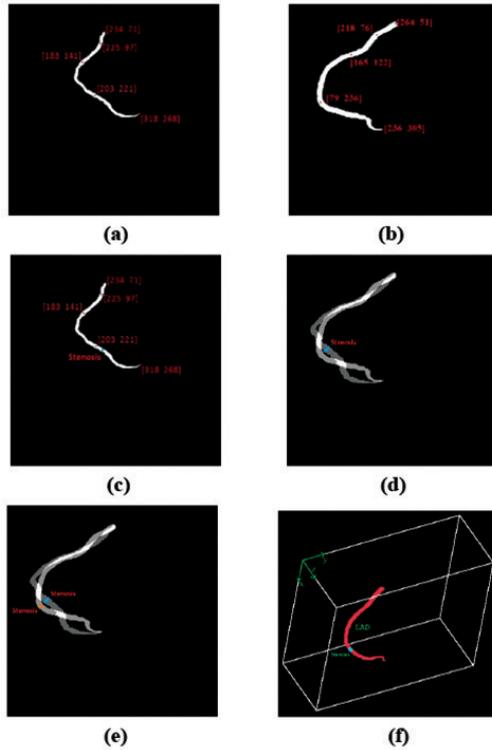
As mentioned earlier, the last phase of this work would be coronary artery registration in CT Angiography and X-ray Angiography, and 3D stenosis position reconstruction. In this phase, X-ray Angiography and CT Angiography datasets were prepared for the same patients. Due to the fact that the above two datasets belonged to the same 12 patients, these were chosen as the datasets for this part of the research.

### **Experimental Design**

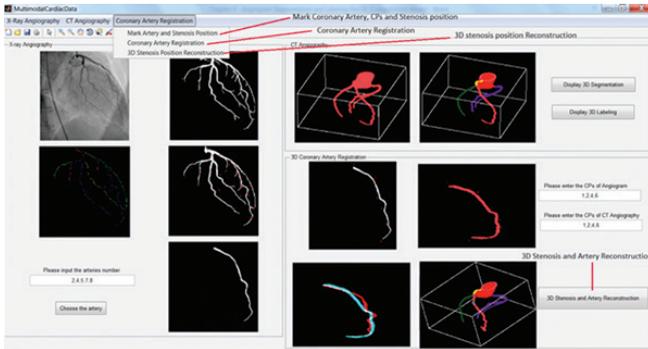
This research work follows the quantitative research design in which the effects of several possible parameters in the proposed methods and algorithms are the focus of the analysis. This section describes the experiments and findings in this research work. Based on the research problems identified, the experiments were divided into the following categories: 1) experiment for tuning the various parameters used in the proposed methods; 2) experiments for validating the proposed methods; and 3) experiments for evaluating the performance of the proposed methods and comparison with well-known existing methods.

In the first category, a set of experiments were designed for tuning the parameters of the proposed methods. For comparative performance evaluation, the optimal parameter values were also used for existing methods, based on the parameter settings described in the corresponding publication. In the second category, the functionality of the discussed method was compared with the ideal situation. Here for the provided set of parameter values the results were compared to the ground truth. In these experiments, for each discussed method, a set of ground truth images were prepared, and

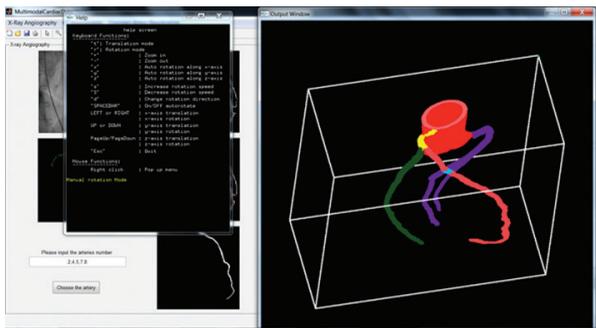
then the discussed method was introduced as the experimental treatment followed by a measurement which determined how well the discussed method was able to perform its expected function. The measurement was based on a set of predefined quality metrics for each individual method. The third category consisted of experiments in which the performance of the discussed method was compared with that of well-known methods and algorithms that are closely related to the proposed methods. That is, for a given set of parameter values, the results produced by the discussed method were compared to that of a particular related work. To this end, two or more methods were applied to the same image dataset or ground truth images and the performance of each method observed. In all experiments the initial parameters were chosen to provide equal conditions for the algorithms under experiment. Images of the results of this part of the research are shown below (refer to Figures 34-36).



**Figure 34** The results of coronary artery registration to locate and 3D stenosis point reconstruction on the CT Angiography. (a) Segmented LAD from angiogram with candidate control points in 2D plane . (b) Segmented LAD from CT Angiography with candidate control points, projected on 2D plane . (c) Marked stenosis position in the angiogram. (d) Registration results using the discussed method for both modalities, shown on plane . (e) Stenosis position estimated in the registration plane on coronary artery from CT Angiography. (f) 3D position of stenosis in the original 3D coordinate system



**Figure 35** The GUI design for the 3D stenosis position reconstruction using CT Angiography and X-ray Angiography registration



**Figure 36** Example of 3D stenosis position reconstruction including the whole coronary arterial artery using the discussed method. Stenosis positions are shown in blue, aorta in red, and LAD, LM, LCX and RCA are labeled in pink, yellow, green and purple, respectively

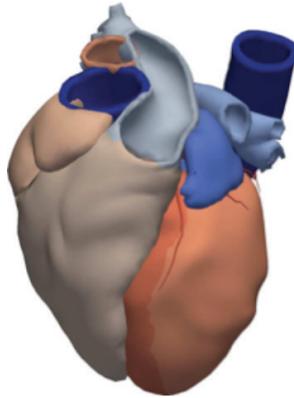
For further clarification and explanation, please refer to Moosavi *et. al* (2013), Moosavi *et. al* (2014a), Moosavi *et. al* (2014b), Moosavi *et. al* (2015) and Moosavi (2016). This work has been copyrighted with the title “AngioFusCTA”, LY2017001378.

### **3D HEART SURFACE VISUALIZATION**

Realistic 3D models play important roles in providing exciting opportunities for learning the heart anatomy and aiding in cardiac surgery training. Several approaches can be used to obtain a realistic heart model even by using 3D computer graphics softwares, 3D scanner devices or image-based modelling algorithms. Computer-Aided Design (CAD) software is a common software used in the creation of 3D models from scratch. The CAD software produces a fairly good model. Although the model can be further improved, via colored surfaces, the final result is still unrealistic, costly and time consuming. On the other hand, the 3D scanner is a device used to collect object data and then project them as a 3D model. Unfortunately, even with its texture, it is still unrealistic due to the scanned model not being from a real object.

Medical imaging researchers use image based modelling approaches to model the heart. These researchers acquire several images of the human body organs for study of the anatomy of the internal organs of patients or to provide information for diagnosis. Data from such devices consists of 2D slices that are used for the reconstruction process to produce a 3D model of the organ under examination, which will convey more information about the organ and ease understanding and learning of the human internal organs especially among novice medical students.

In addition, the 3D model is useful for surgical training and preparation so that surgeons will be familiar with what they will come across in the operating theatre. However, the process is time consuming and several processes are required to derive a final 3D model. Additionally there is also issues of cost and time needed to learn to use these tools or devices. Figure 37 shows an unrealistic solid 3D heart model derived from medical imaging.



**Figure 37** 3D surface of the heart (original image courtesy of Google biodigital human)

Medical applications make extensive use of high quality 3D models. The 3D model is useful for learning the anatomy of human internal organs as well as training for cardiac surgery. In addition, a 3D model helps reduce learning time. Several 3D models are manually created, with the help of available modelling tools. However, it is costly and time consuming to learn to use these tools. An interesting and easier alternative is modelling from images. Modelling from medical images to produce 3D models of human internal organs is done via image sequences acquired from medical imaging devices. The vast development of imaging acquisition devices in recent years has led to an increase in the dimensionality of these images to 3D and Four Dimensional (4D), based on a scan of multiple 2D slices in one axial direction. To generate a more intuitive representation of the obtained images, a 3D model is reconstructed from segmented 2D slices. The input images are acquired as a stack of parallel slices and collectively represent a 3D model of the heart. Then analysis and processing of these slices are required, such as, camera calibration, noise removal, filtering,

features extraction and matching and depth determination. Finally, the model reconstruction is done. However, a reconstructed model from medical imaging such as Computed Tomography Angiography (CTA) requires several processes that are costly and time consuming in terms of data acquisition and data storage, and has the potential to produce unrealistic 3D solid models. In addition, further issues occur during the reconstruction process, such as the highlight reflections from the wet surface of the heart. These reflections deform the reality of the final 3D model and need to be removed before obtaining the final 3D model.

A realistic 3D model is an important factor for educational or clinical purposes since it shows the reality of the human heart which will help the novice medical student to be familiar with what they will face during actual surgery. Realistic 3D model reconstruction is one of the important challenges for researchers in the field of computer graphics and computer vision.

The necessity for a realistic 3D model in the learning environment of cardiac surgery comes with various challenges such as difficulties in creating or obtaining a realistic heart model for each patient, high costs, time consuming and insufficient professional surgeons. These issues motivate researchers to come up with solutions, especially to produce a realistic 3D model of the human heart to help in cardiac surgery training. This is to reduce the long learning curve during cardiac surgery training for novice surgeons. Traditional cardiac surgery performed on plastic models or corpses do not convey much information about the real heart. Further, during cardiac surgery, the professional surgeon can involve two or three novice surgeons to learn and assist during surgery, where one can assist the professional surgeon directly while the rest learn by watching, as shown in Figure 38.



**Figure 38** Novice surgeon watching expert during cardiac surgery.  
Image taken in UKMMC

Another issue that occurs during cardiac surgery is that the surgeons need to locate the vessels' ROI to perform the cardiac surgery and avoid surgical injuries. While the vessels lie over the heart surface in some cases the vessels ROI might be covered by the heart surface fats, and thus needs time to be located. To date, professional surgeons depend on their own expertise to deal with such situations. The literature review demonstrated that identification of the vessels ROI on the real heart surface image is an unsolved problem.

Providing a realistic 3D heart model from a single image, as well as achieving better identification of the vessels' ROI by enhancing the input data can help surgeons during cardiac surgery especially in locating the vessels and performing the surgery. Meanwhile, detection and correction of the specular reflections that occur on the input heart surface image caused by the lighting sources of the OT are also important.

## Research Overview

3D model reconstruction is a difficult and challenging problem in the field of computer graphics and computer vision. The object reconstruction that results in a realistic 3D model is a significant

problem that has not been completely solved. Existing applications, tools or modelling devices are consuming time, cost and effort. Another approach is modelling from images which overcome some of the disadvantages of the previous techniques. Although the time required to reconstruct the 3D model is less using such an approach, it however produces unrealistic 3D models.

The overall research framework for the proposed solution is shown in Figure 39, consisting of data acquisition, pre-processing, specular reflections detection and correction, extracting the pixels information, realistic 3D surface reconstruction, 3D vessel segmentations, reconstruction, fusing and visualization of the 3D human heart surface model.

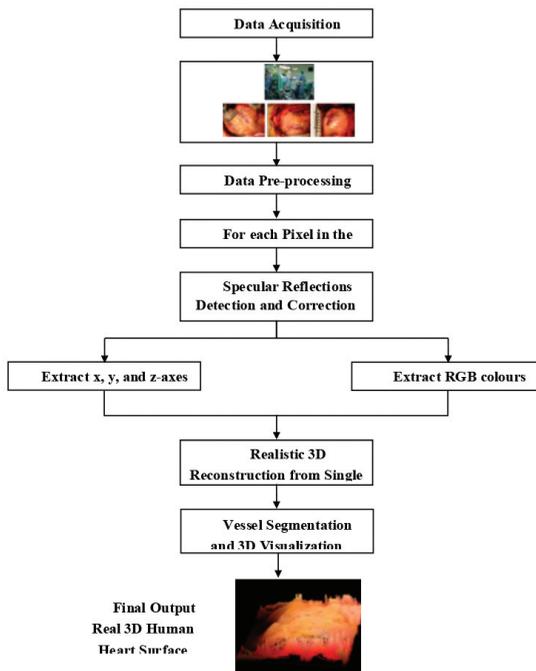
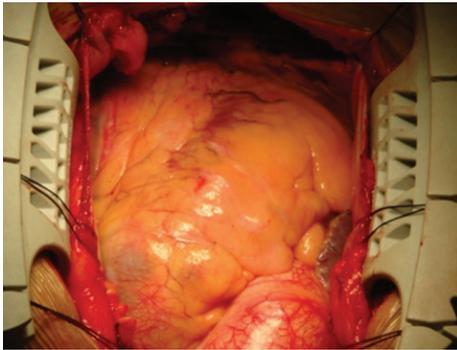


Figure 39 Research framework

In this work, the input for the methodology was a real human heart image. Specular reflections detection and correction was carried out in order to get a realistic 3D reconstructed human heart surface model with 3D vessels over the heart surface. The detection and correction of reflections was considered a significant part of this method, as it could cause a distortion of the depth reconstruction of the heart surface. To illustrate the problem, Figure 40 shows an example of an image of a real human heart with specularities, taken using a digital camera during a cardiac surgery.



**Figure 40** Original human heart image with specularities

The realistic 3D human heart surface model is intended for usage in the learning environment via augmented reality for novice surgeons, to reduce the period required for cardiac surgery training and to enhance their perception of the operating field. A novel and automated method was thus proposed to reconstruct realistic human heart 3D models, which starts with detection and correction of the specular reflections from a single view of the surface of a human heart image.

## **Flowchart of the Research**

The focus of this part of the research was on the problem of reconstructing a realistic 3D model using a single image-view of a real human heart where difficulties arise due to the wet heart surface that produces specular reflections on the surface of the heart image. This can lead to the deformation of the 3D heart surface model. In addition, difficulties in locating the bloodless or blood lacking vessels' ROI where surgery is to be performed is also addressed. The experimental research approach was chosen for this work due to the lack of benchmarking in works on realistic 3D model reconstruction from a single image in the learning system, especially in the medical field. The overall objective in each processing step was experimentally designed and implemented with different parameters' setup and the results were tested quantitatively and qualitatively for most of the steps.

The flowchart has five main steps and each step contains sub-main steps, as shown in Figure 41. The first step is pre-processing which includes image acquisition from OT during cardiac surgery, nominating the images (e.g. images without obstacles) and then image conversion from color image to a greyscale image. In the second step threshold determination to detect specularities on the heart surface was executed. Then, locating the neighbour pixels for the correction process, as well discussing the relations between the light and the 3D extraction process was implemented. The third step is the image analysis from 2D to 3D which involves the extraction of the geometrical features of the points, x, y, z-axes and RGB color channels. The extracted axes produced sharpened edges during the reconstruction process which was followed by the approximation process to smooth the reconstructed surface. The fourth step was the process of segmentation of the vessels' ROI. Finally, original color channels were used in the visualization step for the 3D realistic human heart model with fused 3D vessels on its surface.

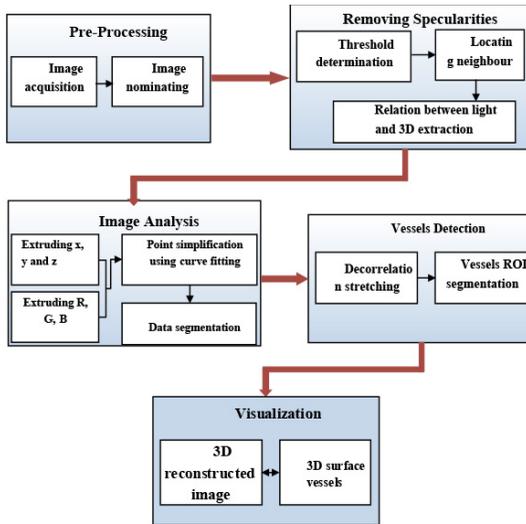


Figure 41 Flowchart of the research

## Data Acquisition

The data used in this research was real human heart color images. The data was collected during open-heart surgery (cardiac surgery) from two Malaysian Government Hospitals, UKMMC (Universiti Kebangsaan Malaysia Medical Centre) and CTC-UiTM (Clinical Training Centre Universiti Teknologi MARA), under the supervision of specialist cardiac surgeons. The datasets included real human heart images for twelve patients. The data for each patient was taken using Sony Cyber-Shot DSC-T30 Digital Camera, with a focal length between 38-114 mm, resolution of 7.2 megapixels and 3x optical zoom with aperture range f3.5-f10. The data was saved in standard JPG format for each image using a single folder for each patient. The preparation and the procedure for data acquisition are described in the following sections.

## Open Heart Surgery (Cardiac Surgery)

The heart has a relatively complex shape. To model even a basic representation of a healthy heart would require a high degree of geometric details. Furthermore, the tissues of the heart also have a complicated structure, consisting of three layers of tissue with distinct physical characteristics as well as coronary arteries and the electrical system.

In cardiac heart surgery, the patient is given general anaesthesia, and then he/she will be taken to the operating theatre where the surgical procedure is going to take place (Figure 42). After the initial covering up and cleaning of the surgical area, the surgeon initially makes an incision in the chest of the patient to expose the heart, then cuts the breastbone using an electrical saw, as shown in Figure 42 (a). The chest is then forced open by a clamp, as shown in Figure 42 (b), (c). This creates the working environment in the chest-cavity for the surgeons. Figure 42 (d) shows the heart within the chest, allowing for easier access to the heart.



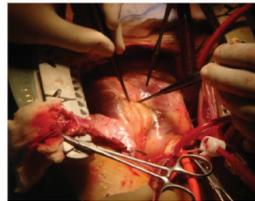
(a) Preparing to open the heart.



(b) Breastbone held open by a clamp.



(c) Opening the membrane surrounding the heart.



(d) Operating on the heart.

**Figure 46** The initial phase of a surgical procedure, images taken in the operating theatre in UKMMC hospital

## Procedure for Acquisition of Real Human Heart Data

In order to enhance the image taken during the surgical procedure, the human heart region needs to be acquired and narrowed down. The heart surface must be seen without any obstacles, such as the surgical tools, surgeons head or hands. The data was retrieved in-vivo from patients, where the chest is opened and the heart clearly visible. Acquiring data during the surgery was either in video format or in still image format while the surgeon's hands or head were away from the heart surface or whenever there were no surgical tools over the heart surface. The input data of the human heart images were acquired from either of two places. First, the regular place was from the upper area of the patient's head. This place is chosen for the data acquisition process as it will not disturb the surgeons during the surgery and the view of the heart is clear, as shown in Figure 43 (a). The second place was decided by the professional surgeon, in case they needed this view to be taken and processed because of its importance, usually taken from the side of the patient beside the professional surgeon, as shown in Figure 43 (b).



(a) Over the patient's head.



(b) Beside the patient's body.

**Figure 43** Camera position. Images taken in the operating theatre in UKMMC hospital

### *Pre-processing of Acquired Data*

The data acquired from the operating theatre during the cardiac heart surgery was in video format form or still images form, captured by digital camera. The video format was converted to a series of 2D frames. Currently, there are many types of software available to convert video format into frames, such as FrameGrabberTester, FrameGrabberDemo, Free Video to JPG Converter, or Video to Picture. In this research the Video to Picture frame grabber software was used to capture the individual digital still images from the digital video stream. The resultant images from FrameGrabber were in 24-bit bmp file format with 640x480-image size.

The data in the form of 2D image format, was saved separately for each patient. These images would be used in the next step in the methodology. The images with obstacles such as surgical tools and surgeons/nurses' hands or heads were manually excluded from the data set collected from the FrameGrabber and from the original images to ensure that the output will be clearly understandable. Then, the images were cropped manually using adobe Photoshop CS4.0, to be used in the experiments in the following chapters.

#### **Specular Reflections Detection and Correction**

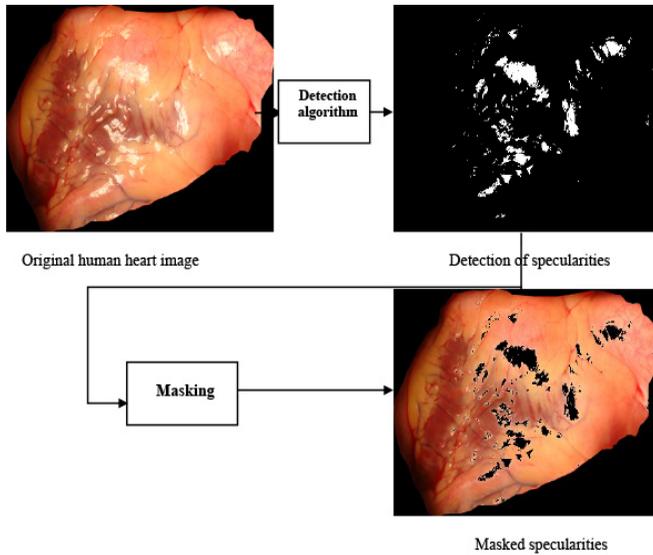
The OT lighting sources emit a huge amount of light rays that reflect from the heart surface, as it is a wet surface. There were thus big and bright regions on different parts of the heart surface. Figure 44 shows the different lighting sources in the OT, such as ceiling lights, overhead surgical lights and surgical headlights which emit huge lighting rays that are reflected from the heart surface, causing loss of some of the original information in the specular regions of the acquired images.



**Figure 44** Different operation theatre lighting sources

### *Reflections Detection Process*

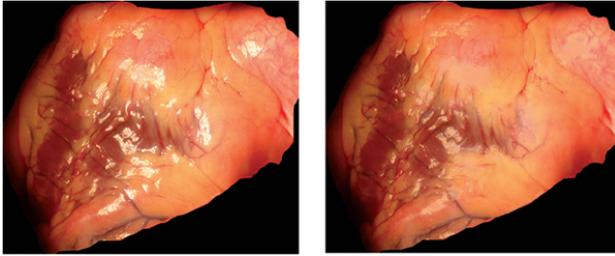
In this section, the input is color images of wet heart surfaces that have specular reflections. The detection of specularities from the single 2D human heart images needed separation of the reflections from the heart surface. Input for this process was a nominated image from the video frames or still images. The detection process of the specular reflection regions relies on an intensity value for each pixel. The specularities are defined by comparing the pixel intensity with threshold values that depend on the blue color channel value and standard deviation value to identify pixels, if they are within the specular reflection regions. The output from the detection algorithm will be a heart image with detected regions of specularities. The final output image will be input for the specularities correction process. Figure 45 illustrates an example of the specular regions' detection process.



**Figure 45** Example of the specular regions' detection process

### *Reflections' Correction Process*

Light intensity locally reflects from a human heart surface and leads to deformation and loss of original information from the surface of the heart. Therefore, a surface correction method was developed that addresses the intensity variations associated with the surrounding neighbors to the specular pixel. The discussed method addresses which of the surrounding pixels were in order to correct the specular pixels. These corrections were applied to the specular pixels. Figure 46 shows an example of a correction of specular reflection by the discussed method.



**Figure 46** Example of the specular regions' correction process

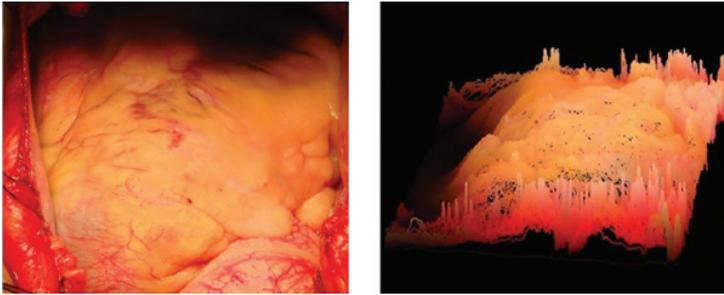
### *Realistic 3D Heart Surface Model Reconstruction from a Single Image*

In this section, the reconstruction process to build a realistic 3D heart surface model using the corrected heart image from the previous step is discussed. A number of researches produced unrealistic 3D model reconstructions using two or more images, especially medical images. The discussed method used only a single view of a real human heart image to build and achieve a fast, accurate and realistic 3D model. This model can be used in a learning environment for novice medical students.

In order to project the 2D image into a 3D model, the model surface required three axes to account for the reconstruction process, as well as a smooth surface that represents the reality of the human heart surface. The discussed method thus used an extraction process to extract the x, y and z-axes from a single 2D image, by using the pixel position values as the x and y-axes, and pixel intensity value as the z-axis.

Each of the pixels that represent the image has values, which describe that pixel and what color it should be. In the binary image, the pixel value is a 1-bit, indicating either background or foreground. For a grayscale image, the value that represents the pixel is a byte, where this value is stored as 8-bit integer numbers spanning

a range from 0 to 255. Color images are represented by separate red, green and blue components for each pixel, and the value of the pixel is a vector of three numbers, each representing 1-byte. An equally significant aspect of the effulgence of the OT lights is that the results of the reconstruction step can lead to a surface with roughness at a large scale, i.e. sharp edges on the surface due to the large cloud of points. These points were thus interpolated with a Bezier curve to produce a smooth surface that depicted a realistic heart surface. Figure 47 shows the realistic result of the 3D human heart reconstructed from a single image.

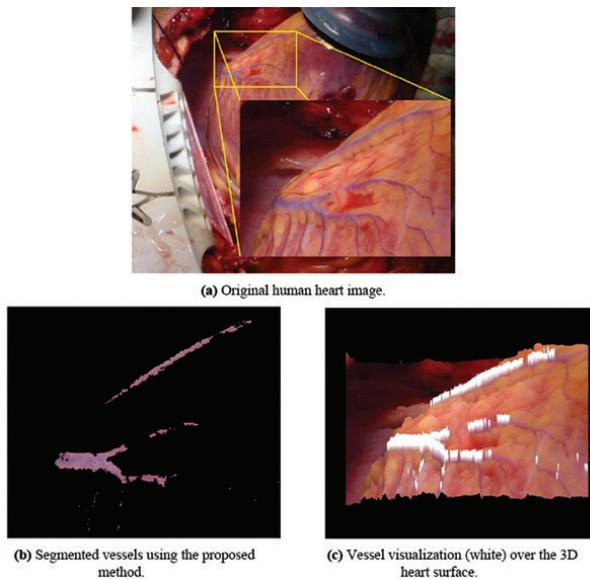


**Figure 47** Result of realistic 3D human heart from a single image

### ***Vessel Segmentation and 3D Visualization***

The vessel segmentations and visualization process are the steps following the 3D reconstruction of the human heart surface. In most cases the fats that cover the human heart surface also cover the surface vessels. However, in some cases the vessels appear clearly on the surface of the heart images where usually the vessels are embossed over the surface. These vessels' regions are darker than the other heart surface regions, where the arteries are reddish due to carrying oxygenated blood while the veins are bluish in color due to the carried deoxygenated blood. In addition, the most important vessels to be segmented are the vessel's ROI where surgery is to be

performed, to avoid surgical injuries. Those vessels will be whitish in colour due to lack of blood. The traditional 3D reconstruction methods do not consider the dark regions, while the discussed method is able to reconstruct these kinds of vessels, by developing a 3D vessel reconstruction method that consists of two steps. The first step is a segmentation process while the second step is the visualization process. Figure 48 shows the process to segment and visualize the vessels over the heart surface model.



**Figure 48** Process of segmentation and visualization of the vessels over the human heart surface

To simplify the work a computer program was developed with Graphical User Interface (GUI), as shown in Figure 49. Figure 50 shows the implementation of the Bezier curve to smoothen the effects of specular reflection.

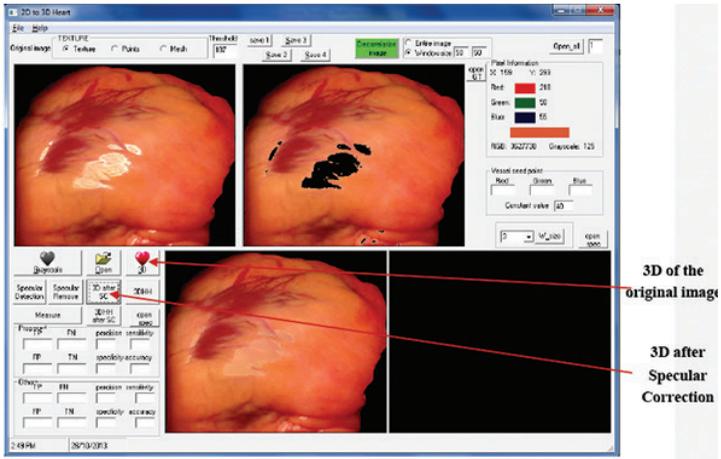


Figure 49 The GUI design for the algorithm

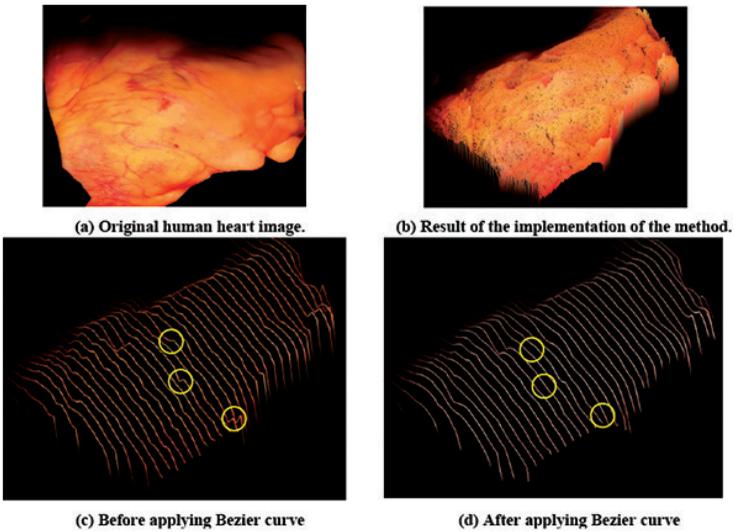


Figure 50 Bezier curve implementation results

There are still many studies that need to be carried out before this part of the results can be used in surgical training in the Augmented Reality environment. There are several investigations already underway for the enhancement of interactions between users and the virtual heart. However, the results of this research can be used as an alternative of 3D visualization using only one camera. It is hoped that this research can be used in other fields besides medicine, especially in architectural design and animation. For further clarification please refer to Al-Surni *et.al* (2013), Al-Surni *et.al* (2014) and Al-Surni (2015). This part of the research has been copyrighted with the title “R3DHHM-Realistic 3D Human Heart Surface Model from a Single Image”, LY2014001845. It won a Gold Medal with the title “Realistic 3D Human Heart Surface Model from a Single Image” at i-Inova 2014, 5th Exposition on Islamic Innovation, USIM

## CONCLUSION

Using Angiography, Echography and CTA images, various research outputs have been produced including image analysis, visualization images and reconstruction images. These works have been published in various journals and have either been copyrighted or patented. To ensure that these works can be used in the real world, a Pictures Archive Communication system (PACs) has been developed (named as CASD-PAC system) and the results have been re-modified as modules and currently the process of integrating each module with the PAC system is underway. It is not easy to penetrate the market where competitors are big international companies but efforts are still ongoing. For further knowledge on this research please refer to Rahmat (2016)

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## **BIOGRAPHY**

Prof. Dr. Rahmita Wirza received her B.Sc. and M.Sc. degrees in Science Mathematics from University Science Malaysia in 1989 and 1994, respectively and received her PhD in Computer Assisted Engineering from University of Leeds, U.K. From 198 to 1990, she worked as a research assistant in the Department of Physics in University Science Malaysia, experimenting on Ozone layer measurements in the Equatorial region, before being engaged as a tutor at Universiti Putra Malaysia. Among her focus research areas are Computer Graphics and Applications, Computer Assisted Surgery and Computational Geometry. Thus far she has led a number of research grants and published her work in International Journals, Proceedings, Book Chapters and Books. A number of research students under her supervision have since been graduated. She has also supervised MSc without thesis dissertations and Final Year Undergraduate students. There are patents filed for a few of her research works and a few have been granted. She is the founder of the Computer Graphic Application Research Group, which later changed to the Computer Graphics, Vision and Visualization Research Group (CGV2). She is also a co-founder of the Computer Assisted Surgery and Diagnostic Special Interest Research Group (CASD). She was one of the task force committee members preparing the draft for the memorandum of agreement between UPM, UKM and IJN for the Computer Assisted Surgery and Diagnostic project spanning 5 years, where the MOA was successfully signed by all parties on 15 February 2013.

To date she has served at UPM for 18 years, fulfilling all the major responsibilities expected of her as a lecturer. She has taught both undergraduate level and postgraduate courses.



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Enablers*  
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Games*  
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Management Towards Precision  
Framing*  
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Environment?*  
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System and the Technological  
Challenges They Pose*  
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Biotechnology: For Profit, People  
and Planet*  
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Wave Probe Made It Simple*  
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with Minimum Collateral Damage*  
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Bacteria*  
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Fibre: Does Malaysia have Enough?*  
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Challenges*  
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Environment*  
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Malaysia: Cabaran Prospek dan  
Implikasi dalam Latihan dan  
Penyelidikan Perubatan serta  
Sains Kesihatan di Universiti Putra  
Malaysia*  
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& Komunikasi ICT untuk Semua*  
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Strategies, Issues & Challenges*  
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Incorporating Economic Valuation  
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Decision Making*  
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Following Diverse Vistas*  
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Engineering the Convenience Foods*  
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Perception Through Landscape  
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*Physical to Biological Building Blocks in Hand & Microsurgery: The Facts, The Face, The Facility, The Field... and The Future*  
20 April 2018



# INDEX

- 3D echocardiography 42
- American Heart Association 5
- angiocardiology 3
- angiogram acquisition 78
- angiography 3
- cardiac surgery 102
- cardiovascular diseases 45
- computed tomography
  - angiography 3, 20, 89, 97
- computer
  - aided design 95
  - assisted medical 1
  - assisted surgery 1
  - science 1
- consistency 32
- conventional coronary angiography 20
- coronary arterial 77
  - arteries 9, 80
  - artery 73
- CT angiography 75, 82
- CT scans 6
- data simplification 65
- detection algorithm 30
- diagnostics 1
- digital stent enhancement 11
- discrepancy 32
- displacement vector flow 53
- dynamic road mapping 11
- echocardiographic data
  - acquisition 41
  - echocardiography 48
  - echocardiography 3
  - echography 112
  - end-diastolic 37
  - end-diastolic 71
  - end-systolic 37, 71
  - experimental design 25
  - extraction algorithm 31
- graphical user interface 110
- image registration 18
- intersection tracking 83
- intravascular ultrasound 20, 89
- left ventricle 35
- magnetic resonance angiography 20, 89
- medical disciplines 1
- one-dimensional parameterization 19
- oxygenated blood 109
- parameter tuning 26
- percutaneous coronary intervention 8
- precision 30
- right ventricle 34
- RV cavity 70
- stroke volume computation 72
- synthesized coronary vessels 19

thoracic and cardiovascular  
diseases 1  
three dimensional  
echocardiography 34  
tracking algorithm 33  
transesophageal echocardiography  
4  
  
velocity vector flow 53  
ventricle volume 59  
vessel segmentations 109  
Virtual Arterial Maps 11  
  
X-ray Angiography 73, 75, 84