CORONARY ARTERY SEGMENTATION FROM NON-CONTRAST CARDIAC CT FOR THE PURPOSE OF CALCIUM SCORING

CHERIAN MATHEW

M.Sc. Master’s Thesis Project
Department of Computing Science
Scientific Visualization Group
Rijksuniversiteit Groningen

SUPERVISORS:
J.B.T.M. Roerdink, Rijksuniversiteit Groningen
Peter van Ooijen, University Medical Center Groningen
Michel Westenberg, Eindhoven University of Technology
# CONTENTS

1 INTRODUCTION 1
   1.1 Coronary Arteries 2
   1.2 Medical Diagnosis 5
   1.3 Diagnostic Research 11

2 METHODOLOGY 13
   2.1 Overview 14
   2.2 Heart Segmentation 17
      2.2.1 Fast Marching 18
      2.2.2 Hole Filling 23
   2.3 Vessel Extraction 26
      2.3.1 Multi-Scale Hessian 27
      2.3.2 Morphological Correction 30
   2.4 Coronary Artery Model Dataset 37
   2.5 Vessel Centre Points Generation 39
      2.5.1 Persistence 40
   2.6 Point Set Matching 42
      2.6.1 Branch and Bound 42
   2.7 Reconstruction of Coronary Arteries 46
   2.8 Summary 48

3 DISCUSSION 49
   3.1 Advantages / Disadvantages 49
   3.2 Measurability 51
   3.3 Guarantees 52
   3.4 Alternatives 53

4 CONCLUSION 55

A APPENDICES 57
   A.1 Input Parameters 57
   A.2 Software Implementation 58

BIBLIOGRAPHY 63
INTRODUCTION

Cardiovascular disease refers to the class of diseases that involve the heart and/or blood vessels (arteries and veins). These include coronary heart disease (heart attacks), raised blood pressure (hypertension), peripheral artery disease, rheumatic heart disease, congenital heart disease and heart failure. Most Western countries face high and increasing rates of cardiovascular disease to the extent that it has now become the number one cause of death globally and is projected to remain the leading cause of death for years to come\(^1\). Heart attacks are one of the main causes of death for people suffering from cardiovascular disease and are mainly caused by a blockage that prevents blood from flowing to the heart. The most common reason for this is the build-up of calcified fatty deposits (commonly known as plaque) on the inner walls of the blood vessels (coronary arteries) that supply blood to the heart, resulting in the narrowing of the arteries. This condition is called atherosclerosis, which could result in either of two potentially life-threatening situations. Firstly, the accumulation of blood clots inside the artery walls due to plaque ruptures, leading to insufficient supply of blood to the heart and secondly, at a more advanced stage, complete blockage of the artery. By the time that this problem is detected, the underlying cause (atherosclerosis) is usually quite advanced, having progressed for decades. The identification and analysis of plaque (known as calcium scoring) has, thus, become the primary focus of research in the diagnosis and cure of atherosclerosis.

This project is a study of the medical diagnosis of the above mentioned condition using a sequence of non-contrast cross-sectional images of the heart obtained by the technique of computed tomography (CT). The problem addressed here involves the identification

\(^1\)http://www.who.int/cardiovascular_diseases/en/
and measurement of calcified plaque located in the coronary arteries as observed in the acquired images. As a potential aid to the diagnosis, a solution is proposed and implemented. This solution is motivated by geometry and consists of multiple steps, each of which is explored in some detail.

This report begins with a quick anatomical view of the heart with particular attention to the coronary arteries. This is followed by a look at the current state of medical diagnosis of atherosclerosis, which includes a detailed description of the computed tomography technique. The current status of diagnostic research on calcium scoring concludes the introductory part of the report. The subsequent chapter describes the proposed solution in a generic manner providing an explanation for each of the steps in detail. This is followed by the results of the implemented solution and a discussion on the various aspects of the solution. The report is concluded by a brief summary.

1.1 CORONARY ARTERIES

The heart can be seen as a regular ovoidal structure located between the lungs in the middle of the chest, behind and slightly to the left of the breastbone. The primary function of the heart is to pump blood, which has been oxygenated by the lungs, to the various parts of the body via the aorta, the body’s largest artery. Electrical impulses from the heart muscle (myocardium) cause the heart to contract and this process is responsible for the repeated, rhythmic contractions of the heart. To do so indefinitely, it requires a constant supply of blood to keep it working. Although a large quantity of blood leaves the chambers of the heart through the aorta, the myocardium is so thick that it requires separate blood vessels to deliver blood deep into it. These vessels, highlighted in fig. 1 are called the coronary arteries. The coronary network is made up of the following two main arteries,

http://www.daviddarling.info/images/coronary_arteries.jpg
1.1.0.1 Left Coronary Artery (LCA)

The LCA begins as the Left Main Coronary Artery (LM) arising from the left part of the aorta. The LM then bifurcates into the Left Anterior Descending Coronary Artery (LAD) and the Left Circumflex Coronary Artery (LCx). In normal anatomy, the LAD makes its way around the pulmonary artery (which carries blood to the lungs to pick up oxygen) and reaches the bottom most part of the heart. The LCx, on the other hand, moves towards the left side of the heart.

1.1.0.2 Right Coronary Artery (RCA)

The RCA originates on the right side of the aorta, slightly lower than the origin of the LM. It travels down the right atrioventricular groove (separating the chambers of the heart) and wraps around the heart.
Figure 2 provides a cross sectional view of a plaque affected artery. The outermost layer is known as \textit{tunica adventitia} (or simply, adventitia) and is composed of elastic fibers. Inside this layer is the \textit{tunica media} (or simply, media) which is made up of smooth muscle cells and elastic tissue. The innermost layer, which is in direct contact with the flow of blood is the \textit{tunica intima}, commonly called the intima and is made up of mainly endothelial cells. The hollow internal cavity in which the blood flows is called the \textit{lumen}. The accumulation of plaque occurs usually within the arterial wall and can protrude out into the lumen.

Plaque is an accumulation and swelling in artery walls that is made up of cells, or cell debris, that contain lipids (cholesterol and fatty acids), calcium and variable amount of fibrous connective tissue. In the early stages of development, plaque is composed of white blood cells, especially macrophages that have taken up oxidized low-density lipoprotein. Macrophages are cells within tissues of white blood cells which engulf and digest cellular debris and infectious agents and also stimulate immune cells to respond to the infection. After they accumulate large amounts of cytoplasmic membranes (with associated high cholesterol content) they are called foam cells.

When foam cells die, their contents are released, which attracts more macrophages and creates an extracellular lipid core near the center to inner surface of each atherosclerotic plaque. Conversely, the outer, older portions of the plaque become more calcific, less metabolically active and more physically stiff over time. One of the consequences of abnormal plaque development occurs when the arterial wall enlargement eventually fails to keep up with the enlargement of the plaque volume. In this case the lumen of the artery begins to narrow, commonly as a result of repeated ruptures of the covering tissues separating the plaque from the blood stream. After a certain period of time, this could result in the rupture of the arterial wall lining, leading to loss of blood flow to the heart. This is

\footnotesize{\textsuperscript{3}http://en.wikipedia.org/wiki/Image:Anatomy_artery.png}
Figure 2: Cross-sectional view of a plaque affected artery

The principal mechanism of many cardiovascular diseases and a primary cause for heart attacks. Another less common outcome is the gross enlargement of the arterial wall (aneurysm), to compensate for the presence of plaque. If the arterial enlargement continues to 2 to 3 times the usual diameter, the walls often become weak enough that with just the stress of the pulse, a loss of wall integrity may occur leading to sudden hemorrhage (bleeding), major symptoms and, in many cases, rapid death.

1.2 MEDICAL DIAGNOSIS

As demonstrated by human clinical studies, most severe events occur in locations with heavy plaque, yet little or no lumen narrowing is present before debilitating events suddenly occur. The majority of events occur due to the gradual accumulation of plaque at areas without narrowing sufficient enough to produce any angina or stress test abnormalities. Due to this reason, the past decade has
seen greater attention being focused on this type of plaque, namely **vulnerable plaque**.

In the field of cardiovascular radiology, **Angiography** is a medical imaging technique in which an X-ray picture is taken to visualize the inner opening of blood filled structures, including arteries, veins and the heart chambers. As blood has the same radiodensity as the surrounding tissues, a radio-contrast agent (which absorbs X-rays) is administered (via a catheter) within the coronary arteries to make
angiographic visualisation possible. The angiographic image, as seen in fig. 3(a)\(^4\) shows projections of the lumen (actually the contrast agent within). Due to the local administration of the contrast agent, the blood vessels and heart chamber walls remain largely to totally invisible on the X-Ray image. Historically, angiography has emerged as an established method to visualise the narrowing of coronary arteries. But, it does not provide any information on the actual size or shape of the plaque residing in the arterial wall. As already mentioned, most severe events occur in locations with heavy plaque, yet little or no lumen narrowing is observed before debilitating events suddenly occur. As a result, methods other than angiography had to be increasingly developed as ways to better detect atherosclerotic disease before it becomes symptomatic.

This development lead to **Computed Tomography (CT)**, which is a technique used to generate slice-by-slice images of the internal anatomy of a human body from cross-sectional X-Ray images (fig. 3(b)\(^5\)). In comparison to Angiography, CT involves the systemic administration of contrast agents to enhance not only the coronary arteries, but also other surrounding structures. Continuing improvements in CT technology including faster scanning times and improved resolution have dramatically increased the accuracy and usefulness of CT scanning and consequently increased its utilisation in medical diagnosis.

**Magnetic Resonance Imaging (MRI)** (fig. 3(c)\(^6\)) and **Intra-Vascular Ultrasound (IVUS)** (fig. 3(d)) are further improvements in cardiac imaging, but both the procedures suffer from the negative aspects of being invasive as well as expensive in nature.

All of the techniques mentioned above involve the surgical insertion of a catheter in or around the coronary arteries (either to introduce a contrast agent into the bloodstream for enhancing the contrast of the images produced or for capturing sonographic

\[\text{http://www.egms.de/figures/journals/tss/2006-3/tss000009.f2.png}\]
\[\text{http://commons.wikimedia.org/wiki/File:Cardiac_mri_slice_bionerd.jpg}\]
images - in the case of IVUS). This is an invasive procedure, which has a certain amount of risk attached to it. Although not common, the contrast agent (usually based on iodine), can also produce undesirable side effects, ranging from anaphylactoid reactions (severe life-threatening allergic reaction) to nephropathy (damage to the kidney). This project attempts to provide a diagnostic solution using CT combined with little or no requirement of contrast agents, which reduces the risk involved as well as the procedural costs.

**Computed tomography**

Sir Godfrey Hounsfield (EMI Central Research Laboratories, United Kingdom) and Allan McLeod Cormack (Tufts University, Massachusetts, USA) shared the 1979 Nobel Prize in Medicine for having (independently) invented the first commercially viable CT scanner.

The word *tomography* is derived from the Greek word *tomos* which means a “section” or “a slice”. In conventional medical X-ray tomography, clinical staff make a sectional image through a body by moving an X-ray source and the storage film in opposite directions during the exposure. This procedure is performed by placing the patient at the center of a rotating machine (as seen in fig.4) which is continuously sending out X-ray beams from different angles. The X-ray source and the storage film, are connected together by a circular rod with the pivot point as focus. This setup ensures that the image created by the points on the focal plane appears sharper, while the images of the other points are removed as noise. The X-rays from the beams are detected after they have passed through the body and their strength is measured. Beams that have passed through less dense tissue such as the lungs have a stronger signature, whereas beams that have passed through denser tissue such as bone will be weaker. This information is then passed through a computer to work out the relative density of the tissues examined.

---

7One lesser known fact is that EMI owned the distribution rights to ‘The Beatles’ music and it was their profits which funded the research

8[http://hcd2.bupa.co.uk/images/factsheets/CT_Scan_427x240.jpg](http://hcd2.bupa.co.uk/images/factsheets/CT_Scan_427x240.jpg)
Values measured by the receptor film can be translated to reflect the physical properties of the anatomical structures and are usually expressed in terms of Hounsfield units (HU). The scale of the HU is defined by the radiodensity value of water fixed at 0 HU and of air, fixed at $-1000$ HU. HU values of other structures include fat at $\sim -100$ HU, blood at $\sim 50$ HU and dense bone at $\sim 1250$ HU. Each set of measurements made by the scanner is, in effect, a cross-section through the body. The circular rod rotates around the body of the patient, with the axis of rotation perpendicular to the rod itself (approximately along the spine of the patient). This results in cross-sectional slices lying on a plane perpendicular to the spinal axis. The computer processes the results, storing them as two-dimensional images. In the case of cardiovascular diagnosis, CT scanners can acquire the entire anatomy of the heart in a single breath-hold of 30-40 seconds. Recent advances in the technique have seen improvements in the resulting resolution of output images. The CT images used in this project have been obtained in DICOM\(^9\) format from a Siemens SOMATOM Definition\(^{10}\) machine using a coronary calcium scan protocol. The spatial resolution of the im-

\(^9\)http://medical.nema.org
\(^{10}\)https://www.medinnovations.usa.siemens.com/products/ct/definition/
ages is about 0.489mm × 0.489mm in the cross-sectional plane with slice widths of about 3mm. The corresponding pixel resolution is 512 × 512 for each cross-sectional x – y plane and about 60 – 80 slices along the spinal axis (z-axis).

1.2.0.3 Contrast Vs Non-Contrast

As mentioned earlier, CT scans acquired in conjunction with the injection of radiocontrast agent into the coronary arteries greatly enhance the quality of the resulting images. Figure 5 provides a comparison of CT scan images of the same patient taken with and without the contrast. It can be clearly seen that in the case of contrast CT, the anatomical structures (like the coronary arteries) are clearly defined and delineated, whereas in the case of non-contrast CT, they appear to be incomplete. Given the difficulties associated with non-contrast CT, it is still seen as a preferable mode of diagnosis due to the non-invasive nature of the procedure implying the reduction of medical risk and a subsequent reduction in cost. One of the main areas of research within radiology today is the possibility of using non-contrast CT (with its benefits) for the purpose of cardiovascular analysis without compromising on the quality of the diagnosis.
This project attempts to provide some ideas for the possibility of diagnosing heart conditions using non-contrast CT scans.

1.2.0.4 Calcium Scoring

Once the CT images are acquired, they are passed on to an expert (usually a radiologist), for analysis and subsequent diagnosis. The main challenge at this step is the identification of calcified plaque, followed by classification of the degree of disease based on a certain type of scoring technique. Calcium Scoring is formally defined as a number reflecting the degree and extent of calcium deposits in the walls of the coronary arteries, as demonstrated by cardiac computed tomography\(^{11}\). The most widely used measurement is the Agatston score \([2]\) which is given by,

\[
AS_{\text{plaque}} = \sum_{i=1}^{n} A_i \times w
\]

where \(A_i\) is the area of a specific plaque in the slice \(i\) and \(n\) is the number of slices in which that plaque is present. The weight factor \(w\) is determined by the maximum intensity value \(I_{\text{max}}\) present in the identified plaque,

- \(130 \text{ HU} \leq I_{\text{max}} < 200 \text{ HU} \Rightarrow w = 1\)
- \(200 \text{ HU} \leq I_{\text{max}} < 300 \text{ HU} \Rightarrow w = 2\)
- \(300 \text{ HU} \leq I_{\text{max}} < 400 \text{ HU} \Rightarrow w = 3\)
- \(400 \text{ HU} \leq I_{\text{max}} \Rightarrow w = 4\)

The total Agatston score is obtained by adding up the scores of all the identified plaque in the entire CT dataset.

1.3 Diagnostic Research

Currently, several commercial as well as non-commercial software packages offer tools for coronary calcium scoring. These tools usually require the user to first (manually) choose some section of the plaque in the CT dataset, with the identification of the entire

\(^{11}\)http://www.radiologyinfo.org/
plaque area being automated using thresholding segmentation and connected components. Even though complete automation of the extraction of the plaque region is difficult to achieve, there has been a considerable amount of research done in this area of calcium scoring.

One of the popular approaches to the problem has been to first isolate the coronary arteries and then detect the plaque inside. To this end, [13] provides an overview of vessel extraction techniques and algorithms. In [21] a new approach to the segmentation of coronary arteries using a skeleton-based, semi-automatic search algorithm (corkscrew algorithm) is described, whereas a topological approach to extracting coronary vessel cores is introduced in [19]. An entirely different approach can be seen in [9], where the calcified plaque present in the arteries is identified using pattern recognition techniques.

These techniques work quite well with datasets that are not very noisy and provide acceptable levels of detail, but when it comes to non-contrast CT data, the low quality and disconnectedness of arterial structures make it difficult for the above mentioned techniques to be applied successfully.
METHODOLOGY

The automated solution to the problem of calcium scoring using non-contrast CT proposed in this project is essentially made up of geometric concepts. The use of geometry as a means to achieve results comparable to manual observation is inspired by the intuition of radiologists. Manual analysis of arterial plaque in cardiac non-contrast CT scans relies heavily on the ability to identify and locate geometrical structures in the given datasets, which in turn is dependent on prior experience and understanding of cardiac CT data. Knowledge of the approximate location of crucial landmarks plays a vital role in the accuracy of the resulting diagnosis. This knowledge leads directly to the virtual reconstruction (in the mind of radiologists) of the mostly disconnected coronary arteries, which in turn leads to the identification of plaque. The proposed solution attempts to replicate this understanding in an automated context, using a pipeline of filters, each of which serves a specific purpose. As a consequence, the main driving forces include,

- **Modelling of manual observation**, implying a geometrical approach.
- **Automation**, implying the reduction of user interaction as much as possible.

The following is a list of pre-requisite information for subsequent chapters:

- **Intermediate results**: All proposed methods in the solution pipeline have been implemented in 3D and are applied to the entire dataset as a whole. For the sake of simplicity and continuity, the intermediate results are provided in the form of 2D slices and come from a single dataset. The 2D cross-sectional images presented in this report have been obtained using custom build software described in A.2 (Appendix A.2)
Volume data: The output of each method in the form of volume data is provided at the end of the method description to visualise the overall effect of the method on the dataset. These resulting volume datasets are not really used as part of the analysis for the corresponding method, but are provided primarily as visual evidence. The 3D volume data snapshots seen in this report have been produced using OsiriX\(^1\).

Volume rendering: Since the pixel resolution of the 2D CT slices is relatively high (512x512) as compared to the number of slices (∼60), it is quite difficult to render the volume in an effective way. This becomes even more problematic when the structures to be identified are as obscure as coronary arteries. Another aspect to consider is that radiologists rarely ever look at rendered volumes of CT cardiac data for the purpose of calcium scoring. Due to all these factors, the volume rendering of the resulting datasets, have been presented in a simplistic format. A consequence of this approach is the visualisation of the artery-like structures in the form of pearl-like strings. This is the effect of the volume rendering software (OsiriX) attempting to scale the datasets uniformly along all dimensions. Since the z dimension, represented by the number of slices, is relatively small, the interpolation used in scaling up this dimension introduces the above mentioned artefact.

2.1 OVERVIEW

The general approach, as seen in fig.6, to identify and measure plaque in a given patient dataset, begins with the segmentation of the heart. This step ensures that unwanted elements such as lung airways, bone structures (and its connecting tissue), etc. are removed from the dataset. The reduction of the dataset also eases computation in the later stages. Heart segmentation is followed by the extraction of vessel-like structures present in the dataset. This step highlights parts of the arteries which are present in the

\(^1\)http://www.osirix-viewer.com
dataset. The next step involves the generation of points, close to the center-line of the extracted vessels. At this point in the pipeline, a high-resolution, high-contrast model of the coronary arteries is also passed through the center-line points generation process. This gives us two 3D point sets - one, of points representing the arteries in the patient dataset and the other, representing the arteries in the model dataset. The point sets are then matched, with the model point set fitted to the patient point set. The closest matching points in the patient point set are selected and considered to represent the coronary arteries. This newly discovered point set is then used to reconstruct the arteries and any plaque found within them is measured.

![General Solution Pipeline](image)

**Figure 6: General Solution Pipeline**

The concrete methods which implement the steps mentioned above can be seen in Fig. 7. These methods have been chosen on the basis of the driving forces outlined at the beginning of this chapter. *Threshold Fast Marching* for heart segmentation is a computation-
ally fast technique which provides accurate results with minimal user interaction. The Multi-Scale Hessian 3D method of identifying vessel-like structures does not require prior directional information and can scale over varying vessel diameters. Morphological Reconstruction helps in eliminating structures other than the vessels themselves. Persistence points provide correct point set representation of required structures (in this case vessels) and also focus on high-intensity regions (like plaque) in them. Since the patient and model point sets are already assumed to be sufficiently close to each other in 3D, the Branch and Bound method of point set matching results in a close approximation of the original artery. The point set is then expanded to a tubular structure and (within a certain error bound) the plaque present inside is measured.

![Chosen Method Pipeline](image)

**Figure 7: Chosen Method Pipeline**
2.2 HEART SEGMENTATION

The segmentation of the heart (including the coronary arteries) from CT datasets is an ongoing field of research. The extraction of the heart region is not only useful in the diagnosis of coronary artery diseases but also in the analysis of systemic diseases such as diabetes, hypertension and cancer.

Snakes[10] or active contours, are curves defined within an image domain that can move under the influence of internal forces coming from within the curve itself and external forces computed from the image data. Segmentation techniques like the one described in [11] deploy a combination of gradient information and geometric curve evolution to detect the boundaries of objects (e.g. the heart) in medical datasets. Another popular technique for segmenting the heart is the use of deformable models, where prior shape knowledge and specification of key features are combined to deform pre-defined heart models to segment the heart. A number of variations of this technique can be seen in [1]. Although the results appear to be promising, the requirement of complex parametric representation (of the evolving contours and deforming models) and the computational load increase when extended to 3D can be discouraging for use in the context of this project. Another issue with the above mentioned methods is that a fairly accurate initial estimate of the heart (initial contour in the case of snakes and feature specification in the case of deformable models) is needed. This aspect could be difficult to balance with the goal of automation, which is one of the aims of this project. Most of these issues can be solved by adopting the technique (along with data-specific modifications) described below.

The Level Set [18] method is a numerical technique for tracking interfaces and shapes. The advantage of the level set method is that one can perform numerical computations involving contours and surfaces on a fixed Cartesian grid without having to parameterise these objects. Also, the level set method makes it very easy
to follow shapes that change topology, e.g. when a shape splits in two, develops holes, or the reverse of these operations. Instead of manipulating the moving front (contour or surface) directly, it is embedded as the zero level set of a higher dimensional function called the level-set function. The level-set function is then evolved under the control of a differential equation [15]. This implies that the method can be easily extended to geometrical objects in any dimension. At any time $t$, the evolving front can be obtained by extracting the zero level-set from the output. Figure 8(a)\(^2\) shows a contour (in 2D) extracted from the level set function (in 3D - represented by the red surface), $f(x, y, t)$ at the zero level set where $f(x, y, t) = 0$. The evolution of the moving front is determined by a speed function based on image features such as mean intensity, gradient and edges in the governing differential equation.

2.2.1 Fast Marching

Fast Marching [17] is a special case of the level set method wherein the propagating front is always moving continuously in a specific direction (either forward or backward). This converts the problem

\(^2\)http://upload.wikimedia.org/wikipedia/commons/c/c7/Level_set_method.jpg
to a stationary formulation, because the front crosses each grid point only once, implying increased speed of computation. This can be clearly observed in fig.9, where the level set technique, though comparatively more accurate, takes many more timesteps to achieve a satisfactory result (more than on the order of 10) than the fast marching method. The output of this method is a time-crossing map that indicates, for each pixel, how much time it would take for the front to arrive at the pixel location. The application of a thresh-

Figure 9: Level Sets Vs Fast Marching

old in the output image is then equivalent to taking a snapshot of
the contour at a particular time during its evolution. This can be seen in fig.8(b)\(^3\) where the shape of a contour in 2D (represented by the closest grid points) can be seen for different timesteps of evolution. In this method the speed function which governs the evolution of the moving front needs to be provided in the form of an image. The speed image needs to be such that the front moves quickly over areas with high speed (intensity) values, i.e. regions to be segmented and slowly over areas of low speed (intensity),\(^3\)

\(^3\)http://www.sciweavers.org/files/imagecache/fmm_imm.jpg

\textbf{Figure 10: Gradient Fast Marching}
i.e. borders of regions of interest. The image is typically computed as a function of the gradient magnitude. Popular functions in the literature include the negative exponent: \(-\exp(x)\), the reciprocal: \(1/x\) and the sigmoid function. Normally, all regions of intensity value below and including those of fat are of no real importance and should be removed prior to the computation of the speed image, but applying this filtering on non-contrast datasets gives rise to two main problems. Due to the fact that the image is noisy, with small pockets of low intensity distributed over the dataset, a speed image based on gradient magnitude is not a good choice. Applying the above functions of the gradient magnitude on such low intensity areas produces corresponding low intensities in the resulting speed image. The fast marching front moves slowly over these areas leading to a segmentation which is not uniform in all directions and can exclude regions of interest (like the coronary arteries), as can be seen in fig. 10. To solve this problem, the dataset is thresholded at a value \((-150\text{HU})\) just below the value of fat \((\approx -100\text{HU})\) to include these noisy low intensity areas. The resulting dataset is then converted to binary form by mapping all intensity values \(< -150\text{HU}\) to 0 and all intensity values \(\geq -150\) to a high constant value (say 1000). Another important reason for this thresholding is that since the arteries are not always connected, it is possible to find sections of the arteries surrounded completely by fatty tissue.

Thresholding at the value of fat removes these artery structures (fig. 11), whereas thresholding at the suggested value below fat ensures that these arteries will be included in the final segmentation (fig. 12). The thresholded binarized image itself can then be used as the speed image for the fast marching process. Another input parameter to the method is a list of initial seed points which will be used to start the propagation. Since it is fair to assume that the heart is usually centered in any CT dataset, the center point of each 2D slice in the dataset can be chosen and added to the set of seed points. The timestep at which the evolution of the propagating front should be stopped also needs to be provided. Segmentation results for increasing number of iterations can be seen in fig. 13.
Since the front is evolving mostly in the $x,y$-plane uniformly in both directions, it is possible to observe experimental values which relate the timesteps to the real distance (spacings in mm) of the $x,y$ grid points, which can be found in the DICOM headers. A value of 80 iterations for a grid spacing (0.5mm, 0.5mm) has been observed to be sufficient in safely segmenting the entire heart. This value can be rescaled for new datasets using their corresponding $(x,y)$ spacings. The aim of this step is to obtain an approximate segmentation of the heart, hence it is possible that structures which
do not belong to the heart (such as a piece from the rib case in the lower part of the images) may be retained. This ensures that the primary structures of interest, namely the coronary arteries, are not eliminated.

2.2.2 Hole Filling

Once the fast marching process has been applied to the dataset, an approximate segmentation of the heart is obtained, containing the
objects of interest (namely, the coronary arteries). But there still exist regions of intensity value between $-150 \text{ HU}$ and $0 \text{ HU}$ (below fat), which are of no practical interest and can be removed. To achieve this, the dataset can be simply thresholded below $0 \text{ HU}$. But, as already observed in the fast marching process, this also generates small ‘holes’ in the dataset which need to be corrected. To achieve this the dataset is converted to binary form by thresholding at $0 \text{ HU}$, which is then passed through a majority voting filter. This filter converts background pixels into foreground only when the number
of foreground pixels is a majority of the neighbors. By selecting
the size of the majority, this filter can be tuned to fill-in holes of
different size.

In this case, a 5x5 window centered at every pixel results in a
smoother image consisting of continuous connected structures in
3D, which is then used as a mask to obtain the final segmented
heart region, as shown in fig. 14.
One of the most problematic issues when dealing with calcium scoring in non-contrast CT data is the loss of information with
respect to the coronary arteries. The arteries are captured as dis-
joint, semi-tubular structures with minimal geometrical information,
which makes them difficult to identify. After the reduction of the
dataset to the heart region in the previous step, the only blood
vessels that are retained in the reduced dataset are the coronary
arteries, implying that the problem of isolating the arteries now
falls under the broader category of vessel extraction. Research in the
field of vessel extraction encompasses various techniques includ-
ing pattern recognition, model-based approaches, tracking based
algorithms, etc. These techniques have been described in the survey
[12]. Most of the methods work well with contrast CT datasets and
provide convincing visual and empirical results, but in the case of
non-contrast data, the lack of sufficient information relating to the
arteries, restrict the accuracy of the methods. The requirement of
user input and/or specific assumptions (e.g. position / orientation
of arteries, intensity values, etc.) for a majority of the methods make
them unsuitable in the context of this project.
The ideal approach would be to extract all the existing structures
of the coronary arteries, even though they may be disconnected
and incomplete. The result should be achieved with no prior direc-
tional or shape information of the arteries and should be scalable
for various artery diameters. Since this is quite difficult to achieve,
the technique proposed at this step of the solution pipeline is split
into two parts. The first part attempts to extract vessel (tube) like
structures from the segmented heart dataset and the output of this
method is then corrected to remove as many unwanted features
as possible, resulting in a dataset which is primarily made up of
coronary artery segments.

2.3.1 Multi-Scale Hessian

The paper [7] describes an approach where the Hessian matrix
is computed at every point in the dataset and used to measure
‘vesselnss’. For image datasets, given that $f(x, y, z)$ represents the
intensity at each point in the dataset, the Hessian matrix can be
represented as,
\[
H(x) := \begin{bmatrix}
\frac{\partial^2 f}{\partial x^2} & \frac{\partial^2 f}{\partial x \partial y} & \frac{\partial^2 f}{\partial x \partial z} \\
\frac{\partial^2 f}{\partial y \partial x} & \frac{\partial^2 f}{\partial y^2} & \frac{\partial^2 f}{\partial y \partial z} \\
\frac{\partial^2 f}{\partial z \partial x} & \frac{\partial^2 f}{\partial z \partial y} & \frac{\partial^2 f}{\partial z^2}
\end{bmatrix}.
\]

\(H(x)\) represents the second order local structure at the given point. An analysis of the eigenvalues of the Hessian can be employed to extract the principal directions in which the local second order structure of the image dataset is decomposed. This analysis extracts three orthonormal directions which are invariant up to a scaling factor, when mapped by the Hessian matrix. The scaling factor \((s)\), is a measurement scale which varies within a certain range and can be used to represent different sizes of vessels. For eigenvalues, \(|\lambda_1| \leq |\lambda_2| \leq |\lambda_3|\), the relations between them can be studied to identify different types of structures. In particular, a pixel belonging to a vessel region will be signaled by \(\lambda_1\) being small (ideally zero), and \(\lambda_2\) and \(\lambda_3\) of a large magnitude and equal sign (the sign is an indicator of brightness/darkness). In CT datasets the vessels can be seen as bright tubular structures against a dark background, implying that both \(\lambda_2\) and \(\lambda_3\) be simultaneously negative.

These concepts are used in [7] to compute a measure of ‘second order structureness’. This measure, along with the knowledge of specific eigenvalue ratios results in a general purpose ‘vesseness’ measure, which is then computed for each point in the dataset. This computation is performed for increasing values of \(s\), to incorporate all possible vessel diameters and is displayed in image form in fig.16 where the vesseness measure ranges from 0 to 255 (higher values represent increasing vesseness for a specific point). The final result of the multi-scale hesssian approach is simply the maximum vesseness measure for every point over all results corresponding to each \(s\). This process usually results in a dataset which highlights the vessel-like structures in the input dataset.
(a) Segmented Heart

(b) Single Scale ($s = 1.25$)

(c) Single Scale ($s = 1.398$)

(d) Single Scale ($s = 1.564$)

(e) Single Scale ($s = 1.75$)

(f) Multi-scale

Figure 16: Multi-scale Hessian Vesseness
On visual examination and comparison, the multi-scale hessian approach does appear to successfully isolate the vessels in the segmented heart dataset, along with other structures which are of no real interest. These structures are primarily areas of high curvature (as seen in fig. 17) which are included in the result due to the fact that the vesselness measure is heavily relying on second order information. In datasets which have curved objects, like CT cardiac datasets (which include objects like the heart ventricles, aorta, etc), this problem is exaggerated. To obtain a better result these structures need to be removed in such a way that the extracted vessels are not affected.

2.3.2 Morphological Correction

Morphological reconstruction for binary images is an image processing technique (described in [20]) which reconstructs a mask image from a marker image using connected operators. Formally, if $I_1, I_2, \ldots, I_n$ are connected components of image $I$, the reconstruction of mask $I$ from marker $J$, namely $\rho(I|J)$, is the union of the connected components of $I$ which contain at least a pixel of $J$, as seen in fig. 18.
One of the techniques used to implement morphological reconstruction is *Opening By Reconstruction*. The technique can be defined using geodesic dilations $\delta_1(J)$ as,

$$\delta_1(J) = I \land \delta(J)$$

This operator is used iteratively until stability, to perform the reconstruction $\rho(I|J)$ given by,

$$\rho(I|J) = \lim_{n \to \infty} \delta^n_1(J) = \delta_1 \ldots \delta_1 \delta_1(J)$$

In practice it is sufficient to apply the above iteration until the smallest integer $n$ is found such that

$$\delta^n_1(J) = \delta^{n-1}_1(J)$$

Since the input to the process is a binary dataset, the result is a reconstruction of any connected component in $I$ which intersects some part of $J$. An opening by reconstruction is computed by selecting marker $J$ which is generated from an opening of $I$ by structuring element (say $X$). Reconstructing from this marker preserves any connected component in which $X$ fits in at least one position.

One of the problems with the standard opening by reconstruction using the above mentioned implementation is that it is slow.
The other, more significant problem, with respect to cardiac CT data is that of leakage. Leakage occurs when spurious thin bridges connect separate image regions, making them inseparable. Inherent noise in the non-contrast CT data along with the low resolution implies that these bridges can occur in the dataset connecting the arteries to other structures. In an attempt to solve both these problems [22] proposes a new formulation of a so-called reconstruction criteria. The sequence of morphological filtering proposed in this section is inspired from and is an approximation of this technique.

The method can be used to eliminate non-vessel structures using the binary form of the segmented heart (generated in fig.14). The task is made much easier in this context, as the dataset contains a single connected component - the heart. With the right choice of mask and marker image it becomes possible to remove the vessel-like structures and retain only the unwanted features. This resulting image is then inverted and applied as a stencil mask on the multi-scale hessian result to remove non-vessel objects.

**NOTE**: Since the objective of the filtering is to eliminate the vessel-like structures, one of the important parameters required for the process is the radius of the arteries. It could be possible to determine the radius from the given datasets (using prior knowledge of the size of known features), but for the purpose of this project and the given datasets, a value of 5 pixels has been seen to give satisfactory results. Another constraint imposed by the given dataset is that due to the low resolution in the z-direction (number of slices) as compared to the x/y-direction (image width/height), it becomes necessary to perform the proposed filtering on a per-slice basis with a 2D structuring element for effective results. The structuring element is chosen to be a 2D euclidean ball.

The steps to generate the final stencil mask are described as follows,

1. The mask image is created by simply eroding \[Erosion(H, 5)\] the binary segmented heart dataset \(H\) by a structuring ele-
ment (in pixels), approximately equal to the maximum radius (= 5 pixels) of the arteries to be removed. A sample mask image slice is seen in fig. 19(b).

2. The marker image is required to be a subset of the mask image and can be generated by performing an opening on $H$, followed by an erosion $[\text{Erosion} (\text{Opening} (H, 7), 5)]$ using a structuring element with radius (= 7 pixels) greater than the one used for the mask image. A sample mask image slice is seen in fig. 19(c).

3. Opening by reconstruction is then performed using the generated mask/marker image datasets, $\rho_5 (\text{Erosion} (H, 5) | \text{Erosion} (\text{Opening} (H, 7), 5))$.

4. Then a dilation with structuring element of radius 5 pixels is applied, resulting in a binary image almost similar to $H$ but without the vessels, $\delta_5 (\rho_5 (\text{Erosion} (H, 5) | \text{Erosion} (\text{Opening} (H, 7), 5)))$.

5. A final conditional dilation is performed with a structuring element of radius 1 pixel, to bring the reconstructed dataset close to edges of $H$, $\text{RWV}(H)$.

In short,

$$\text{RWV}(H) = \delta_{H, 1} (\delta_5 (\rho_5 (\text{Erosion} (H, 5) | \text{Erosion} (\text{Opening} (H, 7), 5))))$$
where,

- Erosion($I, n$) = Erosion of image $I$ by structuring element of radius $n$,

- Opening($I, n$) = Opening of image $I$ by structuring element of radius $n$,

- $\rho_n(I_{\text{mask}}|I_{\text{marker}})$ = Opening by reconstruction of mask $I_{\text{mask}}$ with respect to marker $I_{\text{marker}}$ using structuring element of radius $n$,
\( \delta_n(I) = \) Dilation of image \( I \) by structuring element of radius \( n \),

\( \delta_{I,J}(n) = \) Conditional dilation of image \( I \) by structuring element of radius \( n \) with mask \( J \),

\( RWV(H) = \) Reconstruction of the heart region without vessels.

The intermediary results of the process can be seen in fig. 20. The main advantage of the technique is that it avoids the usual problem of leakage into the vessel-like structures and ensures that they are not included in the final result. The effectiveness of this approach
is based on the assumption that the arteries are usually connected to the heart at the two opposing sides of the aorta.

![Image](image_url)

(a) Heart Segmented Data  (b) Multi-Scale Hessian Data

![Image](image_url)

(c) Morphologically Corrected Data(a)  (d) Morphologically Corrected Data(b)

**Figure 22: Vessel Extraction Volume**

The resulting binary dataset is then inverted and this inversion is used as mask on the multi-scale hessian to obtain a corrected dataset consisting primarily of the required vessel-like structures. As can be seen in fig.21, a large proportion of the unwanted structures are removed. A volumetric representation of the results is presented in fig.22.
2.4 CORONARY ARTERY MODEL DATASET

The structure and shape of coronary arteries play an important role in the diagnosis of heart disease. This has lead to a considerable amount of research being focused towards the development of reliable and exhaustive arterial models. Two methods often cited in the literature include [4], which describes the 3D location of branching points of the coronary artery structure, along with the subsequent [5], which increases the accuracy of the model by adding information about the lumen diameter at different reference points. Structural differences in coronary arteries give rise to a number of possible ambiguous shapes. The use of a priori knowledge in the form of a qualitative model [23], a quantitative model [16], or a combination of both [3], helps to alleviate these ambiguities. For the purpose of this project, any artery model technique can be used, provided it can include as many variations of artery structure as possible.

To this end, the solution methodology implemented here allows for and encourages the use of a large number of models, which potentially represent most of the variations seen in coronary arteries. The software application provides an interface which allows the user to choose high-resolution, high-contrast CT datasets and use these to build coronary artery models. This is done by performing heart segmentation and vessel extraction on the dataset, using the methods already described in sections 2.2 and 2.3 respectively. The unwanted regions can be manually removed by simply erasing them using a rectangular, mouse-controlled erasing interaction as seen in fig.23.

This procedure is performed once beforehand and can be used to build up a comprehensive set of models which correspond to a large number of structurally different arteries. An important reason to use already existing datasets to build models is that the radiologists are already familiar with these datasets and can easily identify the relevant structures. The resulting models are thus a...
reflection of the knowledge and experience of the radiologist, which plays a crucial role in the proposed solution. The motivation behind building a database of coronary artery models is to compare the extracted coronary arteries from the patient to the pre-built models and find the best fit. This is done by introducing the models into the solution pipeline as described in the following sections.

**NOTE**: At this point in the pipeline, it is important to mention that the success of the proposed solution relies heavily on the fact that there exists a high contrast model dataset (in the pre-built database) which is structurally comparable to the dataset under investigation. However this assumption is not unrealistic, since the manual identification of plaque in coronary arteries also depends on whether a dataset with similar structural characteristics has been observed at some point in the past. This assumption is a representation of a radiologist’s experience of having seen many datasets, which is of immense importance in calcium scoring. This implies that for the solution to work, a comprehensive database of varying model datasets is a pre-requisite. However, it would take a considerable amount of time to build such a database. Moreover, this project is essentially a proof-of-concept and is focused primarily on interme-
due results. Due to these reasons, a single model dataset is chosen to be compared. The chosen model dataset is in fact built from the high contrast CT scan of the patient whose (low) contrast dataset is currently under investigation. This may seem to be trivial and unrealistic, since the comparison of a low and high contrast CT dataset of the same patient would be guaranteed to produce good results. But in the context of this project, this comparison is taken to be a first test, to ensure that the solution does not fail, even in the trivial case. Further experimentation details to produce more realistic results are touched upon in the Chapter 3.

(a) Model Cardiac Data  
(b) Model Vessel Data

Figure 24: Model Vessel Volume

2.5 VESSEL CENTRE POINTS GENERATION

The next step in the solution pipeline is the reduction of the volume dataset (obtained as output of vessel extraction) to a 3D pointset. These volume datasets include the result of the automated vessel extraction run on the patient dataset as well as the coronary artery models generated by manually correcting the result of vessel extraction run on the model dataset. Both the patient and model datasets are reduced to representative 3D points which are later compared to each other.
Skeletons and Medial Axis Transforms [8] convert structures in 3D datasets to a set consisting of loci of centers of bi-tangent spheres that fit entirely within the structure being considered. In this process, the structures under consideration need to be in binary form and any effect of information coming from greyscale intensities is lost. This would be an inaccurate approach to employ in the scope of this project as the intensity values of structures play an important role. The vessel-like structures resulting from the vessel extraction step, may not entirely include the vessels present in the original dataset, which can be seen as high-intensity tubular structures embedded in areas of low-intensity. Thus, instead of simply computing centres of the vessel-like structures, it is required to compute the centres of high-intensity regions lying within these structures.

2.5.1 Persistence

Persistence or Persistent Maxima [6] can be defined as the local maxima of the intensity values over all axis-aligned two-dimensional slices of the input image dataset. A discrete topological method is employed to find persistent features that cannot be removed by small perturbations of the data. The use of persistence to generate center points has been implemented in [19] to directly extract the coronary arteries in high-contrast CT datasets. Due to the dis-connectedness of the vessels in non-contrast CT datasets, the method does not give good results when applied to such kind of datasets. Nevertheless, the ability of the method to target and highlight high-intensity regions (in this case, plaque) and its speed of computation in 3D make it an efficient approach for the generation of points lying close to the center of extracted 3D structures. Persistence points of the extracted vessel-like structures for each of the three 2D (XY,YZ,XZ) planar slices are computed as follows:

- A variable \( P(u) \) for each pixel \( u \) is initialized to zero.
- Starting from a set \( S = \emptyset \), pixels of each slice in the current plane (XY or YZ or XZ) in order of decreasing intensity are appended to \( S \).
• In building the set $S$, the connected components (determined based on 8 - neighborhoods) of the union of pixels inserted so far are also stored using the union-find data structure.

• Whenever a new pixel $w$ of intensity $I$ is inserted, the union-find data structure as well as the location of the pixel with maximum intensity are updated in the following steps,
  - All connected components of the neighbors of $w$ of intensity greater than $I$ are merged to one.
  - For each of the merged connected components, if $v$ is its maximum intensity pixel and $I(v)$ is its intensity, $P(v)$ is updated to $I(v) - I$.

• The procedure terminates after all pixels are inserted into $S$.

• After the algorithm terminates, the value of $P(u)$ for any pixel $u$ which is a local maximum will be equal to its persistence. For pixels $u$ which are not local maxima, $P(u)$ will be zero.

![Figure 25: Center Points Generation](image)

This 2D algorithm is run for every slice perpendicular to one of the coordinate axes, recording the results in a 3D array of the same dimensions as the input 3D dataset. This yields three arrays, one per coordinate axis. The entry-wise maximum of these arrays are
then taken, resulting in a 3D array called the persistence volume. Computed persistence points (displayed in red) can be seen in fig.25

2.6 POINT SET MATCHING

This step of the solution pipeline involves the comparison and fitting of the centre-points of vessel-like structures of the patient dataset with those of the model dataset. The problem with this comparison is that the patient dataset contains a large number of unwanted points (outliers) and a small fraction (about 10%) of points close to those in the model dataset (inliers).

2.6.1 Branch and Bound

The Branch and Bound method described in [14] handles the problem of many outlier points and few inlier points, provided the points representing the arteries in both datasets are reasonably close to each other to begin with. The method searches a 12D affine transformation space for the ideal transformation of points from the model (moving) point set to the patient (fixed) point set. The choice of affine (rigid) transformation is due to the fact that cardiac CT scans are usually taken with the heart chamber in approximately the same position and orientation, which lends itself to an easier comparison. Another reason is the assumption that heart chambers and in particular coronary arteries of different patients are structurally similar. The result of this method is the isolation of those points in the patient dataset which represent center points of the coronary arteries.

Assuming that the point sets F (fixed) and M (moving) are both in three-dimensional space, any affine transformation \( \tau \) applied to a point \( m \in M \) can be expressed as a linear transformation \( L \) followed by a translation \( t \), i.e. \( lt(m) : Lm + t \), where \( m \) and \( t \) are 3-element column vectors, and \( L \) is a \( 3 \times 3 \) matrix. Since twelve parameters are needed to define the transformation, this naturally leads to a
twelve-dimensional transformation space, $\Gamma$. Due to the fact that CT slices are captured on the $x$-$y$ plane, the rotational elements are more or less restricted to the rotations of points about the $z$ axes and the rotational elements corresponding to the $x$ and $y$ axes can be discarded. This implies a reduction of $\Gamma$ to a six-dimensional transformation space. The result of the method is a similarity measure ($\text{sim}$) which represents how close the two point sets are in terms of a breakdown point. The breakdown point (also called the distance quantile - $q$) is the pre-defined percentage of points of $F$ that are assumed to be close to points in $M$.

The process can be compared to constructing a search tree, where each node of the tree is identified with the set of transformations contained in some axis-aligned hyperrectangle in the six-dimensional transformation space. These hyperrectangles are called cells. Each cell $T$ is represented by a pair of transformations, $(\tau_{lo}, \tau_{hi})$, whose coordinates are the upper and lower bounds on the transformations of the cell. Any transformation whose coordinates lie between the corresponding coordinates of $\tau_{lo}$ and $\tau_{hi}$ lies in this cell. An initial cell ($T_0$), based on a priori knowledge of the nature of the transformation, is defined such that $T_0$ is assumed to contain the optimum transformation. For the current problem, $T_0$ is set to range over $(-45^\circ, 45^\circ)$ for rotations along the $z$ axis, $(-10, 10)$ pixels for the translation along the $x$ and $y$ axes and $(-4, 4)$ pixels for the translation along the $z$ axis. Given any cell $T$, and given any point $m \in M$, the image of $m$ under every $\tau \in T$ represents a bounding rectangle for $m$, whose corners are defined by $\tau_{lo}(m)$ and $\tau_{hi}(m)$. This bounding rectangle is called the uncertainty region of $m$ relative to $T$.

The algorithm implemented in this context is a simplified version of the branch and bound method, and is described as follows,

1. Build a nearest neighbor data structure for the points of $M$ with respect to $F$. Initialize a priority queue to hold active cells (cells which could potentially contain the optimum transfor-
To begin with, add $T_0$ to the queue and set $\text{sim}_{\text{best}} = \infty$.

2. Remove the largest cell $T$ from the queue and compute the uncertainty regions for every point $m \in M$ with respect to $T$.

3. Consider the point in $M$ denoting the $q^{th}$ quantile in nearest neighbour distance to points in $F$. If the nearest neighbour of this point (in $F$) lies outside its uncertainty region then the active cell is removed from the priority queue and the algorithm returns to step 2.

4. Otherwise, the midpoint transformation (of the cell $T$), $\tau$ is computed and the image of each point of $M$ under $\tau$ is computed. A list of nearest neighbours of these points in $F$ is generated and the $q^{th}$ smallest distance is found. This value is called $\text{sim}_{\text{hi}}(T)$.

5. If $\text{sim}_{\text{hi}}(T) < \text{sim}_{\text{best}}$, update $\text{sim}_{\text{best}}$ and let $\tau_{\text{best}}$ be the associated transformation.

6. Split $T$ into two smaller subcells $T_1$ and $T_2$, by splitting it along the dimension that contributes most to its uncertainty region size. Compute size bounds for $T_1$ and $T_2$.

7. Enqueue $T_1$ and $T_2$ in the queue of active cells and return to step 2.

8. Once the queue is empty the algorithm terminates and the transformed point set is given by $M' = \tau_{\text{best}} M$

The result of the point set matching algorithm is the final transformation $\tau_{\text{best}}$, the corresponding similarity measure $\text{sim}_{\text{best}}$ and the transformed point set $M'$.

Once the transformed point set $M'$ has been computed, a list of nearest neighbours of $F$ in $M'$ is generated. The list is then sorted in the order of increasing distances and all points in $F$ corresponding to distances less then the $q^{th}$ smallest distance are considered to be
the final resulting point set $F'$. This point set is supposed to represent the center points of the coronary arteries in the patient data set. The result of the point matching can be seen in fig. 26, where

![Figure 26: Point Matching Result](image)

the red points indicate the (fixed) persistence points of the patient dataset ($F$), the blue points correspond to the initial persistence points of the model dataset ($M$) and the green (transformed) points belong to the point set $M'$ generated as a result of applying the final transformation $\tau_{\text{best}}$ to $M$. The points belonging to the resulting point set $F'$ are assumed to be representing the coronary arteries.
in the patient dataset and are used to reconstruct the arteries (as discussed in the next chapter).

2.7 RECONSTRUCTION OF CORONARY ARTERIES

![Figure 27: Artery Reconstruction](image)

Once the points representing (the center lines of) the coronary arteries have been computed, the next step is to reconstruct the arteries. This is done simply by constructing a tube around the points using the mask structuring element radius as mentioned
in the morphological reconstruction step (2.3.2). Since the spatial

![Image](image_url)

Figure 28: Artery Reconstruction Volume

scaling of the dataset is not uniform in the three axes (X,Y,Z axes in this case corresponds to 0.489mm,0.489mm,3mm respectively), the radius needs to be scaled accordingly. The results of this step can be seen in fig.27 (2D) and fig.28 (3D). Once the arteries are segmented, all calcified plaque within them can be identified and scored using the Agatson scoring method already described in 1.2.0.4.
2.8 SUMMARY

This project has attempted to solve the problem of automating calcium scoring using non-contrast CT scan data. The core idea of the proposed solution is the generic solution pipeline which has been made concrete by the selection of methods already existing in the literature. The solution pipeline is made up of multiple sub-problems and the chosen methods have been adapted and changed according to the constraints imposed by these problems.

The solution pipeline attempts to reduce the 3D cardiac CT dataset to a set of points which (potentially) represent the center points of the coronary arteries. This has been done both for pre-processed model datasets and patient datasets, following which a similarity test is performed to compare the given patient dataset with the model dataset(s). Due to the inherent noise and lack of detail in the patient non-contrast dataset, the resulting point set of the patient dataset includes false positives, i.e. points which do not belong to the arteries. A successful similarity test determines the points in the patient dataset which should represent the arteries and these points have been used as center points to reconstruct the arteries. All plaque within these regions can then be identified and used to compute the calcium score.

Since the proposed solution is still in the experimental phase, a number of assumptions have been made in implementing each method and verification of results have been mostly visual in nature. Even though the methods are experimental in nature, they have provided enough impetus for further investigation.
DISCUSSION

It is to be noted that the methods and techniques presented in this project have been tried on a specific non-contrast CT dataset of a single patient (with the corresponding contrast high-resolution dataset used as the model). Even though the visual results appear to be promising, they are by no means a guarantee of accuracy, when applied to the variety of datasets that could exist. This aspect is a reflection of the difficulty and complexity inherent in the problem statement and any proposed solution must be accepted only after all possible variations in data have been considered. As it stands, the solution methodology must be seen as a proof of concept and can be used for further analysis and experimentation.

Even though the results obtained so far correspond to a single CT dataset, the applied methods have been observed to be relevant enough for further discussion. This chapter deals with the various questions that may arise as a result of implementing the proposed solution methodology and attempts to answer these by elaborating on the difficulties involved as well as proposing possible future work to improve the effectiveness of the solution.

3.1 ADVANTAGES / DISADVANTAGES

The various individual steps in the solution pipeline have their own set of pros and cons, which can be discussed separately,

1. *Heart Segmentation*: 3D segmentation of the heart chamber (especially in the case of non-contrast CT data) is a complex task. Though the fast marching approach, as proposed in this project, provides a fast and reasonably accurate mechanism to extract the regions of interest, it suffers from the drawback of being heavily dependent on the input parameters, namely
the number of time-steps required and the initial seed points. Incorrect input values could lead to certain (potentially im-
portant) sections of the heart to be left out of the resulting segmentation.

2. *Vessel Extraction* : The multi-scale hessian technique to extract vessel-like structures provides a reliable method of ensuring that the coronary arteries are identified. Unfortunately, the results of this method also include irrelevant structures which could cause problems further down the solution pipeline. An attempt to correct this is made using morphological reconstruction, but the accuracy of the reconstruction is again heavily dependent on the radius of the structuring element used in the process.

3. *Coronary Artery Model* : The proposed idea of using existing high-contrast, high-resolution CT datasets to build models is interesting as it reflects real-world data and provides the user with the chance to generate his/her own representation of coronary arteries. The drawback of building models in such a way is that it is time-consuming and difficult to include all kinds of different artery structures.

4. *Center Line Points Generation* : Center line points generation using the concept of persistence takes into consideration the spatial structure of areas in the dataset as well as the variations in intensity (HU values) within them. This technique results in point-set representations of the arteries which are sufficiently accurate as far as the given dataset is concerned, but may be incorrect in real world terms due to missing information.

5. *Point Set Matching* : Since the branch and bound method (for matching the patient and model point sets) can handle a large number of outlier points, it is a useful technique in this particular instance. However, the difficulty in obtaining right results is directly related to the knowledge of the percentage of outlier points that occur in the dataset. The method can
also be made more precise by discarding the assumptions of affine transformation and rotation only around the z-axis.

6. Overall: Even though the solution pipeline (as proposed) seems to have a logical flow to it, it suffers from the problem of being elaborate in nature. The intermediate methods are, in themselves, quite robust, but when combined together could lead to systemic problems wherein small errors in results of specific methods could lead to dramatic changes in the final result.

3.2 Measurability

The ideal way to confirm the accuracy of scientific methods is to attach a measure to the results, which allow for checking and comparison. In the context of the proposed solution pipeline, the methods put forward in heart segmentation, vessel extraction and center line points generation produce results which are difficult to measure. These results have been visually confirmed to be satisfactory for the test case considered. The final point matching method does involve a similarity measure, $\text{sim}_{\text{best}}$, which defines how close a patient point set is to a model dataset. This measure can be extended to an initial test pattern of say $n$ datasets where both the patient dataset and its corresponding model data set exist. Each patient dataset can then be processed by the solution pipeline using each of the model datasets, resulting in a similarity measure matrix as seen in fig.29. The initial test would be to confirm that the diagonal elements of the matrix are the lowest in each row, i.e. $\text{sim}_{\text{best}}$ is lowest for the $i^{\text{th}}$ patient dataset when processed in combination with its corresponding ($i^{\text{th}}$) model dataset. Once this is confirmed, the solution pipeline can be applied to a new ($n+1$) patient dataset whose corresponding model dataset is not available. This new dataset can be processed all the way until the calcium scoring, which can then be compared with manually obtained results, to check and confirm the real accuracy.
Each of the intermediate methods in the proposed solution pipeline requires a few input parameters which are crucial to the accuracy of the results. These parameters are listed in A.1 (Appendix A.1), along with their experimental values. Even though these values can be improved with testing on multiple datasets, they can be made robust by the provision of theoretical guarantees. In the spirit of the solution proposed, these parameters are related to the geometry of the datasets, implying the possibility of proven geometric bounds on the input parameters and the corresponding behaviour of the methods under these constraints.

Figure 29: Similarity matrix

3.3 GUARANTEES
3.4 ALTERNATIVES

The generic solution pipeline proposed at the beginning provides a basis for the concrete implementation utilizing the proposed methods. The choices of these methods have been driven primarily by the goals laid out at the onset, i.e. modelling of manual behaviour and automation. Other methods which possibly fulfil these goals could also be used instead. Another approach could be to implement semi-automated methods which require minimal user input for the purpose of comparison with the methods proposed in this project. This approach would certainly provide some insights into the ideal functioning of a final solution.
CONCLUSION

The primary objective of this project has been to propose and implement a mechanism to segment coronary arteries in non-contrast CT datasets for the purpose of calcium scoring. Since the procedure of using CT to obtain non-contrast data is minimally invasive and relatively inexpensive, the ability to identify and score calcified plaque in such datasets is of immense importance to both the patient being treated as well as the radiologist / surgeon making the diagnosis.

The proposed solution pipeline has been presented essentially as a proof of concept which needs to be tested and extended. If shaped into a usable tool, the pipeline would be of assistance in the process of diagnosis resulting in a considerable reduction of the time and effort required. Even though the proposed solution is not the final product, the ideas and results described in this project could be further expanded to develop an accurate and comprehensive procedure, resulting in an efficient and reliable system to perform calcium scoring.
APPENDICES

A.1 INPUT PARAMETERS

The following is a list of input parameters and their corresponding values required for the various methods used in this report. The values have been obtained from manual experimentation and observation.

Heart Segmentation

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Threshold value</td>
<td>-150HU</td>
</tr>
<tr>
<td>No. of iterations</td>
<td>80 iterations for (x,y) resolution (0.5mm,0.5mm)</td>
</tr>
<tr>
<td>Majority Filter Size</td>
<td>5x5 window (in pixels)</td>
</tr>
</tbody>
</table>

Vessel Extraction

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hessian Scaling Factors</td>
<td>1.25 , 1.398 , 1.564 , 1.75</td>
</tr>
<tr>
<td>Mask Structuring Element Radius</td>
<td>5 pixels</td>
</tr>
<tr>
<td>Marker Structuring Element Radius</td>
<td>7 pixels</td>
</tr>
<tr>
<td>Reconstruction by Dilation Structuring Element Radius</td>
<td>5 pixels</td>
</tr>
</tbody>
</table>
**Point Set Matching**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$z$ (spinal)-axis Rotation Range</td>
<td>-45 degrees to 45 degrees</td>
</tr>
<tr>
<td>$x,y$-axis Translation Range</td>
<td>-10 pixels to 10 pixels</td>
</tr>
<tr>
<td>$z$ (spinal)-axis Translation Range</td>
<td>-4 pixels to 4 pixels</td>
</tr>
</tbody>
</table>

### A.2 SOFTWARE IMPLEMENTATION

This section describes the software application built for the purpose of implementing the methods and techniques seen in this project. The primary aim of the application is to experiment with given datasets and analyse intermediate results at every step of the proposed solution pipeline. The possibility to experiment with the various techniques has played an important part in developing the proposed solution and also in the visual verification of results.

**Overview**

The software application built for the purpose of implementing the methods and techniques seen in this project has been written in the C++ Programming Language. Most of the methods in the pipeline have been implemented using 'The Insight Segmentation and Registration Toolkit' - ITK\(^1\) library. ITK is also used for input / output of the data sets as well as for some other utility tasks. Visualisation of the data is performed using 'The Visualization Toolkit' - VTK\(^2\) library and the Qt\(^3\) framework has been utilised for building the graphical user interface.

---

\(^1\)[http://www.itk.org/]
\(^2\)[http://www.vtk.org/]
\(^3\)[http://qt.nokia.com/products/]
User Interface

Figure 30 shows a screen-shot of the application which consists of two side-by-side views of the data displayed in 2D slices. Input parameters for each step of the pipeline can be set using the text fields below the views. A pop-up menu is provided for each of the views, which can be used to apply the different techniques seen in the solution pipeline to the corresponding dataset. The pop-up menu is activated by clicking the right mouse button. Navigating through the CT slices in the dataset can be done using the mouse wheel. The mouse left button is used for discarding regions when building model datsets (refer 2.4).

![Figure 30: Software Implementation](image)

Even though the application is meant to be used for experimental purposes, the user interface lends itself to more general purpose functionality. This includes the possibility to compare the given patient dataset with the model dataset. Another (potential) possibility would be for the user to compare his/her calcium score for a particular dataset to the automated calcium score produced by the proposed solution.
Software Design

The application has been constructed using a simplistic software design. Every action performed on the dataset is available in the right-click pop-up menu. Each menu item in this menu corresponds to a task which could be anything from the reading / writing of data to one of the many image processing techniques presented in the solution pipeline.

A.2.0.1 Reading / Writing Data

The CT cardiac datasets used in this project are in the form of a series of DICOM files each representing a single slice. The data is read into the application using ITK’s `itk::GDCMImageIO` class which can handle alphabetically sorted DICOM files. DICOM header information is extracted from the first DICOM file in the series and written to a separate file. Some of the information (i.e. maximum pixel intensity, intensity value shift, slice resolution in pixels) is stored in memory for later use. Some of the intermediate results are saved to file in the VTK file format, which is done using the ` itk::ImageFileWriter` class. The writer also allows the possibility of saving in the PNG format, which has been responsible for all the image results in this report. The corresponding ` itk::ImageFileReader` class is used to read the saved intermediate results when required.

A.2.0.2 Visualisation

The visualisation is handled by VTK’s `vtkImageViewer` which is used to display the current (processed) dataset as a series of images. The image slice to be displayed is chosen by the mouse-wheel action. This image slice is buffered into a custom made Qt widget class called `QVTKOverlayWidget` which updates the widget with the chosen slice. This widget is used for both the view panels in the software. It contains all the interaction logic which has been implemented with the use of the signal-slot mechanism in Qt, where each signal (corresponding to a menu item in the pop-up
menu) triggers a specific slot (corresponding to a function defined in QVTKOverlayWidget).

A.2.0.3 VTK-ITK Connection

The background image processing is mostly handled by ITK and the visualisation is implemented in VTK. To allow the flow of data between these two libraries, the \texttt{itk::VTKImageToImageFilter} class or the \texttt{itk::ImageToVTKImageFilter} is used. Once the format of the data is known the translation of VTK input/output to ITK output/input or vice versa can be performed.

A.2.0.4 Functionality

The functionality of the application essentially includes the implementation techniques of the individual methods in the solution pipeline, which are described as follows,

- The heart segmentation method (section 2.2) has been implemented using ITK’s \texttt{itk::FastMarchingImageFilter} class. This class takes as input a filter which performs the actual fast marching segmentation. The level set result and the fast marching result seen in fig.9 has been generated using the \texttt{itk::ThresholdSegmentationLevelSetImageFilter} and the \texttt{itk::FastMarchingImageFilter} respectively. The ‘Sigmoid of Gradient Image’ image presented as an example speed image in fig.10 is generated using the \texttt{itk::SigmoidImageFilter}. The thresholding of the dataset to remove unwanted structures based on intensity values is done using the \texttt{itk::BinaryThresholdImageFilter} class and the hole filling mechanism (fig.14) is implemented using the \texttt{itk::BinaryMedianImageFilter} class.

- The vessel extraction method (2.3) include the hessian based vesselness technique as well as morphological correction. The vesselness results seen in fig.16 have been generated using ITK’s \texttt{itk::MultiScaleHessianBasedMeasureImageFilter} with the \texttt{itk::HessianToObjectnessMeasureImageFilter} class as input for measuring how closely the objects in the dataset resemble
vessels. The morphological correction is performed using the \texttt{itk::BinaryErodeImageFilter} for erosion, the \texttt{itk::BinaryDilateImageFilter} for dilation and the \texttt{itk::GrayscaleGeodesicDilateImageFilter} for geodesic dilation to produce the results seen in fig. 19 and fig. 20.

- The custom made widget display panel allows the user to remove regions in each image slice by selecting a rectangle in the display panel using the mouse left-click button. This can be applied on contrast datasets which have been filtered through the heart segmentation and vessel extraction methods to generate coronary model datasets as seen in fig. 23.

- The vessel centre points generation technique (2.5) has been implemented using a custom made \textit{Persistence} class which implements the algorithm described in the section.

- The point set matching method (2.6) has been implemented using a custom made \textit{BranchBound} class which implements the algorithm described in the section.


