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AUTOMATED SELECTION OF THE OPTIMAL CARDIAC PHASE FOR SINGLE-BEAT CORONARY CT ANGIOGRAPHY RECONSTRUCTION

by:

Daniel Stassi

A Thesis submitted to the Faculty of the Graduate School, Marquette University, in Partial Fulfillment of the Requirements for the Degree of Master of Science

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ABSTRACT

AUTOMATED SELECTION OF THE OPTIMAL CARDIAC PHASE FOR SINGLE-BEAT CORONARY CT ANGIOGRAPHY RECONSTRUCTION

Daniel B. Stassi

Marquette University, 2014

This thesis investigates an automated algorithm for selecting the optimal cardiac phase for CCTA reconstruction. Reconstructing a low-motion cardiac phase improves coronary artery visualization in coronary CT angiography (CCTA) exams. Currently, standard end-systole and/or mid-diastole default phases are prescribed or alternatively, quiescent phases are determined by the user. As manual selection may be timeconsuming and standard locations may be suboptimal due to patient variability, an automated method is investigated.

An automated algorithm was developed to select the optimal phase based on quantitative image quality (IQ) metrics. For each reconstructed slice at each reconstructed phase, an image quality metric was calculated based on measures of circularity and edge strength of through-plane vessels. The image quality metric was aggregated across slices, while a metric of vessel-location consistency was used to ignore slices that did not contain through-plane vessels. A binary metric based on the edge strength of in-plane vessels was calculated to determine if IQ of in-plane vessels was acceptable. The algorithm performance was evaluated using two observer studies. Fourteen single-beat CCTA exams (Revolution CT, GE Healthcare) reconstructed at 2% intervals were evaluated for best systolic (1), diastolic (6), or systolic and diastolic phases (7) by three readers and the algorithm. Inter-reader (RR) and reader-algorithm (RA) agreement was calculated using the mean absolute difference (MAD) and concordance correlation coefficient (CCC). A reader-consensus best phase was determined and compared to the algorithm selected phase. In cases where the algorithm and consensus best phases differed by more than 2%, IQ was scored by three readers using a 5pt Likert scale.

There was no significant difference between RR and RA agreement for either MAD or CCC metrics (p>0.2). The algorithm phase was within 2% of the consensus phase in 71% of cases. There was no significant difference (p>0.2) between the IQ of the algorithm phase (4.06 ± 0.73) and the consensus phase (4.11 ± 0.76). The proposed algorithm was statistically equivalent to a reader in selecting an optimal cardiac phase for CCTA exams. When reader and algorithm phases differed by >2%, IQ was statistically equivalent.

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TABLE OF CONTENTS

LIST OF TAE	BLES		V
LIST OF FIG	URES	V	Ί
CHAPTER			1
1	INTRO	DDUCTION	1
	1.1	Statement of the Problem	1
	1.2	Objective of the Study	2
		1.2.1 Aim 1: Development of Best Phase Selection Algorithm	2
		1.2.2 Aim 2: Validation of Best Phase Selection Algorithm	2
2	BACK	GROUND	3
	2.1	X-Ray Imaging	3
	2.2	CT Reconstruction	4
	2.3	Common CT Artifacts	5
	2.4	History of CT	7
	2.5	Cardiac Cycle 1	0
	2.6	Coronary Motion1	3
	2.7	Cardiac Gating 1	3
		2.7.1 Prospective Gating 1	4
		2.7.2 Retrospective Gating 1	4
		2.7.3 Effects of Aperiodic Heart Motion 1	7
	2.8	Coronary CT Angiography 1	8
	2.9	Retrospective Best Phase Selection 1	9
3	ALGO	RITHM DESIGN	2
	3.1	Through-Plane Metric	2
		3.1.1 Overview	2

3.1.2	Step 1: Segment cardiac region	24
3.1.3	Step 2: Quantify Through-Plane IQ metric for each image 25	e
	3.1.3.1 Threshold calculation	25
	3.1.3.2 Gamma transform	26
	3.1.3.3 Top hat transform	27
	3.1.3.4 Chamber removal mask	28
	3.1.3.5 Edge strength score	30
	3.1.3.6 Candidate point selection	32
	3.1.3.7 Circularity score at candidate points	33
	3.1.3.8 IQ quantification based on edge strength and circularity scores	35
3.1.4	Step 3: Select slices with through-plane vessels	37
	3.1.4.1 Vessel map creation	38
	3.1.4.2 Slice selection	39
3.1.5	Step 4: Choose best phase	40
In-Pla	ne Metric	42
3.2.1	Overview	42
3.2.2	Step1: Segment heart	43
3.2.3	Step 2: Calculate thresholds	43
3.2.4	Step 3: Accentuate vessels	44
	3.2.4.1 3D top hat transform	44
	3.2.4.2 Chamber removal mask	45
3.2.5	Step 4: Calculate in-plane IQ per voxel	45

3.2

			3.2.5.1	Top hat gradient	45
			3.2.5.2	Match filter	46
		3.2.6	Step 5:]	Limit to in-plane vessel MIP	47
			3.2.6.1	Select slices	47
			3.2.6.2	Locate in-plane vessel regions	48
		3.2.7	Step 6:	Calculate in-plane phase IQ	50
		3.2.8	Step 7:	Convert in-plane phase IQ metric to binary	51
	3.3	Comb	ining Thr	ough-plane and in-plane metrics	53
4	ALGO	ORITHN	A EVALU	JATION	55
	4.1	Obser	ver Best I	Phase Study	55
		4.1.1	Method	S	56
		4.1.2	Results.		57
	4.2	Obser	ver IQ Stu	udy	62
		4.2.1	Method	S	62
		4.2.2	Results.		63
5	DISCU	USSION	N AND C	ONCLUSIONS	69
	5.1	Discus	ssion		69
	5.2	Concl	usions		74
6	REFE	RENCE	ES		75
7	APPE	NDIX 1	: CARDI	AC SEGMENTATION	78
	7.1	Step 1	: Lung re	moval	78
	7.2	Step 2	: Heart-re	egion segmentation	78
	7.3	Step 3	: Rib rem	oval	79

LIST OF TABLES

Table 1- Best phases determined by three observers and the algorithm	58
Table 2- Both pair wise metrics (MAD and CCC) for each combination of measuremen techniques	t 60
Table 3- Overall IQ scores for algorithm and consensus best phase for each observer	64

LIST OF FIGURES

Figure 1- Ring artifact caused by a miscalibrated detector (red). As the gantry rotates, the data associated with the miscalibrated detector form a ring
Figure 2- Right coronary artery with (left) and without (right) motion artifact
Figure 3: Data acquired by detectors for different configurations are shown in blue/red (a/b) Increasing the detector rows or slice thickness by a factor of 4 causes a proportional decrease in the required number of rotations. (c/d) A pitch of 1 (c) leaves no gaps in the acquired data, but takes twice as many rotations to complete as a pitch of 2 (d). (e/f) With a second source and detector, shown in red, the pitch can be doubled while retaining the same longitudinal coverage
Figure 4- The cardiac cycle is split into three stages of systole and four stages of diastole. Systole consists of isovolumic contraction (IVC), maximum ventricular ejection (ME), and reduced ventricular ejection (RE). Diastole consists of isovolumic relaxation (IVR), rapid ventricular filling (RF), diastasis (D), and atrial systole (AS). The duration of each of these stages depends on heart rate. 12
Figure 5- Cardiac scan with prospective and retrospective gating applied. Prospective gating turns on the tube current only for low motion end-systolic and mid-diastolic periods (grey line). Using retrospective gating, slices can be reconstructed from any contiguous set of projections (blue boxes). The center of the retrospective gating window is chosen as a percentage of the R-R interval
Figure 6- Discontinuities occur along the right coronary artery at slab boundaries due to aperiodic heart motion
Figure 7- Consecutive phases only differ by a few projections. With $\sim 180^{\circ}$ reconstruction, these projections are approximately parallel. Motion parallel to the projections cannot be detected by the difference between the images
Figure 8- Overview of the steps to calculate image quality in through-plane vessels at each cardiac phase in a CCTA exam
Figure 9- (a) Original image (b) Image histogram with soft tissue, contrast, and maximum value thresholds marked in black, red, and green respectively
Figure 10- Histogram of median values for each of the three threshold in each exam 26
Figure 11- Steps to image top hat transform (a) Original image (b) Segmented grayscale morphological open (c) Segmented top hat transform

Figure 12- Steps in chamber removal mask creation (a) Original image (b) Grayscale morphological open (c) Initial mask created from the open (d) Points marked as contrast Figure 13- Steps in edge score calculation (a) Original image (b) Top hat transform (c) Top hat transform gradient multiplied by the chamber removal mask (d) Final edge score Figure 14- (a) Match filter (b) Match filter value based on distance from the center of the Figure 15- Candidate point selection (a) Original image (b) Edge strength score (c) Regions of the heart separated with the centroid (d) Nine candidate points in the top hat Figure 16- Examples of circularity scoring (a) Original image with two candidate points circled (b) ROI in the top hat image near the LAD (c) Threshold decomposition of the LAD region with circularity score of 0.518 (d) ROI in the top hat image near the LCX (e) Figure 17- IQ for each vessel is shown as well as images from various phases in the slice. The local maxima in the plots match high IQ phases for the RCA, LAD, and LCX. 37 Figure 18- This example shows how the recursive algorithm searches for vessels in a single direction. The starting location is in the upper right image. Green lines indicate a vessel was found within the search range, while red lines indicate that it was not. When no vessel is found, the search continues for one additional slice to make sure the vessel does not pick up again. Note: the recursive algorithm is looking through the potential Figure 19- The number of through-plane vessels found for each slice are shown. In the central region of the heart, the most through-plane vessels are found for both the right and the left side. The RCA would include slices 21-49, the LAD would include slices 18-39, Figure 20- Overall IQ scores for each phase on the right and left sides of the heart. The best phase for the right vessels is 79%, the best phase for the left vessels is 67%, and the

Figure 22- Steps in in-plane voxel IQ calculation (a) Original image (b) Segmented top)
hat transform (c) Top hat transform gradient multiplied by the chamber removal mask	(d)
Final edge score after applying a match filter	. 46

Figure 23- (a) Match filter (b) Match filter value based on distance from the center of the filter in millimeters
Figure 24- (a) Original image near proximal in-plane RCA (b) IQ score limited to the anterior right quadrant (c) Thresholded IQ score (d) MIP of thresholded IQ scores for the given phase across five slices (12.5mm) surrounding the slice from (a) (e) Sum of MIPs at all phases for this set of slices. The sum of this image is calculated for each set of slices to determine which slices contain the in-plane vessels. (f) The region identified as the location for proximal right in-plane vessels for all phases. If multiple regions are present, the largest one would be selected
Figure 25- (a) Original image near proximal in-plane RCA (b) Unthresholded MIP for the given phase across five slice (12.5mm) surrounding the slice from (a) (c) Unthresholded MIP limited to proximal RCA region from Figure 24f (d) Top points selected to limit to the estimated vessel size
Figure 26- The in-plane score (top) and binary metric (bottom) are shown for the proximal right and left in-plane vessels. The candidate phase was 40% and, since only 8 phases were available for the entire exam, they were all investigated. As seen in the axial slices, 34% is a poor phase for the right side and 48% is a poor phase for the left side. Both of these phases are identified as 'Unacceptable' by the binary in-plane metric. The candidate phase of 40% is accepted
Figure 27- Flow chart of the algorithm for choosing the best cardiac phase for CCTA reconstruction. The through-plane algorithm picks potential phases which are checked to ensure that the in-plane vessel image quality is acceptable
Figure 28- Reader-reader and reader-algorithm plots compared to an ideal 45° line from the origin
Figure 29- Bootstrap histogram of differences between RR and RA mean absolute differences
Figure 30- Bootstrap histogram of differences between RR and RA concordance correlation coefficients
Figure 31- Bootstrap histogram of differences between algorithm and consensus overall IQ
Figure 32- Bootstrap histogram of differences between algorithm and consensus RCA IQ
Figure 33- Bootstrap histogram of differences between algorithm and consensus LAD IQ
Figure 34- Bootstrap histogram of differences between algorithm and consensus LCX IQ

Figure 35- Significant difference in RCA I	Q with 4% pha	ase change (top).	No significant
IQ difference with 6% phase change			

Figure 38- (a) Original image (b) Lung segmentation before morphological closing.	Note
the areas in the heart that are below the lung threshold. (c) Lung segmentation after	
morphological closing. The holes have been removed	82

CHAPTER

1 INTRODUCTION

1.1 Statement of the Problem

In 2004, coronary artery disease (CAD) was the most expensive condition for hospitals to treat, costing over \$44 billion for 1.2 million patients [1]. The gold-standard metric to determine the presence and severity of stenoses is x-ray angiography. Noninvasive Coronary Computed Tomography Angiography (CCTA) exams are often used to exclude significant coronary stenosis because of their high negative predictive value [2]. Cardiac motion can blur the coronary arteries in the CCTA images, making it difficult for clinicians to perform an accurate diagnostic interpretation. Modern CT systems have sufficient temporal resolution to reconstruct volumes at many time points during the cardiac cycle. Ideally, reconstruction will occur during the phase of the cardiac cycle with the least motion. This minimum motion phase varies from patient to patient [3]. The best phase is also related to the patient's heart rate [4]. Heart rate data is often used in prospective gating to limit the range of acquired phases and reduce dose to the patient. It is common to reconstruct many volumes from the acquired phases after prospective gating. In current practice, multiple phases may be reviewed manually to select the volume with the best image quality. This process requires additional computation time to reconstruct each volume. As companies shift towards more time-consuming iterative

reconstruction techniques, minimizing the number of reconstructed phases is essential. A manual best phase selection is also time-consuming for radiologists who must review multiple sets of images. A fully automated algorithm that determines the best phase of the cardiac cycle for CCTA reconstruction is essential to solve this workflow problem.

1.2 Objective of the Study

The objective of this project was to develop an automated algorithm to retrospectively select the best cardiac phase for CCTA reconstruction and evaluate algorithm performance. Based on this goal, two specific aims were identified.

1.2.1 Aim 1: Development of Best Phase Selection Algorithm

Develop an automated algorithm that selects the best cardiac phase for CCTA reconstruction based on coronary image quality.

1.2.2 Aim 2: Validation of Best Phase Selection Algorithm

Validate the algorithm performance by comparing the algorithm output to observer-chosen best phases and image quality assessments.

2 BACKGROUND

2.1 X-Ray Imaging

X-rays are the basis for CT imaging. An x-ray is an electromagnetic wave with a wavelength between 0.01nm and 10nm. As an x-ray beam passes though matter, x-rays are absorbed or scattered based on the material's attenuation coefficient, μ , according to the Lambert-Beer Law:

$$I = I_0 e^{-\mu x}$$
 Eq. 1

where I_0 is the original beam intensity, I is the final beam intensity, and x is the thickness of the material. X-rays occur at different energy levels, and lower energy x-rays are more likely to be attenuated. Therefore, μ is a function of the x-ray energy. X-rays are a form of ionizing radiation. This means that x-rays have sufficient energy to cause an electron to be ejected from an atom. Ionizing radiation can damage DNA molecules which may lead to cancer. Therefore, the radiation dose, or amount of ionizing radiation per unit mass, should be as low as possible.

Projection radiography is a common two dimensional x-ray imaging technique. An x-ray beam is passed through the subject over the region of interest. Before reaching the subject, low energy x-rays that are unlikely to pass through the subject are filtered to reduce patient dose. X-rays outside the desired field of view are removed using collimators. A scintillator converts the final x-ray beam to light, and the light intensity at each spatial location is digitally recorded. This forms an image where contrast is dictated by the attenuation coefficients and thicknesses of materials in the subject. One limitation of projection radiography is the loss of depth information, as attenuation coefficients parallel to the direction of x-ray travel are integrated in the final image. To overcome the limitation of projection imaging, CT scans are used to obtain three dimensional information.

2.2 CT Reconstruction

CT images are maps of the subject's attenuation coefficient at different points in space, which can be calculated using x-ray projections. X-ray projections are acquired at a multitude of angles, covering at least a 180° rotation around the subject. Projections are reconstructed into a CT image with either filtered backprojection or iterative reconstruction techniques. In filtered backprojection, the projection measurements are spread equally along the path that each x-ray travelled through a process called backprojection. The resulting image will be the actual object convolved with a blurring function of 1/r. This blurring artifact can be removed by first convolving each projection with a deconvolution kernel that sharpens the 1/r blurring function. Since convolution is time consuming, the projection data is often transformed into the frequency domain where the sharpening kernel is applied through multiplication. An inverse Fourier Transform is performed on the filtered projection, followed by backprojection to reconstruct the image. Iterative reconstruction starts with an initial guess of the final image and steps through a number of iterations to bring the image closer to an optimal

result. Theoretically, the forward projection of the final image at each angle will exactly match the acquired projection data at that angle. Using this reconstruction approach, the estimated image is updated iteratively to minimize the error between the measured data and the estimated data at each projection angle. CT images typically have a matrix size of 512x512, which makes this process computationally expensive. Using either technique, CT images can be reconstructed from a set of x-ray projections.

2.3 Common CT Artifacts

There are many common artifacts in CT images. Beam hardening occurs because x-ray beams contain a spectrum of energy levels. Low energy x-rays are attenuated after passing through thick sections of materials or through materials with high attenuation coefficient. This forms a spectrum with a higher average energy than the beam that was



Figure 1- Ring artifact caused by a miscalibrated detector (red). As the gantry rotates, the data associated with the miscalibrated detector form a ring.

incident on the object. The high energy beam is less likely to be attenuated by tissue with a lower attenuation coefficient, causing cupping artifacts with low CT number. Metal implants or other materials with high attenuation coefficients can cause streak artifacts due to beam hardening [5]. X-ray beams are often pre-hardened to reduce this effect. Partial volume effects occur when a voxel in the final image contains more than one tissue type. In this case, the measured value is the average of each tissue type. This is also called a blooming artifact because high-valued objects with dimensions smaller than the voxel size expand in the image to fill the entire voxel. Partial volume artifacts occur most often when thick slices are acquired and can be minimized by reconstructing with thinner slices. Ring artifacts



are common in third-generation CT scanners where both the x-ray source and detectors are set on a rotating gantry. This

Figure 2- Right coronary artery with (left) and without (right) motion artifact.

configuration causes each detector to contribute heavily to a circular

region in the final CT image (Figure 1). Therefore, if a detector is miscalibrated, a ring shaped artifact will be present. Ring artifacts are reduced by monitoring detectors for miscalibration and applying algorithms to correct artifacts in the final image. Motion artifacts occur when the subject moves during the scan, causing projections acquired at different times to contain inconsistent data. As seen in Figure 2, motion artifacts are characterized by blurring at the edges of the moving object. Motion artifacts from the lungs are reduced by requiring that the patient holds their breath. This is not possible for cardiac motion, and the image must be taken during the period of lowest motion. In order to obtain optimal image quality, steps must be taken to reduce the effects of each of these artifacts.

2.4 History of CT

CT systems evolved significantly from the first clinical scanner in 1972 to become fast enough to image the entire heart in a single beat [5]. As scanners evolved, the motion and design of x-ray sources and detectors changed. First generation CT scanners used a thin pencil beam of x-rays aimed at one or two detectors. After each recording, the x-ray and detector were incrementally translated across the field of view and the measurement was repeated. The x-ray source and detector were then rotated by 1°, and the process was repeated until 180° of data was obtained. Second generation CT scanners improved data acquisition by sending a narrow fan beam of x-rays at a larger bank of detectors, allowing faster acquisition. Fan beam reconstruction requires projections from 180° plus half of the fan-beam width. Third generation scanners eliminate the translation step entirely. The fan beam was widened to acquire the entire field of view without translation. Both x-ray source and detectors were mounted on a rotating gantry, and data was obtained continuously as the gantry rotated. This rotationonly acquisition greatly reduced acquisition time. Slip-ring systems were employed to eliminate any power and data cables that ran to the gantry. Slip-ring technology allowed the gantry to rotate freely, without cables, while image data were transferred to the stationary data processing computer. Some third generation CT systems contained many detector rows illuminated by a cone beam of x-rays. Cone-beam CT allowed a volume of CT data to be obtained during each rotation. Ring artifacts often occur in third generation CT systems when a detector is not properly calibrated. Fourth generation CT systems

eliminate ring artifacts by using a stationary 360° ring of detectors. The x-ray source is rotated as in a third-generation scanner, but detectors do not move. With this geometry, each detector contributes equally to all spatial locations, eliminating ring artifacts. Due to the increased cost of 360° detector banks and improvement in algorithms for correcting ring artifacts, third generation CT systems are most commonly used today.

The time period over which an image is acquired is called temporal resolution. The temporal resolution of third-generation CT systems are limited by gantry rotation time. Temporal resolution improves with gantry rotation speed because a wider range of projection angles can be acquired over a smaller period of time. CT gantries are heavy, causing centrifugal forces up to 10G. This mechanical limitation on temporal resolution led to the introduction of electron beam CT (EBCT). In EBCT, rotation of the x-ray beam is controlled electronically rather than mechanically, eliminating gantry rotation. An electron beam is swept across an anode, which converts the electrons into a fan beam of x-rays. This approach decreased temporal resolution to 30-50ms. However, EBCT systems have decreased longitudinal resolution due to fewer detector rows and are highly specialized to cardiac applications. These considerations limit the use of EBCT in CCTA examinations [6].

Three dimensional fields of view can be acquired in many ways with a third generation CT scanner. Increasing the number of rows in the detector array increases the number of slices that can be acquired at one time, increasing temporal resolution. The height of the x-ray cone beam also increases with increasing detector rows, which causes cone-beam artifacts due to undersampling in the longitudinal direction. Modern CT scanners can have up to 320 detector rows and use specialized reconstruction algorithms to reduce cone beam artifacts [7]. Initially, thicker sections of anatomy were analyzed in step and shoot mode. In this mode, the x-ray source is rotated around the patient to acquire a slab of data. Next, the patient is translated to position the next slab onto the detector array. This process is repeated until the required anatomy is imaged and the reconstructed slabs of data are stitched together to form a full three dimensional volume. Helical acquisition eliminates the translation and stitching stages in step and shoot mode. The patient is slowly translated while the gantry rotates during the entire acquisition, therefore the source and detector move in a helical trajectory with respect to the subject. Specialized reconstruction algorithms are used to reconstruct a volume of images. The speed of translation relative to the detector slab width is called the pitch.

$$Pitch = \frac{Table Translation per Rotation}{Slice Width * Detector Rows}$$
Eq. 2

A pitch of one acquires 360° of projection data at each slice while a pitch of two acquires only 180° of projection data at each slice. Dual source configurations are often used with helical CT. These systems contain an additional x-ray source and set of detectors in the gantry ring, doubling the amount of data taken per gantry rotation. In a dual source helical acquisition, the pitch can be doubled, halving acquisition time. The effects of pitch, dual sources, and increased detector rows are summarized in Figure 3.



Figure 3: Data acquired by detectors for different configurations are shown in blue/red (a/b) Increasing the detector rows or slice thickness by a factor of 4 causes a proportional decrease in the required number of rotations. (c/d) A pitch of 1 (c) leaves no gaps in the acquired data, but takes twice as many rotations to complete as a pitch of 2 (d). (e/f) With a second source and detector, shown in red, the pitch can be doubled while retaining the same longitudinal coverage.

Some modern CT scanners have wide enough detectors to cover the entire heart without helical acquisition. This allows a full volume of the heart to be acquired in approximately one half rotation of the gantry [7]. The improved temporal resolution offered by these techniques aids in reducing motion when imaging the heart.

2.5 Cardiac Cycle

The left and right atria and ventricles of the heart supply oxygenated blood to the entire body. The atria serve as primers for the ventricles, increasing ventricular filling [8]. The right ventricle pumps deoxygenated blood through the pulmonary artery to the lungs. Oxygenated blood then passes through the left side of the heart where the left ventricle pumps it through the aorta, to the rest of the body. The myocardium on the left side of the heart is much thicker than the right side because the left side must generate more pressure to pump blood to the entire body. Atrio-ventricular (AV) valves separate the atria from the ventricles while semilunar valves separate the left and right ventricles from the aorta and the pulmonary artery, respectively. There are three main coronary arteries that supply blood to the heart. The right coronary artery (RCA) services the right ventricle and posterior left ventricle, running along the right AV groove. The left coronary artery splits into the left anterior descending (LAD) and left circumflex (LCX) arteries. The LAD supplies blood to the anterior left ventricle, running along the left AV groove [3]. Plaque buildup in these arteries is a common cause of CAD. Understanding the movement of these structures is essential to solve the challenges of imaging the heart.

Motion of the heart during the cardiac cycle can be characterized by seven stages of atrial and ventricular systole and diastole. Ventricular systole begins with a stage of isovolumic contraction where pressure in the ventricles builds up. The semilunar valves will then open during ventricular ejection, which causes blood to flow out of the ventricles through the semilunar valves. Most of the blood is expelled during the first third of ventricular ejection, which is called the period of rapid ejection. A longer period of reduced or absent ejection follows [9]. Ventricular diastole begins with isovolumic relaxation. In this stage, the ventricles relax, reducing pressure. This causes the semilunar valves to close and the AV valves to open. Once the AV valves open, there is a period of rapid filling of the ventricles. Diastasis, a period of reduced or absent ventricular filling, follows. The cycle completes with a period of atrial contraction. A summary of these stages are shown below in Figure 4.



Figure 4- The cardiac cycle is split into three stages of systole and four stages of diastole. Systole consists of isovolumic contraction (IVC), maximum ventricular ejection (ME), and reduced ventricular ejection (RE). Diastole consists of isovolumic relaxation (IVR), rapid ventricular filling (RF), diastasis (D), and atrial systole (AS). The duration of each of these stages depends on heart rate.

The duration of each cardiac stage changes nonlinearly with heart rate. As heart rate increases from 50bpm to 90bpm, the duration of diastole will decrease by 11.2ms/bpm while the duration of systole will decrease by just 0.21ms/bpm [10]. Therefore, variation in patient heart rate reduces the periodicity of the cardiac cycle. The relative durations of each cardiac stage also vary between patients [3]. These factors make it challenging to consistently locate a cardiac stage from the ECG signal.

2.6 Coronary Motion

Coronary artery motion has a detrimental effect on the image quality of cardiac CT exams. Many studies have investigated the movement of different sections of the coronary arteries during the cardiac cycle. The RCA and LCX have higher average velocities due to their location on the AV groove [3]. There are typically two periods of low motion for all vessels: end-systole and mid-diastole [3], [11]. The period of low motion during mid-diastole occurs during diastasis, when the ventricles are slowly filling. The length of diastasis is highly dependent on heart rate [12]. The period of low motion during end-systole consists of the period of reduced ventricular ejection and isovolumic relaxation [10]. Since the duration of systole is less dependent on heart rate, the end-systolic period of low motion is typically longer than diastasis for high heart rates. Motion causes artifacts in CT imaging. Therefore, scans should be taken during quiescent stages of the cardiac cycle for the best image quality.

2.7 Cardiac Gating

Cardiac gating is used to reduce patient dose and improve temporal resolution of CT images of the heart. An ECG is taken during acquisition to determine the stage of the cardiac cycle at all times during the scan. Prospective cardiac gating is primarily used to reduce patient dose while retrospective cardiac gating improves image quality by improving temporal resolution.

2.7.1 Prospective Gating

Prospective gating reduces dose by turning the x-ray tube current down or off during high motion stages of the cardiac cycle. Early implementations of prospective gating reduced tube current by ~80% during periods of high motion. More recent implementations turn the x-ray tube off entirely between heartbeats, reducing dose by up to 83% [13]. Prospective gating can be applied to both step and shoot and helical acquisitions, but greater dose reduction occurs in step and shoot mode [14]. Past ECG information must be used to predict periods of high motion. Typically, tube current is turned on during end-systole and/or mid-diastole. The exact timing of these cardiac states is predicted based on heart rate, ECG data, and a priori knowledge about the cardiac cycle. Arrhythmias and heart rate variability can cause errors in these predictions. Also, at heart rates >90 bpm, the timing of low motion cardiac states is extremely variable. Because of these factors, prospective gating is paired with retrospective gating to acquire a volume with minimal motion artifacts.

2.7.2 Retrospective Gating

Retrospective gating trades off dose for image quality. Additional projections are acquired for each slice, so that the volume can be reconstructed at different states of the cardiac cycle. Consider a CT system with fan angle, φ , and rotation time τ operating in step and shoot mode. Projections from each slab of data are acquired for the entire cardiac cycle. Only projections from $180+\frac{1}{2}\varphi^{\circ}$ are required for reconstruction, producing a temporal resolution of $(\frac{1}{2}+\frac{1}{720}\varphi)\tau$. Reconstruction can occur from any contiguous set of projections over this time span. The set of projections chosen for reconstruction is called the reconstruction window. The center of a reconstruction window is often chosen based on a percentage of the R-R interval (Figure 5). Each slab is reconstructed using the same window to produce a full cardiac volume. Volumes can be reconstructed at multiple time points, often called phases, and compared either manually or automatically. Only the volume with the best image quality is used for patient assessment. The same concept can be applied to helical acquisitions with reduced pitch. For heart rates greater than 75bpm, the limited temporal resolution of the scanners may not be sufficient to image the heart without motion artifact [6]. Segmented adaptive scanning can be used to improve temporal resolution.



Figure 5- Cardiac scan with prospective and retrospective gating applied. Prospective gating turns on the tube current only for low motion end-systolic and mid-diastolic periods (grey line). Using retrospective gating, slices can be reconstructed from any contiguous set of projections (blue boxes). The center of the retrospective gating window is chosen as a percentage of the R-R interval.

Segmented adaptive scanning uses data from multiple heartbeats to reconstruct each slab (step and shoot) or slice (helical). Consider a step and shoot mode acquisition where projections are taken for n consecutive heartbeats in each slab. Dose is increased by a factor of n. Ideally, temporal resolution is reduced by a factor of n because more projection data is available. However, if the gantry rotation is synchronized with heart rate, the same projection angles will be acquired during each reconstruction window. Therefore, the gantry rotation speed must be adjusted to ensure that each heartbeat acquires a different set of projection angles for each reconstruction window [6]. For helical acquisition, the pitch must be decreased to as low as 0.3 for segmented adaptive scanning. Because of the low pitch, it can be difficult to complete a full cardiac examination within a single breath hold. Segmented adaptive scanning relies on accurate reconstruction windows.

There are many ways to retrospectively select a reconstruction window for multiple heartbeats. Ideally, the center of the reconstruction window, also called the phase, will occur during the same cardiac state for each heartbeat. This can be challenging because of heart rate variability. The center of the reconstruction window is typically chosen as either a percentage of the R-R interval or a fixed delay after the QRS complex. The percentage-based approach assumes that the duration of each stage of the cardiac cycle is proportional to the R-R interval. However, the length of diastasis tends to show a much higher variability with heart rate. This can produce up to a 180ms error if heart rate variability is ± 8 bpm [15]. Estimating cardiac state as a fixed delay from the QRS complex assumes that all stages of the cardiac cycle have constant duration besides diastasis and atrial systole. Neither of these approaches accounts for the nonlinear changes in cardiac state duration. Vembar proposed a delay algorithm that combines the R-R percentage and fixed delay approaches, but it is not implemented clinically [3]. Because of difficulty in identifying a consistent cardiac state, heart rate variability can have a significant impact on image quality in multi-beat acquisitions.

2.7.3 Effects of Aperiodic Heart Motion

Cardiac gating for multi-beat exams relies on the assumption that heart motion is periodic. Violations of this assumption can have a considerable impact on image quality.

The heart center varies slightly from beat to beat. Also, heart rate variability can cause changes in the cardiac state across multiple beats. Both of these factors cause inconsistencies in the data. In segmented adaptive scanning, data from multiple heartbeats are used to reconstruct a single image slice. If data from different heartbeats contain misregistered locations of cardiac structures, the image is blurred. In all gated multi-beat acquisitions, slabs of data from different heartbeats are collected and stitched together.



Figure 6- Discontinuities occur along the right coronary artery at slab boundaries due to aperiodic heart motion.

Discontinuities can occur in cardiac structures at slab boundaries (Figure 6). Reducing the number of heartbeats and choosing an accurate reconstruction window are important factors in cardiac CT image quality.

2.8 Coronary CT Angiography

Coronary CT angiography (CCTA) is a common application of cardiac CT used to visualize the coronary arteries. CCTA is used to screen for CAD because of its high negative predictive value (97%-100%) for coronary stenoses [2]. X-ray angiography is the gold standard for coronary artery imaging, but is invasive, expensive, and poses additional risk for the patient. CCTA exams require fast temporal resolution and fine spatial resolution to visualize the coronaries without motion artifact. As heart rate increases, the duration of the low motion cardiac state decreases. This requires faster temporal resolution. For this reason, many studies have found an inverse correlation between heart rate and CCTA image quality[16], [17]. Patients with high heart rates are given beta blockers to reduce heart rate before scanning. Heart rate variability also reduces image quality in multi-beat acquisitions due artifacts from gating [18]. To overcome these challenges, specialized cardiac CT systems are optimized to have fast temporal resolution while maintaining high spatial resolution.

Some modern CT systems are able to image the heart within a single beat. These systems avoid the challenges of heart rate variability and aperiodic heart motion. Prospective and retrospective gating are both used. Prospective gating selects a wide window of data around either end-systole (>85 bpm), mid-diastole (<65 bpm), or both (65-85 bpm). Retrospective gating reconstructs cardiac volumes at several phases of the cardiac cycle, and the best phase is chosen either manually or with an automated algorithm. This process produces the best image quality with the lowest dose.

2.9 Retrospective Best Phase Selection

Several approaches are currently used to automatically detect the best phase of the cardiac cycle for CCTA reconstruction. Each approach quantifies a metric of cardiac motion and chooses the time of minimal motion as the best phase for reconstruction. The kymogram approach calculates the motion of the center-of-mass of the heart from raw projection data, replacing the ECG as a synchronization signal [19]. The volume is reconstructed from time points with the lowest center-of-mass motion. Since this approach does not require image reconstruction at multiple phases, it is computationally



Figure 7- Consecutive phases only differ by a few projections. With ~180° reconstruction, these projections are approximately parallel. Motion parallel to the projections cannot be detected by the difference between the images.

efficient. However, a large difference (12.5%) is seen between manually and automatically chosen reconstruction phases [20]. Another approach uses the difference between low-resolution heart volumes at consecutive phases to estimate the motion of the heart [21]. When the heart is stationary, consecutive phases will have similar values, resulting in small values in the difference volume. Because consecutive phases only differ by a few projections of data, motion parallel to these projections will not be

detected (Figure 7). This causes the metric of heart motion to be coupled with motion direction. The image quality of the coronary arteries has also been estimated and optimized for motion correction based on entropy and positivity [22]. This requires reconstruction and coronary segmentation at all possible phases, which may be time consuming. The best phase for reconstruction can also be estimated based on the patient's heart rate. A model of the cardiac cycle can be used to determine the phase corresponding to end-systole or mid-diastole. However, there is a high patient variability in the exact location of these states, which may result in the reconstruction of suboptimal images [4]. Because of the limitations of current approaches, it is still common for a radiologist to review volumes from multiple phases and manually choose volume with the best image quality. A fully automated algorithm is needed that identifies the phase of the cardiac cycle with the best image quality for CCTA examinations.

3 ALGORITHM DESIGN

The proposed algorithm considers two types of vessels: through-plane vessels and in-plane vessels. Through-plane vessels travel longitudinally through each axial slice of the heart, while in-plane vessels travel along the transverse plane within an axial slice. The best phase is found by calculating the image quality of through-plane vessels directly and pairing this with a binary metric that determines if image quality of in-plane vessels is acceptable. This avoids the dependency on motion direction seen in the phase difference approach. The automatic phase detection algorithm consists of two independently-calculated metrics that quantify image quality (IQ): through-plane vessel IQ and in-plane vessel IQ. These metrics are evaluated jointly to select the best phase for CCTA reconstruction.

3.1 Through-Plane Metric

3.1.1 Overview

The through-plane metric quantifies IQ for vessels travelling longitudinally through the volume. Circular cross-sections of the vessel will be visible in axial images. Blurring caused by motion artifacts makes vessels appear less circular with softer edges. Because

of this, the through-plane metric is based on the circularity and edge strength of the vessels.

A summary of the steps used to calculate the through-plane score is shown in Figure 8. CT images reconstructed from all phases of interest at select slices from the CT exam are input to the through-plane metric. In each input image, through-plane IQ is calculated for the RCA, LAD, and LCX. Next, slices that don't contain through-plane vessels are excluded. Through-plane IQ scores from slices that contain through-plane vessels are combined to determine a score for the right and left vessels at each phase. The right and left scores are then combined to calculate an overall through-plane score for each phase. The steps are described in detail in the sections below.



Figure 8- Overview of the steps to calculate image quality in through-plane vessels at each cardiac phase in a CCTA exam

3.1.2 Step 1: Segment cardiac region

The proposed algorithm does not require a full 3D dataset. Therefore, standard 3D cardiac segmentation algorithms cannot be used. A 2D segmentation algorithm for axial slices of the heart was developed and is described in detail in Appendix 1. The segmentation algorithm takes a single axial slice as input and locates the cardiac region based on the contour between the heart and lungs.
3.1.3 Step 2: Quantify Through-Plane IQ metric for each image

3.1.3.1 <u>Threshold calculation</u>

Once per slice, three thresholds are calculated: a soft tissue threshold, a contrast threshold, and a maximum value threshold. The soft tissue and contrast thresholds will be used to create the chamber removal mask while the maximum value threshold is used in the gamma transform. The soft tissue threshold is the approximate value of the background tissue in the heart. The contrast threshold is the approximate value in the chambers of the heart. The maximum value threshold is the largest value in the image that does not include contrast pooling or calcification. Each threshold is calculated using the segmented image histogram divided into bins with a width of 30 HU. The soft tissue threshold is the first peak in the segmented image histogram. The contrast threshold. The maximum value threshold is the highest histogram bin that contains at least 0.05% of the total image points. An example of each of these thresholds can be seen in Figure 9. Figure 10 shows the consistency of the soft tissue, contrast, and maximum value thresholds across exams.



Figure 9- (a) Original image (b) Image histogram with soft tissue, contrast, and maximum value thresholds marked in black, red, and green respectively.



Figure 10- Histogram of median values for each of the three threshold in each exam

3.1.3.2 Gamma transform

The gamma transform attenuates very high values in the image that can overpower the results of gradient and filtering operations used to calculate the edge strength score. A gamma transform is performed on each image. High values are often due to calcification or contrast swirling and will be greater than the maximum value threshold. A gamma

transform is performed on values above the maximum value threshold (MVT) to mitigate this effect.

$$\begin{cases} MVT + (x - MVT)^{\gamma} & \text{if } x > MVT \\ x & otherwise \end{cases}$$
 Eq. 3

Lower γ values give more sudden thresholds, removing gradient information above the MVT, but better rejecting high values in the image. Values ranging from 0.5-0.8 provide similar results. In the current algorithm implementation $\gamma = 0.7$.

3.1.3.3 <u>Top hat transform</u>

The top hat transform focuses on small, high-valued regions in the image by identifying and removing large, constant-valued structures with a grayscale opening operation. This step of removing large structures helps to identify vessels. The top hat transform, T(f), is applied to the image, f, with structuring element s where • denotes the grayscale opening of the image.

$$T(f) = f - (f \circ s)$$
Eq. 4

Grayscale opening operations consist of consecutive erosion and dilation operators, where erosion chooses the minimum value in the region defined by the structuring element and dilation chooses the maximum value. By subtracting the opened image from the original image, the top hat transform will include only high-valued details that are smaller than the structuring element.

In the proposed algorithm, the top hat transform is performed on each un-segmented, gamma transformed image, because segmentation can partially remove large structures, making them appear to be small structures during the top hat transform. A circular structuring element was chosen that was large enough to completely remove throughplane vessels during the erosion operation. Therefore, the radius was larger than the vessel radius including blurring due to motion and the point spread function in the CT. Based on a vessel radius of ~5mm [23] and a spread of ~5mm, a radius of 10mm was chosen for the structuring element. This means that structures larger than 20mm in every dimension were removed. The image was resized to 128x128 for this operation then scaled back to 512x512 using bicubic interpolation for computational efficiency. An example of the top hat transform calculation is shown in Figure 11.



Figure 11- Steps to image top hat transform (a) Original image (b) Segmented grayscale morphological open (c) Segmented top hat transform

3.1.3.4 Chamber removal mask

In the next step of the algorithm, a chamber removal mask is created to de-emphasize the chambers of the heart as well as any contrast swirling from each image. This helps focus on through-plane vessels. As mentioned previously, the morphological open of the image

will include large structures, making it a good indicator of heart chamber location. The first step in generating the chamber removal mask is to transform the values of the morphologically opened image that is generated during the top hat transform. (Figure 11b). The values are scaled so that the range from the soft tissue threshold to contrast threshold in the open image is mapped to a range from one to zero (Figure 12c).

Contrast swirling can cause inconsistent values in the chamber that may appear as small structures during the opening operation. This is why the edges of the right atrium are still present in the mask in Figure 12c. To account for this, any values connected to a chamber that are greater than the maximum value threshold are marked as regions of contrast swirling. Regions of contrast swirling are dilated and given a value of zero in the mask (Figure 12d). The initial mask is smoothed with a 5mm x 5mm averaging kernel to assure that the edges of the chambers are removed. The resulting mask has zeros in areas representing heart chambers and ones in areas where the background is soft tissue.



Figure 12- Steps in chamber removal mask creation (a) Original image (b) Grayscale morphological open (c) Initial mask created from the open (d) Points marked as contrast swirling and removed in the final mask (e) Final chamber removal mask

3.1.3.5 Edge strength score

The edge strength score is used along with a circularity score to calculate through-plane IQ for each through-plane vessel in each image. The edge strength score is also used by the algorithm to identify regions that could be through-plane vessels. The top hat image, chamber removal mask, and a match filter are used to calculate the edge-strength score, as illustrated in Figure 13. In the first step of the edge-strength score calculation, the gradient of the top hat transform is calculated using a Sobel filter and then multiplied by the chamber removal mask (Figure 13c). The chamber removal mask is applied after the gradient because, otherwise, strong gradients would occur at the edges of the heart and heart chambers. Next, a match filter is applied that has a maximum response to circular

disks in the gradient image (Figure 14). The match filter is radially symmetric with a positive response to values within a 4mm radius of the center (Figure 14). The maximum response is at the expected vessel radius of 0.75mm-1.5mm. Gradients outside this range are likely due to blurring and therefore elicit a weaker response. The negative lobe of the filter at radii of 4mm-7mm reduces the response from structures that are larger than 8mm in any direction. The convolution of the match filter with the top hat image gradient gives the edge strength score at each point in the image.



Figure 13- Steps in edge score calculation (a) Original image (b) Top hat transform (c) Top hat transform gradient multiplied by the chamber removal mask (d) Final edge score after applying a match filter



Figure 14- (a) Match filter (b) Match filter value based on distance from the center of the filter

3.1.3.6 Candidate point selection

In this step, candidate points are identified in the edge-strength score image. Pixels with the highest edge strength scores are likely to be vessels. However, the edge strength score will give a high response to any structure whose longest dimension is less than 8mm, even if it is not circular. Therefore, candidate points from each side of the heart with high edge strength scores are analyzed further to determine their circularity. For each image, a binary mask is created with pixels within the segmented cardiac region set equal to one. The centroid of the binary mask is considered as the center point that defines three regions of the heart (Figure 15c): the right side contains the RCA, the left anterior quadrant contains the LAD, and the left posterior quadrant contains the LCX. Pixels that are greater than each of their eight neighbors are found in the edge strength image and identified as regional maxima. The three highest valued regional maxima in each of the three regions are chosen as candidate vessel center points (Figure 15d). If less than three points are chosen, processing time will decrease, however the algorithm will be less likely to correctly identify the vessel.



Figure 15- Candidate point selection (a) Original image (b) Edge strength score (c) Regions of the heart separated with the centroid (d) Nine candidate points in the top hat image

3.1.3.7 Circularity score at candidate points

The circularity score is a measure of compactness calculated for each candidate point, as illustrated in Figure 16. In [24] a measure of compactness is proposed for a binary image (Eq. 5) where a value of one is the most compact and higher values are less compact.

$$Compactness = \frac{Perimeter_d^2}{4\pi Area_d}$$
 Eq. 5

A square 27mm x 27mm ROI around each candidate point in the top hat image is considered (Figure 16b/d). First, the center of the vessel is identified as the largest value in a 2mm radius of the candidate point. Next, the ROI is thresholded into four levels based on a percentage of the vessel center value: >50%, >40%, >30%, and >20%. A value of 50% was chosen so that, in calcified vessels, the highest thresholded image will contain the entire vessel region. If a higher threshold was chosen, only calcified regions would be selected. As the threshold is decreased, a larger portion of the vessel edges and any blurring due to motion is included. Therefore, these four images show the shape of the vessel and the magnitude of motion artifact. Fewer thresholds could be used to improve processing time, but there will be more uncertainty in the magnitude of the motion artifacts. This uncertainty will lead to a less accurate circularity metric. For each level, regions above the threshold are labeled with a connected-components algorithm using 4-connectivity, and the region that contains the center of the vessel is selected. The compactness of each of these four binary regions is calculated (Eq. 5) and compiled into a measure of circularity (Eq. 6).

$$Circularity = \frac{1}{\sum_{d=2}^{5} d} \sum_{d=2}^{5} d * [2 - max(Compactness_d, 2)]$$
Eq. 6

Compactness_d refers to the compactness of the selected region when the ROI is thresholded at d*10% of the center vessel value. Values greater than two for the compactness are extremely poor circles that should not be considered. Therefore, compactness values are transformed so that the original range of one to two corresponds to zero to one. An increased weight is placed on higher thresholds because distortion seen at lower thresholds is lower in magnitude and, therefore, should have a lower effect on the circularity metric. The final circularity metric varies from zero (non-circular) to one (exactly circular).



Figure 16- Examples of circularity scoring (a) Original image with two candidate points circled (b) ROI in the top hat image near the LAD (c) Threshold decomposition of the LAD region with circularity score of 0.518 (d) ROI in the top hat image near the LCX (e) Threshold decomposition of the LCX region with circularity score of 0.772

3.1.3.8 IQ quantification based on edge strength and circularity scores

After edge and circularity scores are calculated, they are multiplied together for each candidate point to determine the final through-plane IQ metric. Multiplication is chosen instead of addition to select regions where both edge strength and circularity are high. This approach prevents noncircular regions with strong edges from having high throughplane IQ metrics. The candidate point from each vessel region (Figure 15c) with the highest through-plane IQ score is chosen to represent through-plane IQ for the vessel. The through-plane IQ calculation is executed for a particular slice at all phases. At this point in the algorithm, through-plane IQ for all input phases across a slice can be compared for each vessel, as seen in Figure 17.





Figure 17- IQ for each vessel is shown as well as images from various phases in the slice. The local maxima in the plots match high IQ phases for the RCA, LAD, and LCX.

3.1.4 Step 3: Select slices with through-plane vessels

In order to compare phases across the heart volume, the through-plane IQ metrics must be aggregated across relevant slices. This step of the algorithm locates slices that contain through-plane vessels. This will allow slices without through-plane vessels to be ignored in the aggregate through-plane IQ calculation for each phase. The locations with high through-plane IQ for the RCA, LAD, and LCX at each slice and phase (as output by the previous step) are used to locate the relevant slices by creating vessel maps as described in the following sections.

3.1.4.1 Vessel map creation

Vessel maps are created at each phase to identify the location of the RCA, LAD, and LCX. Consider a perfectly through-plane vessel for a single phase. In slices that contain the vessel, high through-plane IQ points will be in the exact same location in the axial plane. In all other slices, high through-plane IQ points will be at random locations because the IQ score is based on noise. Therefore, through-plane vessels can be identified by a set of slices with high IQ points at the same axial location. In reality, the axial location is allowed to vary so that the vessel is travelling at less than a 45° angle from the z-axis. Vessel maps are found by recursively searching for points with similar axial locations. Each vessel point from slices within 50mm of the center of scan in the z-direction is used as a starting point for this recursion. The recursion stops when two slices in a row cannot find a nearby point (Figure 18). Once this is repeated for all starting points, a list of potential vessels is available for a particular phase. Any potential vessels that span less than 10mm in the z-direction are discarded. This process is repeated for all vessels at all phases.



Figure 18- This example shows how the recursive algorithm searches for vessels in a single direction. The starting location is in the upper right image. Green lines indicate a vessel was found within the search range, while red lines indicate that it was not. When no vessel is found, the search continues for one additional slice to make sure the vessel does not pick up again. Note: the recursive algorithm is looking through the potential vessel points, not the original images.

3.1.4.2 Slice selection

Vessel maps can be used to determine which slices contain each through-plane vessel. The number of phases that found each vessel (RCA, LAD, LCX) at each slice are determined based on the vessel maps (Figure 19). High values indicate that many different phases found a through-plane vessel in that slice. Ideally, all phases will find the through-plane vessels at the exact same slices. This would result in a rectangular function in Figure 19. However, poor image quality at some phases causes deviations from a rectangle. All slices with a value over 25% of the maximum for each vessel are considered to have through-plane vessels.



Figure 19- The number of through-plane vessels found for each slice are shown. In the central region of the heart, the most through-plane vessels are found for both the right and the left side. The RCA would include slices 21-49, the LAD would include slices 18-39, and the LCX would include slices 23-47.

3.1.5 Step 4: Choose best phase

This step calculates an aggregate through-plane IQ score for each phase. At this point in the algorithm, through-plane IQ has been calculated for each cardiac phase in all slices. The slices that contain through-plane vessels for each vessel have been identified. Next, the through-plane IQ values (Figure 17) are summed across all slices that contain through-plane vessels. This results in an aggregate vessel IQ score for each phase for the RCA, LAD, and LCX. The scores for the LAD and LCX are added to give an overall left side score. The best phase for each side is the phase with the largest IQ score on that side (Figure 20). The results from the right and left sides are normalized by their mean and summed to find the overall IQ. The phase with the highest through-plane IQ metrics is the candidate best phase.









Figure 20- Overall IQ scores for each phase on the right and left sides of the heart. The best phase for the right vessels is 79%, the best phase for the left vessels is 67%, and the best overall phase is 79%. The bottom images show sagittal cross-sections of the RCA at 67% and 79%. IQ is similar for the RCA at both phases.

3.2 In-Plane Metric

3.2.1 Overview

While the through-plane algorithm can assume a circular region with a single point per slice, the in-plane vessels may have varying sizes and shapes, including

bifurcations. Due to the unknown vessel shape, the in-plane metric is expected to be less robust than the through-plane metric. Therefore, the objective of the in-plane metric is to determine if the proximal left and right in-plane vessels are acceptable for the candidate best phase. The shape of the vessels varies considerably due to branches and turns. Blurring due to motion will cause the edges of these vessels to be softer. Each slice from the superior half of the scan is required to ensure that the in-plane vessels are present for all phases and to enable 3D image

processing. Regions that contain in-plane vessels are identified in all phases, and a gradient-based IQ metric, similar to the edge score metric for the



Figure 21- Overview of the steps to determine if image quality is acceptable for right and left proximal in-plane vessels at a candidate cardiac phase.

through-plane algorithm, is calculated. This metric is compared across phases to determine a binary score of 'Acceptable' or 'Unacceptable' for both the right and left vessels. A logical AND of the right and left vessel results gives the final determination of whether the in-plane vessels are 'Acceptable' at a given phase. A summary of the steps to calculate the in-plane score is shown in Figure 21.

3.2.2 Step1: Segment heart

Proximal in-plane vessels originate in the aorta and curve longitudinally as they near the edge of the heart. Therefore, only through-plane vessels will be present near the edge of the heart. To account for this, using the output of the cardiac segmentation in Appendix 1, all pixels within 6mm of the edge of the heart are removed. This process is carried out in 2D for each axial slice at each phase. This step produces a mask that can be applied to limit the ROI to the heart.

3.2.3 Step 2: Calculate thresholds

Thresholds are calculated in the same manner as for the through-plane metric (Section 3.1.3.1). However, the histogram is created using volume data instead of slice data. The outputs of this step are a soft tissue threshold, a contrast threshold, and a maximum value threshold.

3.2.4 Step 3: Accentuate vessels

The goal of this step is to process the CT data to provide better contrast between the coronary arteries and other tissue. A top hat transform and chamber removal mask, similar to those used in the through-plane metric, are applied as described in the following sections. This produces a volume of images for each phase that highlights small, high-valued regions and a mask that can be used to remove heart chamber locations.

3.2.4.1 <u>3D top hat transform</u>

A three dimensional top hat transform is applied. The structuring element is spherical with radius based on the average radius of the proximal coronaries, blurring due to motion, and the point spread function of the CT system. The proximal left has a diameter of 4.5 ± 0.5 mm, while the proximal RCA has a diameter of 3.9 ± 0.6 mm [23]. Allowing for a spread of ~5mm, a radius of 10mm is chosen for the structuring element. This means that structures larger than 20mm in every dimension will be removed. A 3D transform is advantageous because structures that span many slices but are small in the axial plane would be retained with a 2D transform.

3.2.4.2 Chamber removal mask

The chamber removal mask is a multiplicative mask ranging from 0-1 that will remove heart chambers. This mask is calculated for each axial slice as previously explained for the through-plane metric (Section 3.1.3.4). However, the method to remove contrast swirling is not implemented because it may also remove in-plane vessels connecting to the aorta.

3.2.5 Step 4: Calculate in-plane IQ per voxel

A measure of in-plane IQ based on the gradient magnitude of each top hat image from Step 3 is calculated. This metric is similar to the edge strength score from the through-plane metric without the circularity assumption. A summary is shown in Figure 22. This step produces a measure of in-plane vessel IQ at each voxel.

3.2.5.1 Top hat gradient

The 2D gradient of each axial slice from Step 3 is calculated using a Sobel filter. A 2D gradient is used instead of a 3D gradient because thick slices can cause inaccurate gradient measurements in the slice direction. The gradient is then multiplied by the chamber removal mask to ignore heart chambers. A 2D match filter is applied to each top hat gradient image. The match filter is similar in design to the filter used in the through-plane metric with the negative lobes removed. This is because the negative lobes reduce output from non-circular regions. The positive lobe is approximately 4.5mm wide to encompass the entire vessel radius. Gradients 1.5-2.5mm from the vessel center produce the strongest response because this is the expected vessel radius. This filter produces high values in the center of vessels with strong gradients.



Figure 22- Steps in in-plane voxel IQ calculation (a) Original image (b) Segmented top hat transform (c) Top hat transform gradient multiplied by the chamber removal mask (d) Final edge score after applying a match filter



Figure 23- (a) Match filter (b) Match filter value based on distance from the center of the filter in millimeters

3.2.6 Step 5: Limit to in-plane vessel MIP

A maximum intensity projection (MIP) of in-plane IQ scores is calculated with a projection straight down the longitudinal axis using only regions near in-plane vessels. Since vessels are in-plane, they should not travel underneath one another. If this were to happen, taking a MIP at this projection angle would cause information about the weaker overlapping vessel to be lost. Because vessels do not overlap, calculating the MIP reduces the dimensionality of the data to 2D without signal loss.

3.2.6.1 Select slices

Selecting a small range of slices for MIP calculation reduces noise in the image and makes identification of in-plane vessels easier. The slices of interest vary between the right and left side, therefore a separate MIP is created for each. The heart center is determined in the same manner as it was in the through-plane metric (Section 3.1.3.6). Since the proximal RCA originates from the anterior aorta, only points anterior to the heart center are considered for the right side.

Slices that contain in-plane vessels will have many locations with high in-plane IQ scores. Low in-plane IQ scores are removed by automatic thresholding using Otsu's method (Figure 24c). MIPs are calculated for the right and left sides from every possible slab of five contiguous slices (12.5 mm) for each phase (Figure 24d). A 12.5 mm slab is sufficiently thick to contain in-plane vessels at all selected phases. This slab thickness must account for slight deviations from in-plane as well as longitudinal movement of the vessels across phases. In-plane IQ scores are summed within each MIP and across all phases (Figure 24e). This produces one score for each of the left and right sides and for each slab. The slabs containing the in-plane vessels will have many locations with high scores. Therefore, the slabs containing the in-plane vessels are identified as the slabs with the highest in-plane IQ scores.

3.2.6.2 Locate in-plane vessel regions

Next, a mask is identified that contains the in-plane vessels in all MIPs.

Since a small range of phases (~16% of the cardiac cycle) is being used, the vessels will be in a similar location for all phases. Therefore, a single common mask is identified for the in-plane vessels for each side of the heart that will be used in all phases. A connected components algorithm with 8-connectivity is applied to locations where the thresholded MIP summed across all phases (Figure 24e) is greater than zero. The largest region, circled in green in Figure 24f, is selected as the location for the proximal in-plane RCA for all phases. Next, the size of the vessel is estimated for each phase. The number of pixels that are greater than zero in the thresholded MIP for each phase (Figure 24d) logically ANDed with the estimated vessel location (Figure 24f) is the size of the vessel at that phase. The average value across all phases is the estimated vessel size.



Figure 24- (a) Original image near proximal in-plane RCA (b) IQ score limited to the anterior right quadrant (c) Thresholded IQ score (d) MIP of thresholded IQ scores for the given phase across five slices (12.5mm) surrounding the slice from (a) (e) Sum of MIPs at all phases for this set of slices. The sum of this image is calculated for each set of slices to determine which slices contain the in-plane vessels. (f) The region identified as the location for proximal right in-plane vessels for all phases. If multiple regions are present, the largest one would be selected.

3.2.7 Step 6: Calculate in-plane phase IQ

The previous step provides slice locations, transverse locations, and the approximate size of in-plane vessels. To calculate in-plane phase IQ at each phase, MIPs are calculated for each phase using the given slice locations and the voxel IQ scores without applying Otsu's thresholding method. MIPs are limited to the identified transverse locations. The average score in each MIP from the top n highest valued points is the final in-plane phase IQ score where n is the estimated vessel size. This is repeated for each phase and each side of the heart. A summary of these steps is shown in Figure 25 and the resulting scores are shown in Figure 26.



Figure 25- (a) Original image near proximal in-plane RCA (b) Unthresholded MIP for the given phase across five slice (12.5mm) surrounding the slice from (a) (c) Unthresholded MIP limited to proximal RCA region from Figure 24f (d) Top points selected to limit to the estimated vessel size

3.2.8 Step 7: Convert in-plane phase IQ metric to binary

Since the in-plane phase IQ metric is less reliable than the through-plane metric (due to the non-circular vessel shape), it is converted to a binary metric of acceptable / unacceptable to check if in-plane phase IQ is acceptable for a given phase. This is done by comparing the candidate phase score to the scores at nearby phases, therefore the acceptability threshold is a relative metric. An absolute in-plane IQ score threshold cannot be used because the magnitude of the score depends on image contrast, including the presence of calcifications. Using more nearby phases gives a more accurate binary metric but increases processing time. If vessels are not found in most phases for a particular side of the heart, the in-plane score is considered unreliable. In this case, the IQ of in-plane vessels is unknown for this side of the heart and all phases are considered to have 'Acceptable' results. Otherwise, IQ scores are normalized by the mean and an adjustable acceptability threshold, typically ~0.90, is applied to each side. This determines if the results are acceptable at each phase separately for the right and left side. A logical AND is used to combine the binary metrics from the right and left sides, identifying phases where both sides contain vessels that are 'Acceptable'. An example of in-plane scores and their conversion to a binary metric is shown in Figure 26.





Figure 26- The in-plane score (top) and binary metric (bottom) are shown for the proximal right and left inplane vessels. The candidate phase was 40% and, since only 8 phases were available for the entire exam, they were all investigated. As seen in the axial slices, 34% is a poor phase for the right side and 48% is a poor phase for the left side. Both of these phases are identified as 'Unacceptable' by the binary in-plane metric. The candidate phase of 40% is accepted.

3.3 Combining Through-plane and in-plane metrics

A flow chart of how the through-plane and in-plane metrics work together is provided in Figure 27. The through-plane metric is calculated for all phases. The best through-plane phase is chosen as a candidate best phase. The binary in-plane metric is calculated for the candidate best phase and the six nearest phases to ensure that in-plane IQ is acceptable. Since the volume was reconstructed every 2% of the cardiac cycle, this covers a range of 14% of the cardiac cycle. If in-plane IQ is not acceptable, the next best through-plane phase is considered. Typically, the phase with the best through-plane score that has acceptable in-plane IQ is chosen as the best phase.



Figure 27- Flow chart of the algorithm for choosing the best cardiac phase for CCTA reconstruction. The through-plane algorithm picks potential phases which are checked to ensure that the in-plane vessel image quality is acceptable.

In the unusual case where the next best through-plane score is below 75% of the maximum score and no phase has yielded acceptable in-plane vessels, the acceptability threshold of in-plane metric is decreased. The in-plane check is repeated, restarting with the best through-plane phase. Calculations will continue in this manner until a phase is found with a high through-plane score and acceptable in-plane vessels.

4 ALGORITHM EVALUATION

The proposed algorithm was implemented in MATLAB and evaluated using fourteen previously acquired, anonymized, single-beat datasets provided by GE Healthcare. Each exam was acquired using the GE Revolution CT system. Six cases contained only diastolic phases, one case contained only systolic phases, and the remaining seven cases contained both systolic and diastolic phases. A 200x200x160mm CT volume was reconstructed with slice thickness of 2.5mm and matrix size 512x512 for phases at intervals of 2% of the R-R interval. Heart rates ranged from 60bpm to 79bpm with an average of 70±6.8bpm.

Two studies were conducted to evaluate the accuracy of the proposed algorithm. Since coronary image quality in the clinical setting is evaluated qualitatively, observers were used to provide a gold standard metric. The observer best phase study evaluated the phase difference between observers and the algorithm. The observer IQ study evaluated image quality of both observer and algorithm selected best phases.

4.1 Observer Best Phase Study

The observer best phase study evaluated the agreement in best phase between the algorithm and observers. The agreement between algorithm and observer was compared to the inter-observer agreement to determine if the algorithm can be considered as

effective as an observer. A consensus observer best phase was also identified by the observers, who were blinded to the algorithm best phase, and compared to the algorithm best phase.

4.1.1 Methods

Three observers identified the best systolic and diastolic phases for CCTA reconstruction for each dataset. Next, the three observers worked together to identify a consensus best phase for each exam. Individual reader best phases were analyzed using two pairwise statistics that compared reader-algorithm (RA) and reader-reader (RR) agreement: mean absolute difference (MAD) and concordance correlation coefficient (CCC). The MAD is the absolute value of the difference in phase. The CCC is a modified version of the Pearson correlation coefficient that fixes the best fit line at 45° from the origin. If the results of different measurement techniques are plotted on each axis, the metric will represent the reproducibility between techniques. In this study, each measurement technique was either an individual reader or the algorithm. The CCC is a value between -1 and 1 where the deviation from a 45° line is represented by a deviation of the CCC from a value of 1. CCC can be calculated using the equation below where σ_{12} is the covariance, μ_x is the mean of measurement technique x, and σ_x^2 is the variance of measurement technique x [25].

$$CCC = \frac{2\sigma_{12}}{\sigma_1^2 + \sigma_2^2 + (\mu_1 - \mu_2)^2}$$
 Eq. 7

Both metrics were calculated for every possible pair-wise combination of the four measurement techniques. This provided three sets of RA metrics and three sets of RR metrics. If the algorithm is as effective as an observer, there will be no difference between RA and RR metrics. The difference between each RR and RA metric was calculated to produce a population of nine differences. A bootstrapping analysis with 10000 iterations was used to estimate the mean RR and RA difference for each metric. The 80% confidence interval was calculated by taking the 1000th smallest and the 1000th largest estimated mean difference for each metric [26]. The confidence interval was analyzed to determine if the RA pair-wise metrics were significantly different than the RR pair-wise metrics.

4.1.2 Results

Table 1 shows the best phase determined by the algorithm and each reader for systole and diastole in each exam. The algorithm best phase was within 2% of the consensus best phase in 15/21 of cases. The average absolute difference between consensus and algorithm best phases was $2.29\% \pm 2.47$. The average systolic best phase was $42.6\pm3.2\%$ for consensus and $41.9\pm3.4\%$ for the algorithm. The average diastolic best phase was $75.8\pm2.8\%$ for consensus and $77.3\pm2.7\%$ for the algorithm.

		Best Phase (% R-R Interval)				
	Exam ID	Reader 1	Reader 2	Reader 3	Consensus	Algorithm
	74	76	72	72	72	74
	64	76	72	72	72	80
	89	74	70	74	74	78
	61	80	80	74	80	78
e	94	81	75	73	79	73
Ю	100	78	78	74	78	78
st	154	78	76	74	74	76
Dia	71	71	77	75	77	73
	101	75	77	79	79	79
	104	76	74	74	74	76
	156	77	73	73	73	79
	168	82	78	78	78	78
	193	73	75	75	75	81
Systole	64	38	40	40	40	40
	89	48	48	48	48	48
	61	40	44	44	44	44
	100	42	44	42	42	42
	154	40	40	40	40	40
	156	39	45	37	39	37
	168	46	46	40	46	44
	174	38	42	42	42	40

Table 1- Best phases determined by three observers and the algorithm

The RR and RA agreement compared to the ideal 45° line is shown in Figure 28. There were two clusters around 42% and 75% for systolic and diastolic best phases.





Figure 28- Reader-reader and reader-algorithm plots compared to an ideal 45° line from the origin.

The pairwise MAD and CCC metrics are shown in Table 2. The average RR MAD was 2.60 which was higher than the average RA MAD of 2.57. The average RR CCC was 0.9317 which was also higher than the average RA CCC of 0.9299.

	MAD	CCC
Reader 1 / Reader 2	2.76	0.9321
Reader 1 / Reader 3	3.24	0.9275
Reader 2 / Reader 3	1.81	0.9356
Reader 1 / Algorithm	2.67	0.9327
Reader 2 / Algorithm	2.76	0.9235
Reader 3 / Algorithm	2.28	0.9334
Mean Reader/Reader	2.60	0.9317
Mean Reader/Algorithm	2.57	0.9299

Table 2- Both pair wise metrics (MAD and CCC) for each combination of measurement techniques

Bootstrapping results showed no significant difference in RR and RA values for CCC and MAD (p>0.2). The 80% confidence interval of the mean difference in MAD between RR and RA metrics was -0.233 to 0.296 with a mean value of 0.032. Positive values indicate that RR variation is greater than RA variation. The histogram of expected MAD differences between RR and RA metrics is shown in Figure 29.


Figure 29- Bootstrap histogram of differences between RR and RA mean absolute differences

The 80% confidence interval of the mean difference in CCC between RR and RA metrics was -0.0006 to 0.0042 with a mean value of 0.0018. Positive values indicate that RA variation is greater than RR variation. The histogram of expected CCC differences between RR and RA metrics is shown in Figure 30.



Figure 30- Bootstrap histogram of differences between RR and RA concordance correlation coefficients

4.2 Observer IQ Study

The observer IQ study evaluated image quality in cases where the observer consensus best phase and the algorithm best phase did not agree. Subjective observer IQ scores were evaluated for each vessel and for the overall study to determine if subjective IQ was equivalent for the different observer and algorithm best phases.

4.2.1 Methods

In exams where the consensus observer best phase and the algorithm best phase differed by more than 2%, three observers evaluated image quality on a five point Likert

scale for the RCA, LAD, LCX, and overall where 1 indicated an inevaluable vessel, 2 indicated significant motion artifact, 3 indicated moderate motion artifact, 4 indicated minor motion artifact, and 5 indicated no apparent motion artifact. The consensus and algorithm chosen phases were presented in random order, and readers were blinded to the phase of each volume. The average and standard deviation of scores for each vessel and for the overall study were calculated. Bootstrapping was used to determine if there was a significant difference in image quality between algorithm and consensus best phases. The difference between IQ scores for algorithm and consensus best phases from each reader was used as input to the bootstrapping analysis. The bootstrapping analysis was performed with 10000 iterations, and the 80% confidence interval was calculated by taking the 1000th smallest and the 1000th largest estimated mean difference for each vessel and overall. The confidence interval was analyzed to determine if the algorithm best phase IQ was significantly different than the consensus best phase IQ.

4.2.2 Results

The overall vessel IQ scores from each observer are shown in Table 3 for algorithm and consensus best phases. Average image quality for the algorithm chosen best phase was 4.01 ± 0.65 overall, 3.33 ± 1.27 for RCA, 4.50 ± 0.35 for LAD, and 4.50 ± 0.35 for LCX. Average image quality for the consensus best phase was 4.11 ± 0.54 overall, 3.44 ± 1.03 for RCA, 4.39 ± 0.39 for LAD, and 4.50 ± 0.18 for LCX.

			Algorithm Best Phase				Consensus Best Phase				Difference			
Exam	Consensus BP	Algorithm BP	R1	R2	R3	Average	R1	R2	£3	Average	R1	R2	R3	Average
64	72	80	3	4	4	3.7	3	4	5	4.0	0	0	-1	-0.3
89	74	80	3	3	3	3.0	3	3	4	3.3	0	0	-1	-0.3
94	79	73	4	5	4	4.3	3	4	4	3.7	1	1	0	0.7
71	77	73	5	4	5	4.7	4	5	5	4.7	1	-1	0	0
156	73	79	4	5	5	4.7	4	5	5	4.7	0	0	0	0
193	75	81	4	4	4	4.0	4	5	4	4.3	0	-1	0	-0.3

Table 3- Overall IQ scores for algorithm and consensus best phase for each observer

Bootstrapping results showed no significant difference between consensus and algorithm IQ for overall IQ or IQ of the RCA, LAD, or LCX. The 80% confidence interval of the mean difference in overall IQ score between algorithm and consensus phases was -0.22 to 0.11 with a mean value of -0.06. Negative values indicate that consensus phase had a better overall score compared to the algorithm phase. The histogram of expected overall IQ differences between algorithm and consensus phases is shown in Figure 31.



Figure 31- Bootstrap histogram of differences between algorithm and consensus overall IQ

The 80% confidence interval of the mean difference in RCA IQ score between algorithm and consensus phases was -0.39 to 0.11 with a mean value of -0.11. Negative values indicate that consensus phase had a better RCA score compared to the algorithm phase. The histogram of expected RCA IQ differences between algorithm and consensus phases is shown in Figure 32.



Figure 32- Bootstrap histogram of differences between algorithm and consensus RCA IQ

The 80% confidence interval of the mean difference in LAD IQ score between algorithm and consensus phases was -0.06 to 0.28 with a mean value of 0.11. Positive values indicate that algorithm phase had a better LAD score compared to the consensus phase. The histogram of expected RCA IQ differences between algorithm and consensus phases is shown in Figure 33.



Figure 33- Bootstrap histogram of differences between algorithm and consensus LAD IQ

The 80% confidence interval of the mean difference in LCX IQ score between algorithm and consensus phases was -0.11 to 0.11 with a mean value of 0.00. Positive values indicate that algorithm phase had a better LCX score compared to the consensus phase. The histogram of expected LCX IQ differences between algorithm and consensus phases is shown in Figure 34.



Figure 34- Bootstrap histogram of differences between algorithm and consensus LCX IQ

There were no cases where a reader's score differed by more than one point from

algorithm to consensus best phase.

5 DISCUSSION AND CONCLUSIONS

5.1 Discussion

The observer best phase study investigated whether intra-reader variation was greater than the variation between reader and algorithm. Bootstrapping results showed no significant difference in RR and RA values for CCC and MAD (p>0.2). This suggests that the algorithm was as effective as a reader in selecting the best phase. In Figure 28, both RR and RA plots show clusters around end-systolic and mid-diastolic phases. This is expected because these locations are known low motion stages of the cardiac cycle.

All three observers agreed on the best phase in 2/21 cases. In both cases, the algorithm agreed with observers. This suggests that the algorithm was able to exactly identify the best phase when one phase is clearly superior. The consensus best phase agreed closely with the algorithm best phase with a mean difference of $2.29\pm2.47\%$. This is an improvement on previous automated retrospective best phase algorithms in literature. The kymogram algorithm demonstrated a mean difference of 12.5% [20]. Seifarth found that one version of the motion map algorithm (Cardio BestPhase, Siemens Medical Solutions) had a mean difference of $6.1\pm5.9\%$ for systolic phases and $5.0\pm4.7\%$ for diastolic phases. The phase difference was over 5% in 46% of systolic and 36% of diastolic exams compared to a difference of over 2% in just 29% of exams in this study [27]. In contrast, Hoffman found that, using a motion map algorithm, the best phase

would be within 6.8% of the consensus best phase 95% of the time [28]. However, Hoffman allowed the algorithm to pick up to four phases and observers to pick up to three phases. Only the nearest algorithm and observer phases were considered, which may account for the lower variation seen compared to the Seifarth study. The proposed algorithm is unique because the best phase is identified based on vessel image quality directly. Other approaches estimate coronary motion which is then used to determine vessel image quality.

The best phase study quantified results based on a phase difference between algorithm and reader best phases. The phase difference is not always proportional to the IQ difference. A 4% phase difference can have a significant effect on image quality, while two phases 6% apart can have similar image quality (Figure 35). The observer IQ study was conducted to ensure that, when the algorithm and consensus phase differed by >2%, both phases had equivalent IQ.



Figure 35- Significant difference in RCA IQ with 4% phase change (top). No significant IQ difference with 6% phase change.

The IQ study found no significant difference in subjective observer IQ between algorithm and consensus phases when the phase difference was >2% for overall IQ or IQ of the RCA, LAD, or LCX. Previous IQ studies showed mixed results with the motion map algorithm. Seifarth found a significant difference between algorithm and consensus IQ, while Ruzsics did not find a significant difference[29].

In the current study, difference between algorithm and consensus best phases was only >2% in diastolic phases. This is likely because the low motion period in end-systole is typically very short. Diastasis tends to be longer, especially at low heart rates. The two exams with the lowest heart rates (60bpm) had a phase difference >2%. Because of the longer low motion interval, there is a wider window of phases that yield equivalent low motion results. The overall and RCA IQ were slightly better in the consensus best phase (4.11 vs. 4.01 and 3.44 vs. 3.33, respectively). The average LCX score was identical for both phases (4.5). Finally, the average LAD IQ score was better in the algorithm best phase than the consensus phase (4.50 vs. 4.39). The RCA IQ was likely lower than the LAD or LCX IQ due to higher average velocities in the right coronaries [3]. An axial slice from each exam is shown in Figure 36 at both algorithm and consensus best phases. From observation, none of the algorithm selected best phases show significantly worse IQ than the consensus phases.



Figure 36- Algorithm and consensus best phases with >2% difference

There was no exam where two readers agreed that the overall IQ of the algorithm best phase was worse than the consensus best phase. However, in exam 94, two out of three observers gave the algorithm best phase a better score than the consensus best phase. This suggests that there was no exam where the algorithm chosen best phase was perceived as worse than the consensus best phase.

There were several limitations in this study. Prospective gating was used in all exams, which limited the available range of phases. However, using prospective gating significantly reduced patient dose. A gold standard metric of image quality is not available for coronary imaging. Therefore, image quality had to be assessed by readers qualitatively. The intra-reader variability in IQ scores was reduced by using three readers. Also, when selecting the best phase, readers can exhibit a bias towards typical end-systolic and mid-diastolic locations. This bias was eliminated in the IQ study by blinding the readers to the phase of the volume.

There are many opportunities for improvement in the algorithm. Processing time can be reduced by using parallel processing and converting the code from MATLAB to C. Also, the algorithm could be generalized for multi-beat cases. Multi-beat imaging poses unique challenges because IQ can vary between slabs. Furthermore, IQ scores could be scaled to allow comparison of IQ across multiple exams. The scaling factor could be based on the contrast in the aorta. The algorithm will also need to be tested with additional single-beat datasets before clinical implementation. Further studies could also compare the algorithm best phase to phases selected by motion map and kymogram algorithms.

The algorithm can also be better integrated into the CT reconstruction process. The left and right scores could be used to determine when separate best phases should be selected for each side of the heart. The in-plane and through-plane IQ metrics could be used to determine whether motion correction is worthwhile. The vessel points from the algorithm could be used as input to the coronary segmentation algorithm, providing seed points for each artery. The segmentation algorithm could then verify that the correct points were found for the RCA, LAD, and LCX. If the vessels were not located correctly, the algorithm results could be flagged as unreliable.

5.2 Conclusions

There was no significant difference between the proposed algorithm and a reader in best phase selection for CCTA exams. The difference between observer and consensus best phase was favorable compared to results of previously published retrospective best phase detection algorithms. In cases where the algorithm-selected and consensus best phases differed by >2%, there was no significant difference in overall IQ or IQ of the RCA, LAD, or LCX.

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7 APPENDIX 1: CARDIAC SEGMENTATION

An algorithm for cardiac segmentation based on an axial slice of the heart was developed because full 3D data may not be available. An initial segmentation was performed to remove the lungs and spine. The location of the ribs were then determined once per slice and removed for images at all phases for the slice. The steps for segmentation are summarized in Figure 37.

7.1 Step 1: Lung removal

First, the lungs are removed from each image. The lungs are identified by applying a threshold at 550HU to the image, where regions of low CT number are identified as potential lung regions. Regions above the threshold are labeled with a connected-components algorithm using 4-connectivity, and the region with the largest area is selected. A morphological closing is performed on the region because shading can cause values within the cardiac region to fall below the threshold (see Figure 38).

7.2 Step 2: Heart-region segmentation

In this step, the heart contour is identified based on the location of the lungs. The Euclidian distance, D, from any point on the image to the closest point on the lungs is

calculated. The region with distance above a threshold, D_{Thresh} , was identified as the center of the heart (Figure 37c). D_{Thresh} was defined as the product of the maximum distance and a scaling factor α . If α is too large, the shape of the heart will not be preserved, while too small an α will cause parts of the ribs and spine to be included in the heart region. In the current algorithm implementation $\alpha = 0.8$.

$$D = \sqrt{(x_1 - x_2)^2 + (y_1 - y_2)^2}$$

$$D_{Thresh} = \alpha * max(D)$$

Eq. 8

The initial heart segmentation includes all values not in the lungs that are within a Euclidian distance of $D_{Thresh}*(1+\beta)$ from the central heart region (Figure 37d). This removes any regions that branch off of the center of the heart where β is the tolerance for branching regions. Too large a β will include large parts of the ribs and spine while too small a β will remove outer edges of the heart. In the current algorithm implementation, $\beta=0.15$.

7.3 Step 3: Rib removal

The ribs are removed by finding points on the right and left side of the heart where the ribs connect to both the heart and lungs, hereafter referred to as rib connection points. This is only done once per slice because the ribs will be in the same location for each phase. The ribs are identified as regions in the top half of the image that were removed by the initial heart segmentation, are not a part of the lungs, and intersect both the initial segmented region and the edge of the field of view. The lowest and most central points on this region are identified for the right and left side of the image and labeled as the rib connection points (Figure 37e). If no appropriate points can be found, the ribs are not present and the segmentation is complete.

Otherwise, a line is automatically drawn between the rib connection points and all points above it are removed. This line should not go through bone or the center of the heart. Furthermore, it should avoid passing through any chambers of the heart if possible. This logic is implemented by drawing the line as a minimum cost path (Figure 37f). The initial cost for each pixel in the heart region is equal to the reconstructed CT number. This gives additional cost when passing through chambers of the heart. Points outside the initial heart segmentation are not considered as possible paths for the line. Values above 1300 are not considered as possible paths for the line to assure that the path does not travel through bone. To discourage the path from going through the center of the heart, an image is constructed whose value is equal to 700 in the heart center, defined previously as the region where D>D_{Thresh}, and decreases linearly to zero halfway between the center of the heart and the lungs. A maximum value of 700 is chosen to allow no greater than a 100% increase in cost, assuming soft tissue values \geq 700. This image is added to the previously defined cost image. The cost weighted distance is calculated for each rib connection point using a geodesic time algorithm[30] where the distance between points (x_1,y_1) and (x_2,y_2) is calculated using quasi-Euclidian distance, a piecewise variation of Euclidian distance.

$$\begin{cases} |x_1 - x_2| + (\sqrt{2} - 1)|y_1 - y_2| & if |x_1 - x_2| > |y_1 - y_2| \\ (\sqrt{2} - 1)|x_1 - x_2| + |y_1 - y_2| & otherwise \end{cases}$$
Eq. 9

 $\Omega uasi - Euclidian Distance =$

The two cost weighted distance functions are summed and the minimum cost path is selected as the pixel with the smallest value for each column between rib connection points. The final segmentation is achieved by including the region below this path and performing a morphological open to smooth the edges of the segmentation (Figure 37g).



Figure 37- Steps in the segmentation process (a) Original image (b) Image after lung removal (c) Distances of every point on the image from the lungs. The blue outline shows the central heart region that is above the distance threshold. (d) Initial segmentation of the image with ribs still present. The red outline shows the expansion from the center of the heart. (e) Mask of the parts of the ribs removed during initial segmentation. Red dots show the rib connection points. (f) Cost function where the minimum cost path between rib cutoff points is shown in green. (g) Final segmentation with ribs removed.



Figure 38- (a) Original image (b) Lung segmentation before morphological closing. Note the areas in the heart that are below the lung threshold. (c) Lung segmentation after morphological closing. The holes have been removed.