博士論文

Study of relationship between each segment of ECG and reconstruction phase on 320-row coronary CT.

（３２０列冠動脈CTに心電図の各セグメントと再構成位相の関連に関する研究）

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CHAPTER 1 INTRODUCTION

1.1 BACKGROUND

Incidents of coronary artery diseases are one of the leading cause of death [1]. One of the common methods for evaluation of coronary artery disease is CT coronary angiography [2]–[4]. And radiological advancement has dynamically changed the benefit of the study on many aspects [5]. Accuracy for diagnosis of coronary stenosis through CT angiography is quite high [6]–[12]. After introduction of the CT coronary angiography ECG guidance has also been added. Considering morbidity and mortality this non-invasive angiographic procedure stepped ahead of traditional catheter coronary angiography [13]. Even it is considered as a second line investigation after treadmill tests [14]. Getting optimum quality image from CT coronary angiography is not an easy task. Numerous protocols are followed for different cases [15]. One of the main causes is the rapid movement of the heart [16]–[18]. Heart rate can widely vary. This continuous array of variation makes the CT angiography very challenging. Not only that, the reconstruction of the coronary vessels requires much better data to be processed to track down the details of the narrow vessels as well as their pathologies. Data from different axis of the heart are also required for tracking down a clear path of the vessels. It is known that slower movements can extract better quality images. Aiming this theory, medications like beta blockers have been used before the study to control the heart rates which is not always possible [19]. In such condition, ECG gating can help to ease up the process. For many years electrocardiography (ECG) has been synchronously used with CT coronary angiography (CTCAG) and is the modality of choice for detection of coronary conditions specially for coronary arterial stenoses [16], [20]–[27]. Plaque characterization is also possible through this study [28]–[31]. Patients may get exposed with high amount of radiation during the procedure if measures not taken [32], [33]. The radiation dose for performing CT is reduced through the advancement of technology [34]–[41]. Recent scanners are multi-detector-row CT scanners which can slice more thinner and have shorter rotation time, resulting faster scan during a single breath hold. And the spatial resolution covers the entire heart volume [42]. Prospective ECG-triggering is widely used to reduce radiation dose [32], [33], [39], [43]–[55]. Here the X-ray beam is kept on only in specific segment of cardiac cycle. And the remaining portion is not being used [56]. It is still uncertain when to keep the X-ray beam on or off. Because the heart beats are not rhythmical every time. This criterion has made it difficult to predict. There are specific protocols by which the expert radiologists can attempt to predict before every scan. To get the best reconstruction phase the scanning protocol may require to include multiple beats to be scanned which also increases the chance of radiation exposure [57]–[59]. But as faster scanner has been gradually introduced a preselected phase of the cardiac cycle can be used to get the best output. From the previous literature it was known that if the heart rate (HR) becomes low then the possibility of getting sharp image becomes high [59], [60]. Besides, there were subjective and objective studies stating that 10–30% dose can be reduced with "FIRST" method (Forward projected model-based Iterative Reconstruction SoluTion) [61]. It is also proved as a promising reconstruction method by different studies [62]–[65].

P. A. Araoz *et al*. studied among 30 high heart rate as well as 30 low heart rate patients in the aim of getting the best phase of image. They divided the patients in two groups at the point of 70 beats per minute. They reconstructed all the cases from 30% of the reconstruction phase upto 70% with 5% increment. They gave a sharpness score to the vessels they examined and the vessels they included in the study are the right coronary artery (RCA), left main (LM), left anterior decending (LAD) and circumflex (Cx) arteries. And after analyzig the data they found that the best quality image is found in end diastolic phase for the patient having heart rate less than 70 beats per minute. And for the high heart rate patients the best quality image is seen at end systolic phase. They also stated a range of reconstruction phase along with the cardiac phase [60].

Effectiveness of CT angiography in patients with in-stent restenosis is also studied and proved informative. A study performed on 169 vessels evaluated by CT coronary angiography showed significant ability of detecting in-stent restenosis [66].

A study also used a relatively different method to find out optimal quality image. They used kymogram which is a raw data-based motion signal. The study used data of 90 patients. Using the fully automated computer-assisted approach they concluded that the method can identify the best quality image while the CT scan examination is on process. The study incorporated patient specific selection of tube current which will use the minimum amount of radiation for bringing out of the examination for every individual [67]. As the most static stage is a diastolic phase, so it represents the opportunity for optimum reconstruction phase [68], [69]. But when the heart rate is high, it becomes difficult to find out the best one which is also common in patients with arrhythmia [16], [59], [70]–[72]. And for such cases individual patient dependent variation was accepted [58], [68], [73], [74]. Most of the acquired data do not play any role on image processing rather than producing artifacts. X-ray current modulation can play vital role in this step [75]–[77]. And usually between 40% to 90% of the cardiac cycle is selected for full use of tube current [76], [78]. As this range is very long there comes concern about radiation [79]. For correcting the unnecessary portion of the radiation, the range should be narrowed down. As most part of this range does not play any role in acquiring the necessary image it would be beneficial if the range could be narrowed down. And for this purpose, the study used kymogram signal. Some of the other studies also used kymogram as alternative to ECG for signal synchronization [80], [81]. Few studies also used it for evaluating reconstruction phase [82], [83]. The study proved the ability of kymograph for detecting optimum image though they suggested for a full potential evaluation. It mainly dealt with the tube current for achieving optimum image rather than analyzing segment wise evaluation of coronary cycle for a better image.

Another study with retrospective ECG gating was performed among 125 patients in which there was reconstruction from 20% to 80% of the R-R interval with 5% interval. It performed Pearson correlation analysis and it found no correlation between mean heart rate and image quality between left anterior descending and right coronary artery except left circumflex artery. The study also determined that best image is found in diastole and the heart rate should be below 80 beats per minute. And if the heart rate is up to 85 beats per minute then 50% of the coronary segments shows better image at diastole. Heart rate above 80 beats per minute had quality images towards end-systole [59]. This study used a 64 slice CT scan machine and 140 HU as threshold level of signal attenuation. It also measured the image quality through a scoring system and it was mentioned that it might have subjective bias. The data were analyzed through Pearson correlation analysis by

SPSS. The study also stated that there was a negative effect between heart rate variability and image quality for all coronary segments [59]. It also highlighted that the heart rate regularity plays important role determining the image quality. One of the limitations of the study was they excluded coronary artery stenoses and also excluded the patients having heart rate above 102 beats per minute. For reducing the radiation dose, some of the studies used prospective helical ECG gating rather than retrospective gating [84]–[86].

Another study of 70 patients attempted to evaluate reconstruction image on both relative and absolute timing. They used a four-step grading system. And performed Spearman correlation, Wilcoxon other tests for analysis. The range of R-R interval was 40% to 75% for the study. The study concluded that the best quality image is found at mid-diastolic level for low heart rate patients. And for high heart rate patients the best image is formed at end-systolic and early-diastolic phase of the cardiac cycle. They included coronary stenosis cases and it significantly been able to detect them for 50% cases having 86% specificity and sensitivity [58]. 64-slice CT scanner was used here. Another study performed in 80 patients with 20% to 80% of the R-R interval with 5% increment in a 64-slice scanner which found no significant correlation between image quality and HR variability in right coronary artery and left anterior descending artery except left circumflex artery [87]. The ECG protocol is reviewed by a person who was not involved in the image processing and can be considered as a third reviewer. The threshold for image acquisition was 100 HU for this study. All patients of this study also received sublingual isosorbide dinitrate.

A study with 100 patients attempted to evaluate the influence of heart rate on motion artifact. They used 64-slice scanner. It found the optimum quality image at 65% to 75% of the R-R interval and concluded that best image is found at late-diastole of the cardiac cycle if the heart rate is below 60 beats per minute. And for higher heart rates the optimum quality image is observed at the late systole. And for the whole evaluation they included 25% to 75% of the R-R interval in the study [88]. CT angiography has role in detecting ischemia as well as exclusion of risk stratification [89]–[94]. Several few studies also revealed that least motion artifact is observed in systole for higher heart rate patients [16], [59], [60], [69], [74], [88], [95]–[102]. Unlike the other studies, this study also used sublingual trinitrates for vasodilation but it included 20% to 90% of the cardiac cycle for image evaluation. Like some other studies, it followed a score-based system for classification of the artifacts. The study concluded that limitation of short segment data acquisition is not possible in high heart rate patients [88].

A study performed with 80 patients all of them having high heart rate showed that better image is found at systole. It followed a gradation system for differentiating the image quality. The heart rate ≥70 beats per minute was considered as high heart rate [103]. One of the important limitations of this study was the number of patients which is only 35 that may question the statistical significance.

There was a study in which the patients were divided in three groups according to heart rate. It concluded that if the heart rate is ≤ 70 beats/min then best quality image is found in diastole. However, the study could not suggest to scan systolic phase for high heart rates of the other two groups, rather it suggested to scan both diastolic and systolic phase for patients with high heart rates [104].

A study on 43 patients as well as phantoms were performed with filtered back projection, hybrid iterative reconstruction as well as knowledge based iterative reconstruction revealed that the last mentioned one is best for noise reduction and image improvement [38].

It has been proved that slower heart rates can achieve high image quality [17], [59]. An srticle mentioned that vessels are best visible if the heart rate is below 65 beats per minute (b/m) [105]. Study also showed that reconstruction at end-systolic and early-diastolic intervals produces high quality image in patients with low heart rates [58]. On the other hand, some of the studies concluded that the best quality image is found at mid-diastolic level [58]–[60], [95], [100], [101], [106], [107]. Some studies concluded that motion artifact at this level is also reduced by ECG gating [69], [108], [109]. Data acquisition can be limited to diastole in slow heart rate patients [58], [88], [104]. Few literatures also included their work on the basis of systolic or diastolic phase of the cardiac cycle. Due to the availability of faster scanner it is thought to be possible to scan and reconstruct a more specific portion of the cardiac cycle which means scanning a specific portion of the ECG wave.

1.2 OBJECTIVE

The purpose of this study is to evaluate the diagnostic phases and correlate them with cardiac or ECG phases with Multi Detector CT coronary angiography.

The study would reduce radiologists' effort for preselecting the protocol for each patient to find the accurate phase as well as reduce the radiation dose, scan time and might have produced an auto-reconstruction algorithm for the future CT scanner if the scan range could be narrowed down.

1.3 DOCUMENT ARRANGEMENTS

In chapter 2, I have mentioned the basic history of coronary angiography imaging. In chapter 3, I have mentioned the materials as well as the research method of this study. Also, the relation of ECG gating with heart rate as well as basic process of data acquisition has been stated. In chapter 4, I have stated the analysis of the collected data elaborately along with the steps of image evaluation and different comparisons. In chapter 5, I have plotted the results in different ways. In chapter 6, the results were discussed for a better outcome and finally conclusions have been made in chapter 7.

CHAPTER 2 BASIC THEORY

2.1 ECG GATING

ECG gating is one of the best methods among the dose-saving strategies for reducing the radiation dose during the radiological procedures. ECG tracking is a widely used technology in various medical conditions. And using the ECG tracking device for a coronary study is more relevant. In performing coronary studies, the examiner can track the cardiac beats, different stages of the cardiac cycle as well as some other parameters. And there is an ECG tracking device which is very easy to set up with the patient and does not require any special precaution and also usually does not create patient discomfort. Just after adding the leads on the anterior chest wall of the patient with the help of gel, the ECG tracker can collect the cardiac data continuously and visualize them on the monitor. The examiner can decide and set the protocol of the study after watching the cardiac beat nature from that monitor which helps to find out the best moment of the cardiac phase that would be enough for the best quality image. This is how ECG gating helps the whole process to run easily without causing any extra effort or requiring extra time.

There are two types of ECG gating that can be used in coronary CT angiography. One is retrospective and the other is prospective ECG gating. The first one is a conventional technique in which the x-ray beam is kept on along the entire cardiac cycle.

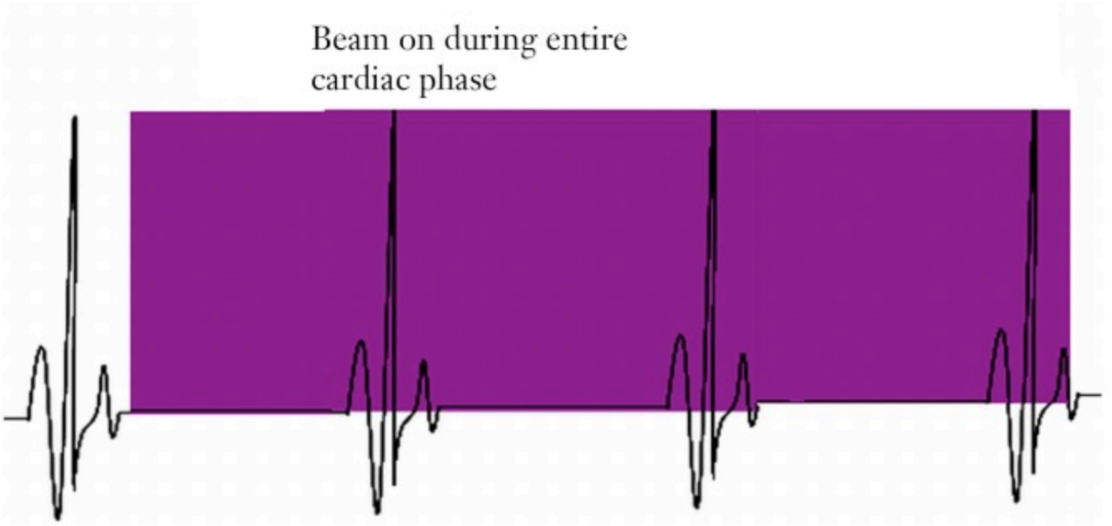


Figure 1 Conventional retrospective ECG gating.

In conventional retrospective ECG gating (Figure 01) the x-ray beam is kept on along the entire cardiac cycle [49]. As a result, the patient gets radiation exposure for a longer time. The X-ray beams may be kept on from two beats to multiple beats and sometimes continuous along the whole length of the study.

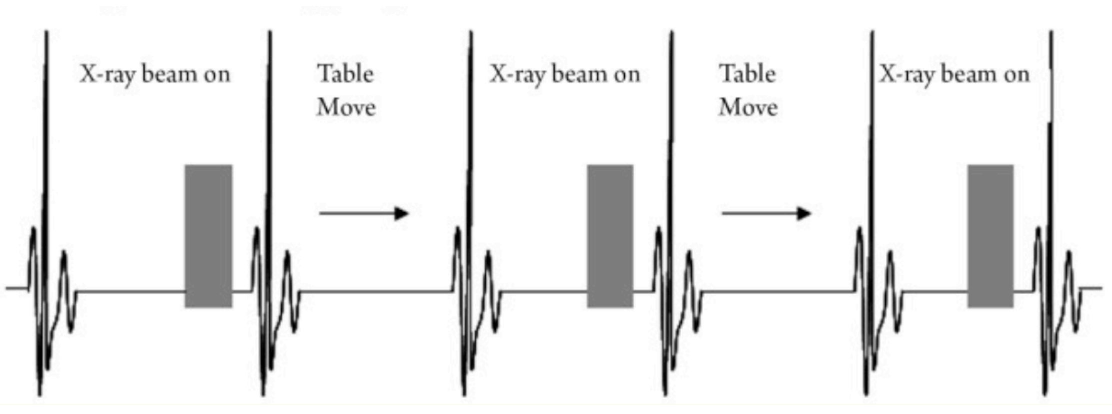


Figure 2 Prospective ECG gating.

On the other hand, in prospective ECG gating (Figure 2) the x-ray beam is kept on in a specific portion of the cardiac cycle. The x-ray beams are turned off at the other portion of the cardiac cycle. It can be considered as a partial scan [49]. Recent study shows that it significantly reduces the radiation dose [53], [110]–[119].

2.2 NORMAL ECG AND ITS MEASUREMENTS

2.2.1 Normal ECG

Though ECG is the oldest investigation for evaluation of the heart, it provides many information on present days. This is one of the common routine investigation. So, it is not necessary to discuss it too elaborately. Besides, the advanced monitors and indicators provide lots of information for the investigator. However, as this study is related to the measurements of different segments of the cardiac cycle, knowledge about the main waves of the ECG should be recaptured.

During normal sinus rhythm, depolarization of the right atrium followed by left atrium takes place. So, the first wave coming from atria are named P wave. After that, there is AV nodal delay resulting a horizontal line and this is named as PR interval. This portion is one of the static phases of the heart. Depolarization of the ventricles are named as QRS complex. Initially the Q wave have a negative deflection. The next is R wave with an upward deflection and again S wave as a downward deflection. It slightly goes negative at its end point and then comes along the isoelectric line. And after that, there is a last electrical wave called the T wave and the duration is called ST segment which is usually isoelectric. (Figure 3) There are some standard measurements of the waves and intervals.

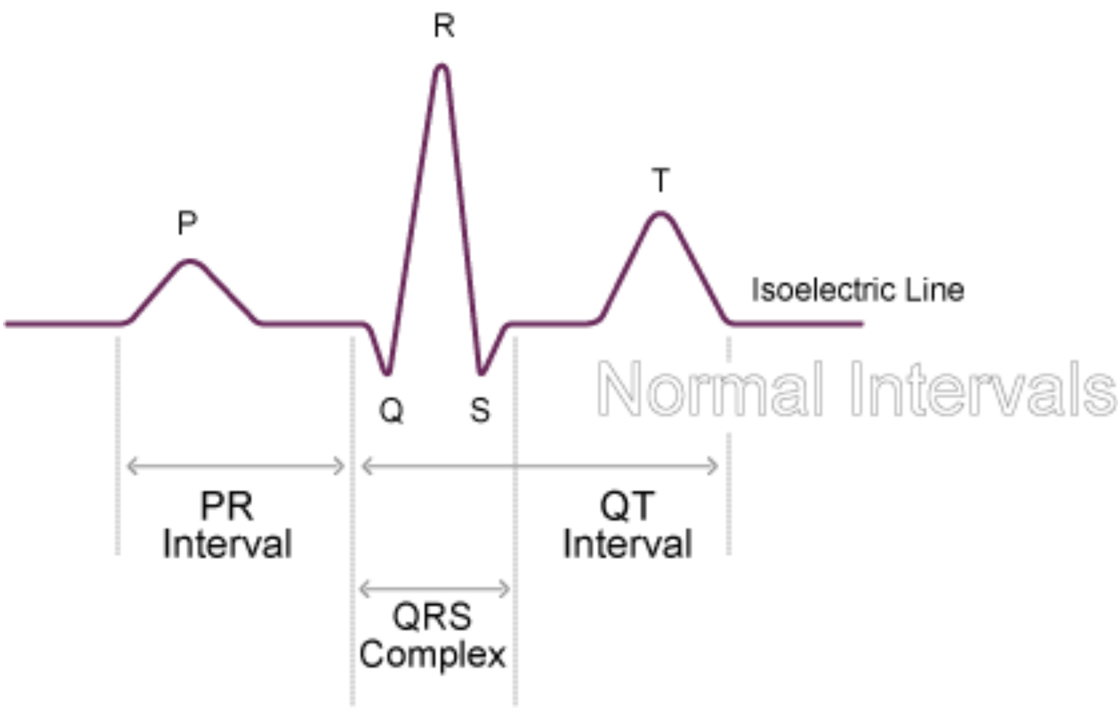


Figure 3 Normal ECG waves with intervals [120].

2.2.2 Measuring Q-T interval

- The QT interval is measured in lead II or in lead V5 and V6 in successive beats of the cardiac cycle. (Figure 4)
- When the U waves are large, (more than 1mm) and if it is fused with the T wave then it should be counted.
- But if the U waves are small those should be excluded.
- From the beginning of the QRS complex, the starting point of QT is considered and it ends up to the end of the T wave.

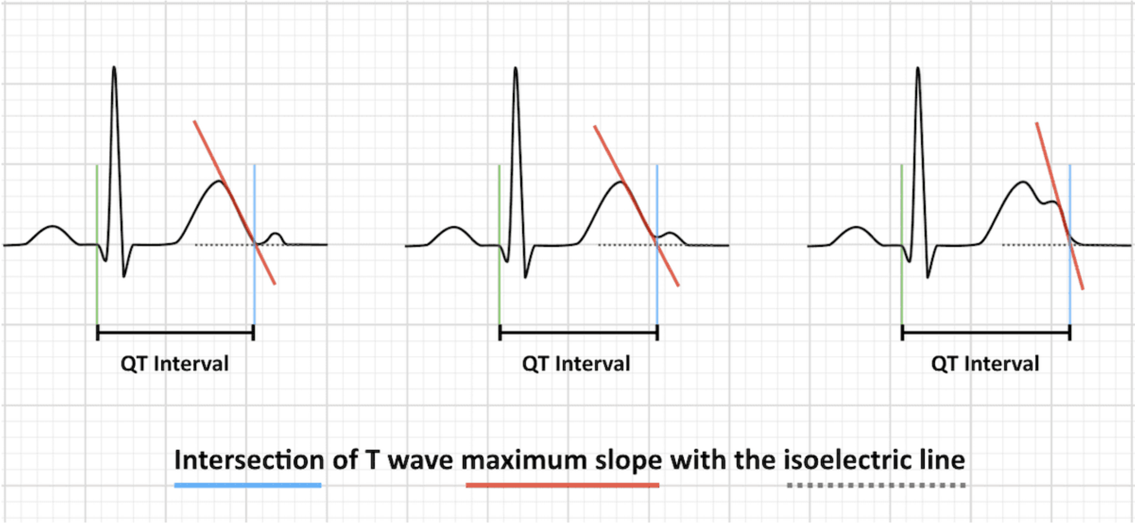


Figure 4 Different patterns of measuring Q-T interval [121], [122].

2.2.3 Measuring P-R interval

- P-R interval is measured from the start point of the P wave and ends at the start of the QRS complex. (Figure 5)

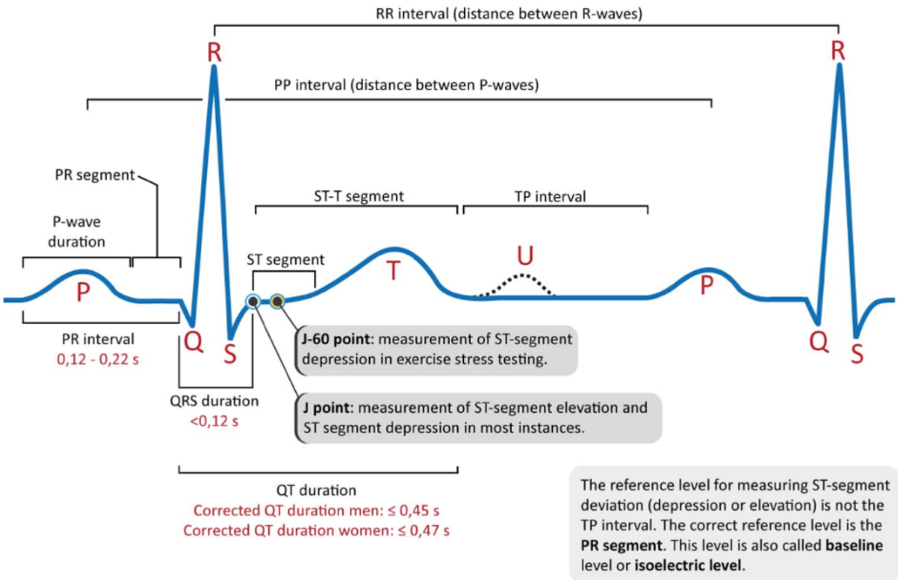


Figure 5 Measuring of P-R interval [123].

2.2.4 Measuring R-R interval

It is the distance measured from the peak of one R wave to the peak of another R wave of the next cardiac cycle. (Figure 5). In this study we measured the R-R interval for all the patients. Then the reconstruction phases are plotted. Length of R-R interval can vary from beat to beat. So, we measured only those in which the X-ray beams were kept on.

2.3 ECG VIEWER

This is not an instrument rather a software which is used for the study. This software can measure different aspects of the ECG wave very easily and accurately. After collecting patient data through a portable hard drive, they are transferred in a computer and then opened with this software for accurate measurement. This software has reduced the study time in a great extent and the data could be easily plotted from there to a spreadsheet. One of the special features of this software is, it can mark the portion of the ECG wave when the x-ray beam emitted from the CT machine. So, we can easily find out which waves have to be measured. Because, the other waves are irrelevant to get measured as they don't have any role on image reconstruction process. We wanted only those waves during which the images were captured by the CT machine for future reconstruction for getting the diagnostic images. The software can also measure the related intervals of those focused waves.

CHAPTER 3 MATERIALS AND METHODS

3.1 STUDY POPULATION

Initially 200 patients were selected from the patients who are referred by the clinicians. The patients were selected during the period of January 2017 to July 2018. After admitting to the Radiology department, the initial measurements including the patient weight and others were taken. Then written consent was taken from the patients. Examining the prescription and questionnaire of the study, the radiologists decides whether the patient will go for a helical scan or not. In this process 44 patients were selected by the radiologist for helical scan and 18 patients were indicated for helical scan. So, they were excluded from the study. Three patients were excluded due to different types of severe arrhythmia.

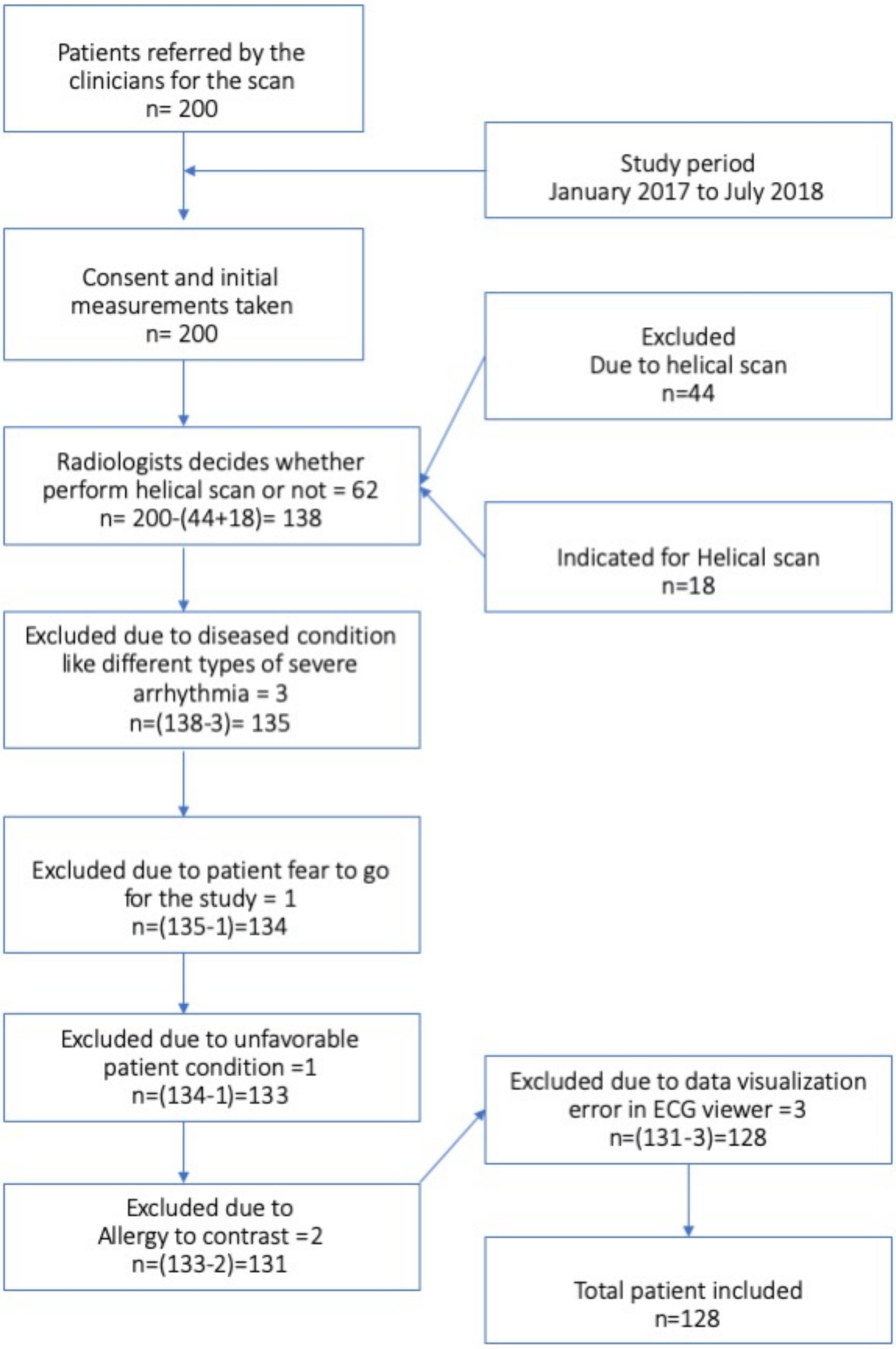
Patients of severe arrhythmia have been excluded especially supraventricular tachycardia, ventricular fibrillation, ventricular tachycardia. However, our intention was to include patients of all categories. For this purpose, some of the patients of severe arrhythmia who can follow the instructions and can hold the breath properly in initial practice session just before the start of the actual scan were included. They were asked to hold the breath for few seconds and then the cardiac cycle pattern was observed by the radiologist and the radiographer. Then if the decision is inclusive, two or four beats were covered in the actual scan so that one of them gives the best result.

Patients with renal dysfunction, and known allergic reactions to the contrast medium are excluded from the study. Patients indicated for helical scan are also excluded from the study because in helical scans the patient is scanned continuously from starting to the end point. So, it is out of the point of interest of this study as we are trying to evaluate a specific portion of the cardiac phase.

One patient did not agree to perform the due to fear of the process. One was excluded due to unfavorable condition. Two patients had history of allergy for contrast materials. So, they were excluded from the study. Three patients were excluded as their data were not being viewed properly on the ECG viewer software. In this process total of

72 patients were excluded from the study. And finally, 128 patients were included in the study. A complete flow chart is added below for this whole process. The study was performed at the University of Tokyo Hospital which is a highly equipped hospital with various types of patients available. For this reason, the study was able to include fair amount of coronary cases in a limited span of time. The patients usually come to the Radiology department after getting referred from the clinicians and surgeons. Then after some official procedures we get their details in the patient database including their registration numbers. They were given a specific appointment for performing the investigation and after completion of a check list the process takes place.

The flow chart below shows the steps of patient inclusion and exclusion.


Patients referred by the clinicians for the scan n= 200
Study period January 2017 to July 2018
Consent and initial measurements taken n= 200
Excluded Due to helical scan n=44
Radiologists decides whether perform helical scan or not = 62 n= 200-(44+18)= 138
Indicated for Helical scan n=18
Excluded due to diseased condition like different types of severe arrhythmia = 3 n=(138-3)= 135
Excluded due to patient fear to go for the study = 1 n=(135-1)=134
Excluded due to unfavorable patient condition =1 n=(134-1)=133
Excluded due to data visualization error in ECG viewer =3 n=(131-3)=128
Excluded due to Allergy to contrast =2 n=(133-2)=131
Total patient included n=128

3.2 DURATION OF THE STUDY

The CT images has been obtained in routine clinical practice during an 18-month period from January 2017 to July 2018 and analyzed in a retrospective approach. All the patients underwent CTCAG through the 320-row slice CT (Aquilion One vision edition, Toshiba, Japan). Approval from the ethics committee has been received for the study. The IRB approval number is 2561-(18).

3.3 STUDY PROCEDURE

Along with the completion of the check list, a written informed consent for CT scan is taken from the patients including the routine questioners. Regular measurements including the blood reports and weight of the patients are collected. The radiologist and the technologist performing the study evaluate the collected information and decide for the feasibility of the examination. In the meantime, patient preparation takes place. The patients are carefully instructed about the procedure.

An IV channel is kept open and the CT scanner is equipped with contrast and saline injector. A doctor connected the channel with the injector and tested whether it had been correctly working or not. Sublingual β-blocker was applied to the relevant cases whenever applicable following safe administration protocol. It is administered by a cardiologist present during the study. One or two sprays of nitroglycerine are administered to the patient sublingually after a little counselling by the cardiologist himself. Beta blocker have some adverse effects though it regulates and reduces the heart rate. It is not administered in some conditions including the patients with severe asthma.

The technologist in presence of the radiologists investigated the heart rate and monitoring the ECG pattern and other features decides for a protocol for the patient. After taking a pilot scan they make changes to the settings of the different parameters of the study including the tube current, voltage as well as the number of beats the scan would take place.

After a thorough checking, the radiologist finally gives proper instruction to the patient about the procedures and comes out from the CT room. Then the study starts, contrast was injected and the patient was instructed for a breath hold after a certain time for a few seconds. At the same time the ECG beats are recorded the leads of which are already attached on the chest of the patient. The ECG recording is controlled by a remote control. When the patient is asked for a breath hold the ECG recording is started by pressing the remote. This is how the ECG data are collected at the same of the scan proceeds. When the enhancement in the vessels reaches a certain limit of Hounsfield Unit the scanner is started and collects the necessary imaging data. So, through these processes the CT scanner collects the imaging information and the ECG machine collects the details of the cardiac cycle.

Just after the scanning is done, the patient is asked to release his/her breath hold status and the examination is ended from the patient's side. The radiologist then views the data and checks whether the images were correctly collected or not. Then the images were reconstructed for the best phase for the visualization of the coronary vessels. There is specific software for the reconstruction process and data were transferred to the specific computer containing the software. The reconstruction process is performed. The whole process is performed by the radiologist.

The reconstruction process is finished in few minutes. Then the radiologist can view the reconstructed data and can make the diagnostic evaluation. During the reconstruction process the radiologist determines the best phase on which the reconstruction of the data should take place for the best image quality. That specific point is kept recorded in the data collection sheet. It is also saved in the software for future rechecking.

The image is considered optimal when the image visualization level is acceptable for the necessary diagnosis. The radiologist has reviewed all the coronary arteries along with the most prone areas where artifacts can be found. The image data are continuously reconstructed and checked until the lumen of all the arteries are well visualized or the stents and internal plaques are well detected. Images from all of the patients are evaluated in the same way until the diagnosis could be made satisfactorily. And these images are considered as the best optimal images which are clinically important.

Besides the processing and reconstruction of the data the ECG data were collected from the ECG machine which were recorded during the examination procedure. The data was first collected from the ECG machine by a portable USB drive and then it is transferred in a different computer that we used for the research. We also used a special software named "ECG Viewer". (Figure 6). This software has the ability to analyze the different aspects of the ECG data. We can also measure the different phase of the cardiac cycles. It also shows the point of coronary cycle in which the x-ray beam was active. So, if multiple beats were used for scanning in a specific case then we can detect on which point among those beats the x-ray beams were active.

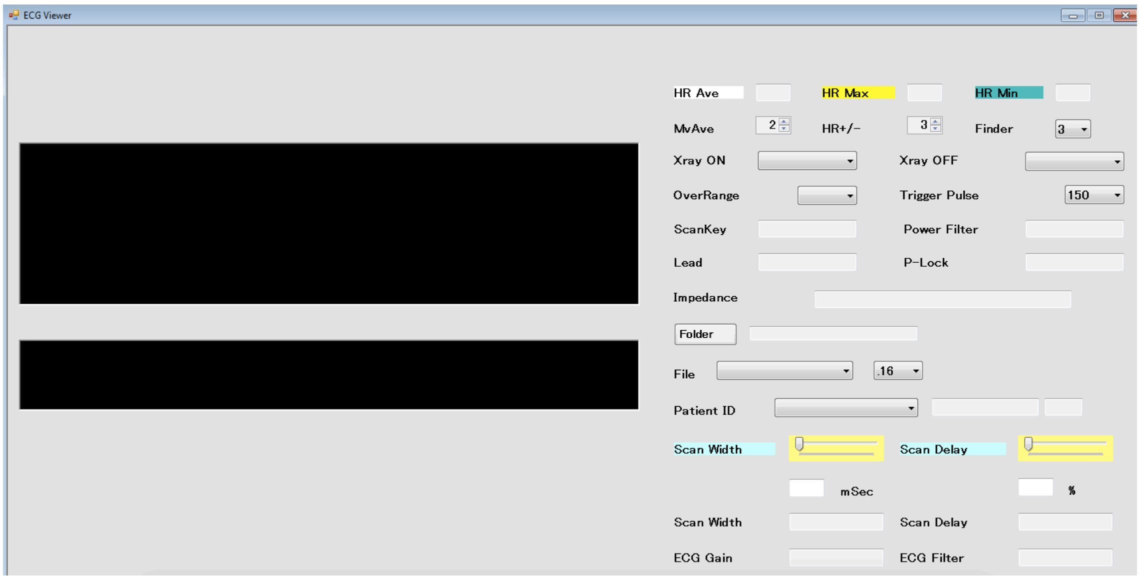


Figure 6 Image of the home screen of the ECG Viewer software.

When the ECG data were transferred to the ECG viewer software we can open and view the data of any patient through the software. In this process, we opened the data of every patient and measured our required parameters and wrote them in a tabulated form on the data collection sheet. Then the data were analyzed statistically through JMP software.

Then the data were analyzed statistically through JMP software (JMP pro Version 14.0). Various statistical methods have been used. The distribution of the diagnostic phases of both groups were analyzed by using the distribution analysis system of the JMP software. Bivariate fit of the reconstruction phases and heart rate were analyzed using the Fit Y by X of JMP. Correlation between heart rate and the diagnostic phase was performed by using the multivariate method of JMP (The Pearson Correlation Coefficient). Also, the common statistical issues were solved by using the existing facility of Microsoft Excel software (Version 2016 Office Home and Student edition).

3.4 RELATION WITH HEART RATE

Radiation is a very common issue discussing malignancy as it is a matter to be concerned among the causative factors related to produce malignancy [49], [124]–[126]. Various dose-saving strategies is applied in the field of radiological examination procedures. And through many techniques, the radiation dose has also been reduced significantly [40]. Among them, ECG-triggering is one of the best effective technique [49], [50]. Prospective ECG-triggering can be determined by following some criteria and careful patient preparation [49]. In prospective ECG-triggering the X-ray beam is kept on in a specific segment of the cardiac cycle. The beam is off on the other segments. If the patient is ECG gated, the radiologist and the technologist can evaluate the cardiac beat pattern of the patient. Then it is possible to decide whether it will be enough to scan a single beat or not. If the cardiac cycle pattern of the patient is regular, then the examination can be proceeded with a single heart beat scan. But if the heart beat is irregular or very high, then the radiologist or the technologist have to decide to scan multiple beats or even for a continuous helical scan. As there is a protocol change for the change of heart beats and pattern of heart beats, there may be a possibility of having any relation between them when we search for a best phase for reconstruction of the coronary scan image data. As reconstruction is performed only at a specific portion of the cardiac cycle, it means that there may be a specific portion of the cardiac cycle on which we can get the best quality image. The heart is a continuously moving organ opening a door of motion artifact [21], [23], [59], [88], [98], [127]. However, there are some points at which it is most stable or relatively slower. Side by side, there are advancement of the CT scanners that delivers good quality image even at the state of motion. By the advanced technology of removing motion artifacts and faster scanning capabilities more accurate evaluation of the correlation of cardiac phase and reconstruction phase should be performed [17], [23], [98], [127]. If there is any further better relation among them, then less portion of the cardiac cycle can be scanned for getting the best image as well as less amount of radiation will be enough for carrying out the purpose of the examination which will ultimately reduce the time of radiation exposure and will play good role on reducing the radiation hazard. For faster scanner synchronized with ECG will open the possibility of reducing the scanning time by targeting the relevant portion of the cardiac cycle.

3.5 CT DATA ACQUISITION

The angiography was performed with a second-generation 320-row CT (Aquilion ONE ViSION edition; Toshiba Medical Systems, Tochigi, Japan) along with ECG gating. CT scan tube potential was 80 KVp; gantry rotation time was 275 ms; and tube current was determined by auto exposure control.

Standard scanning protocol was followed using specific settings of detector collimation, table feed per rotation, and rotation time. About 80–100 ml of non-ionic contrast medium (320mg/ml, 370mg/ml iodine) was injected intravenously. The flow rate was 3.0 ml/s via a 20G catheter in a cubital vein. No post-contrast saline injection was used. When the density level in the ascending aorta at the level of carina reaches to 200 Hounsfield units (HU), the patient was asked to take an inspiratory breath hold for about 20–30s during data acquisition. The scan direction was cranio-caudal and it covered the area from the level of the right main pulmonary artery to the lower end of the heart. Previous study also showed that CT imaging with ECG triggering had high diagnostic accuracy [49]. Radiation dose was also significantly reduced with prospective triggering technique as the data acquisition takes place in specific part of the cardiac cycle [47], [49], [54], [128]. It is to be noted that, the previous studies were performed in relatively slower CT machines. For this reason, they could not get better image when the heart rate was higher. Usually their recommendation for prospective ECG was for the patients having heart rate less than 70 or 65 beats per minute [49]. And the recent scanners are faster than those. For this reason, it is obvious that possibility of reducing the radiation dose is more in the newer faster scanners [26], [129]. As the scanner we used for this study is faster than those that were previously used, there could be a better chance of having a good correlation and that could play big role in radiation dose reduction issues.

3.6 IMAGE RECONSTRUCTION

After the acquisition of the scanned data, the reconstruction process was performed by an expert radiologist who decided the best phase for the image quality to make the correct diagnosis. The reconstruction parameters varied from 160–200 mm Field of View (FOV) depending on the body configuration of the patient. 1 mm slice thickness was kept with 0.5 mm of increments.

The ECG data were recorded simultaneously as the study progresses. Recording started just at the starting of the contrast introduction and stopped when the examination ended. And the patient was asked to release the holding breath. Single beat or continuous beats were scanned as necessary. After collecting the data, they were shifted to a software named 'ECG Viewer' for assessing the different aspects of the ECG wave invented by Chronos Medical Device, Chiba, Japan. Different intervals of the ECG were measured irrespective of heart rate and later on arranged and compared with the reconstruction phase. P-R and Q-T were measured for the patients having heart rate ≤ 75 beats per minute. And in addition, S to the end of T had been measured for the patients who had heart rate higher than 75 beats per minute. These measurement parameters were selected from the analysis of the previous studies.

Figure 7 Image of the ECG Viewer software with the measuring parameters.

By the ECG viewer software, we can measure the different aspects of the ECG wave along with the reconstruction phase. The red lines are the automatically measured portions. The yellow lines indicate the moment when the patient was exposed with the X-ray beams. (Figure 7). For this study, we measured only those cardiac cycles when the X-ray was kept on. First the R-R is measured following the diagnostic phase and then PR and QT intervals were measured respectively.

CHAPTER 4 ANALYSIS

4.1 SUBJECTIVE IMAGE ANALYSIS

Subjective image quality was finalized by a cardiovascular radiologist who has 15 years of experience in pediatric and cardiovascular radiology. The radiologist was kept blind about the details of the CT datasets, which were provided in a randomized order.

4.2 IMAGE EVALUATION

All the image data that were reconstructed by a method called FIRST and were transferred to a computer workstation for post-processing (ZAIO M900, Zaiosoft, Tokyo, Japan). Evaluation of the coronary arteries was performed on this workstation by thin-slab maximum intensity projection and sagittal or coronal multi-planner reformation images. The right coronary artery (RCA: proximal and distal portion), left main coronary artery (LMCA), the left anterior descending artery (LAD: proximal portion and 1st diagonal branch) and the left circumflex artery (LCX: proximal portion and obtuse marginal artery) was studied. The proximal portion of the RCA, distal portion of the RCA, proximal portion of the LAD and proximal portion of the LCX were defined as segments #1 and #2, #3 and #4PD, #6 and #7, and #11 and #13, respectively, in accordance with the classification used by the American Heart Association. The radiologist also evaluated the other relevant patient specific parameters case by case.

A board-certified radiologist evaluated the reconstructed images. For calcified or stented coronary arteries continuity and visibility of the vessel walls were also evaluated.

The table below shows that various conditions have been diagnosed through the study among which LAD stenosis are the most frequent. About 26 patients had stenosis in LAD. On the other hand, 3 patients had stenosis in RCA. It is to be noted that there were some cases of stenting, meaning that they were previously diagnosed as patients of stenosis and had gone through stenting. So, we kept them in a separate group as the aim of the scan was to detect whether there is any new In-Stent Restenosis or not. Among those patients, 7 patients had restenosis and 5 had no restenosis. Patients having three or two vessels disease are also plotted separately in different rows. Patients having uncommon diagnosis has been kept in other categories on the table. Normal findings were observed in 39 patients. (Table 1).

Table 1: Radiological Diagnoses of the 128 studied patients.

Conditions	No of pts	% of total
LAD 50% stenosis	19	14.84%
LAD 75% stenosis	4	3.12%
LAD 75-90% stenosis	3	2.34%
RCA 75% stenosis	1	0.78%
RCA 75-90% stenosis	2	1.56%
In-Stent restenosis	7	5.47%
No In-Stent restenosis	5	3.91%
3 vessels disease	12	9.38%
2 vessels disease	14	10.94%
Single vessel disease	8	6.25%
Normal findings	39	30.47%
Others	14	10.94%

4.3 COMPARISON OF THE RECONSTRUCTION

The patients were divided into 2 groups according to their average HR (beats/min). One group consisted patients having heart rate ≤ 75 beats/min (n=98), and another group consisted above 75 beats/min (n=30). The average HR in each case was defined as the average for the total cardiac cycle during data acquisition.

The table below showing that, among the 98 patients who had heart rate ≤ 75 beats/min, 66 were male and 32 were female. And among the other 30 patients having heart rate more than 75 beats/min, 20 patients were male and 10 were female. So, in our study, total number of male patients was 86 and number of females was 42. (Table 2) History of smoking or diabetes or the other conditions were collected in a questionnaire supplied from the hospital which is filled up for all patients. But as their details are irrelevant with this study so those are not mentioned here in detail.

Table 2: Patient's age with heart rate.

HR	Male	Female	Total
≤ 75 beats/min	66 (51.56%)	32 (25%)	98 (76.56%)
> 75 beats/min	20 (15.63%)	10 (7.81%)	30 (23.44%)
Grand total	86 (67.19%)	42 (32.81%)	128 (100%)

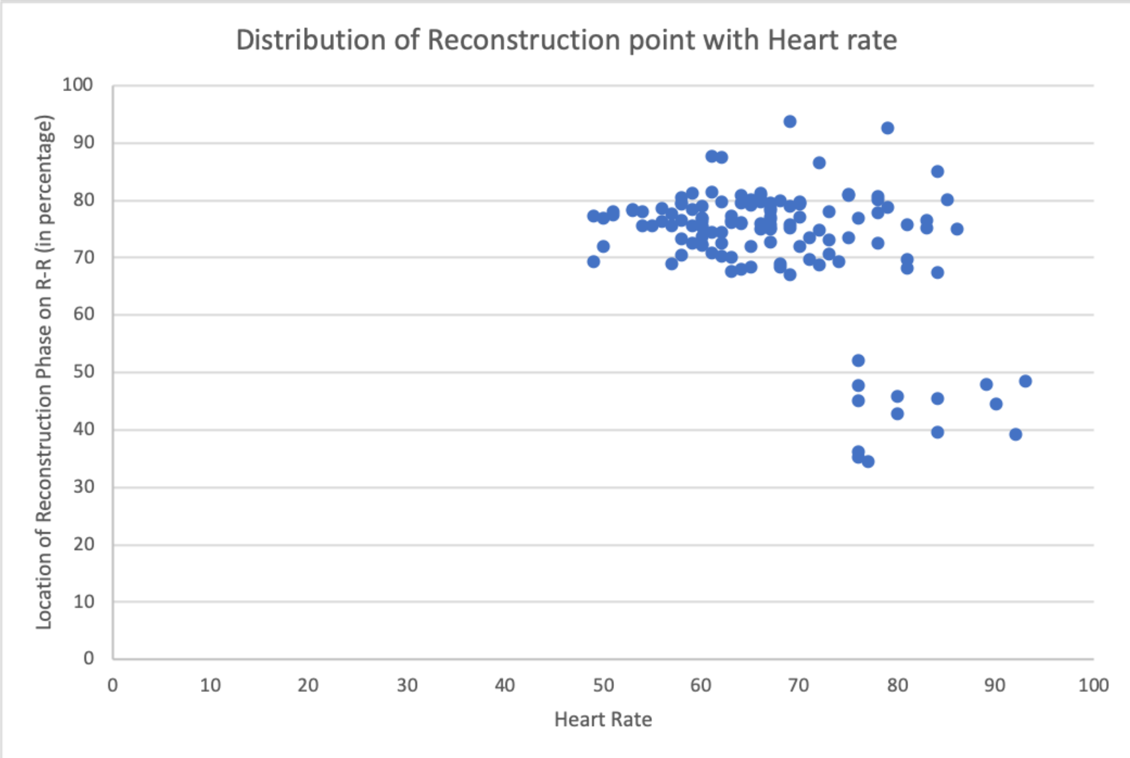


Figure 8: Distribution of diagnostic phase (Reconstruction Phase in percentage of R-R) with HR in all 128 pts.

The heart rate and diagnostic phase was plotted in the above figure. The blue dots indicate the diagnostic phase of all 128 patients of the study. (Figure 8). Here we see that the diagnostic phases are closely aggregated in low heart rate patients and relatively scattered in high heart rate cases.

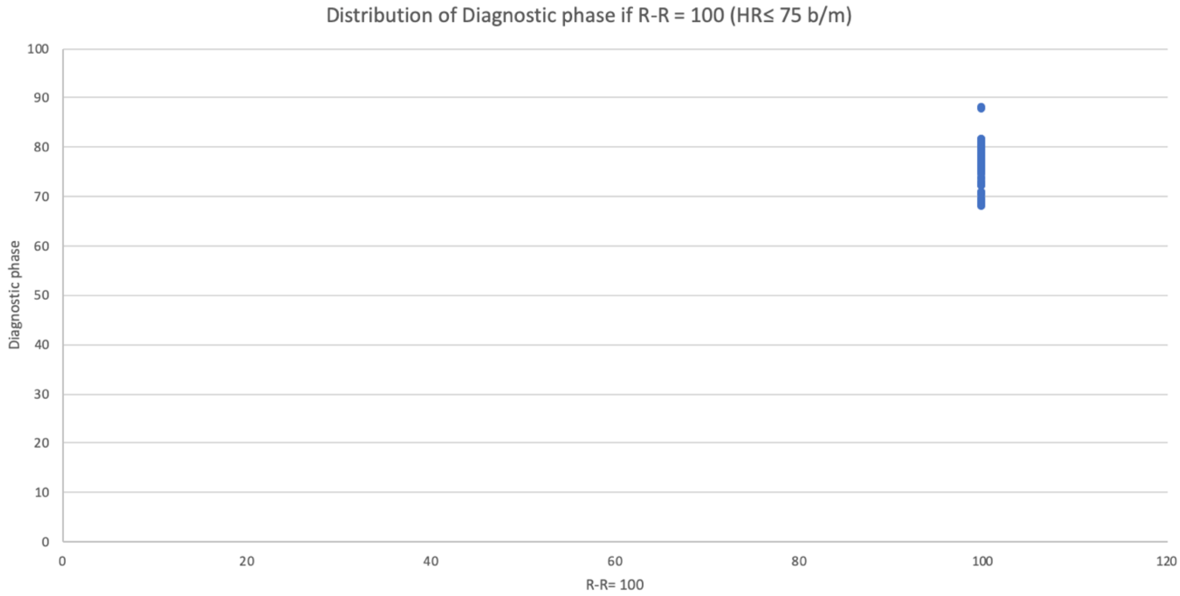


Figure 9: Distribution of diagnostic phase location if R-R= 100. in patients with HR ≤ 75 beats per minute.

The figure above attempted to visualize the distribution of the best image reconstruction point on an R-R scale in 98 patients having heart rate ≤ 75 beats per minute. Here it is clearly visible that most of the points are closely aggregated between 66% to 82% of the R-R interval. And the mean distribution is 74 ± 4 (SD) (Figure 9). Three patients show reconstruction above the range. It is also observed that among the 98 patients, the optimal image was found before the P wave in 62 patients (63.26%). And 19 cases (19.39%) found over the P wave and 9 cases (9.18%) after that. Image at the end of the T wave was found in only 8 cases (8.16%).

Also, the second group is as follows.

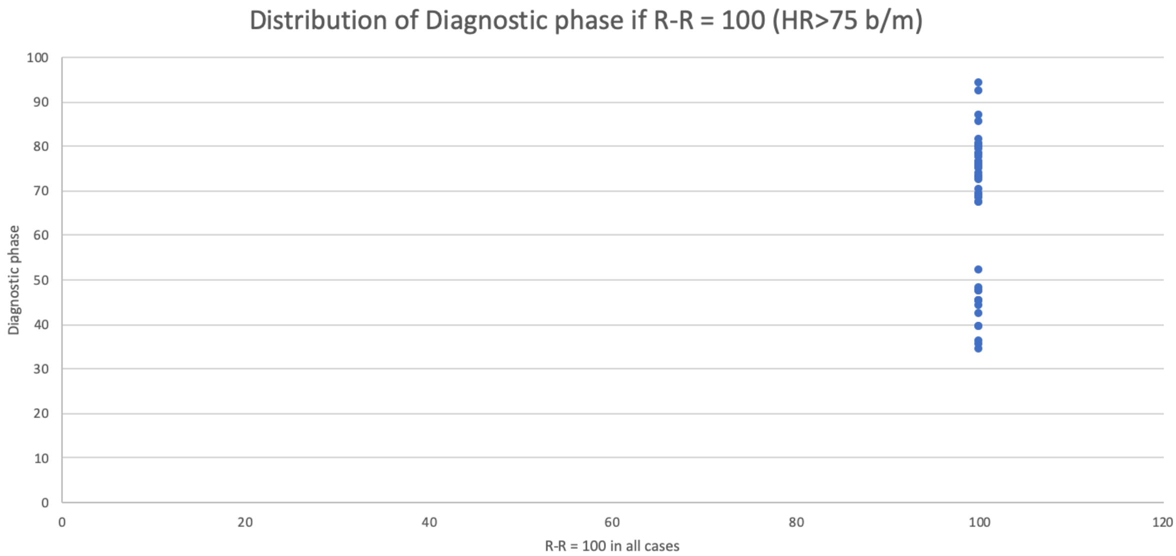


Figure 10: Distribution of diagnostic phase location on R-R length in patients with HR > 75 beats per minute.

The figure above attempted to visualize the distribution of the best image reconstruction point on an R-R scale in 30 patients having heart rate > 75 beats per minute. (Figure 10). Here it is clearly visible that most of the points are irregularly scattered though the frequency is observed at QT. And the mean distribution is 61 ± 18 (SD) (Figure 10). It could be mentioned that, among the 30 cases, reconstruction phase of the 9 cases (30.0%) were after the T wave, 8 cases (26.67%) were at the slope of T wave, 3 cases (10.0%) were at the end of the T wave, 2 cases (6.67%) were over the T wave, 3 cases (10.0%) were before the T wave, 1 case (3.33%) over P wave and lastly 4 cases (13.33%) showed before P wave.

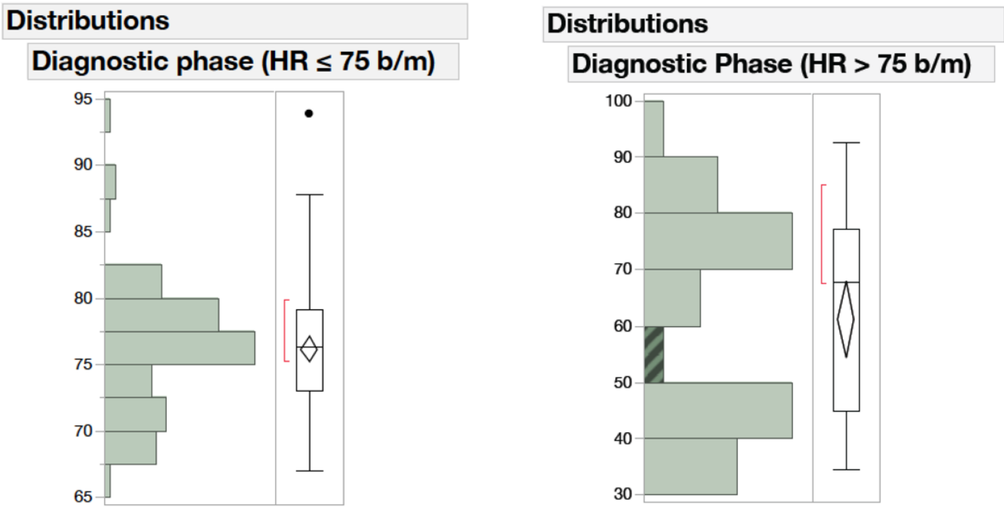


Figure 11 Distribution of the diagnostic phases in two groups.

The distribution charts showing that the mean diagnostic phase is 74 ± 4 (SD) in patients having HR ≤ 75 b/m and 61 ± 18 (SD) in patients having HR > 75 b/m. So, the distribution is scattered in higher heart rates. One patient has the diagnostic phase at 93%. (Figure 11).

The chart below shows the relation between R-R interval and the Reconstruction phase. Here we see that they appear symmetrical on the left side which is asymmetrical on the right side. (Figure 12). The horizontal numbers indicate the patients' serial number arranged per heart rate. That means, up to the first 98 patients the heart rate was ≤ 75 beats per minute and after that the heart rate was higher. It is clearly seen that the relation became asymmetrical when the heart rate became very high.

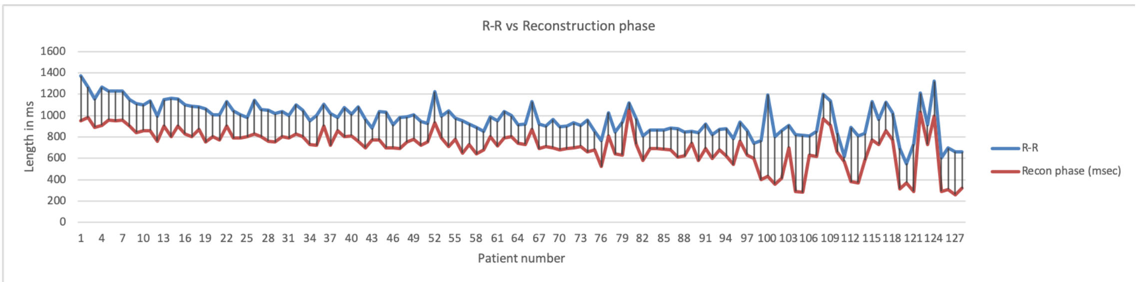
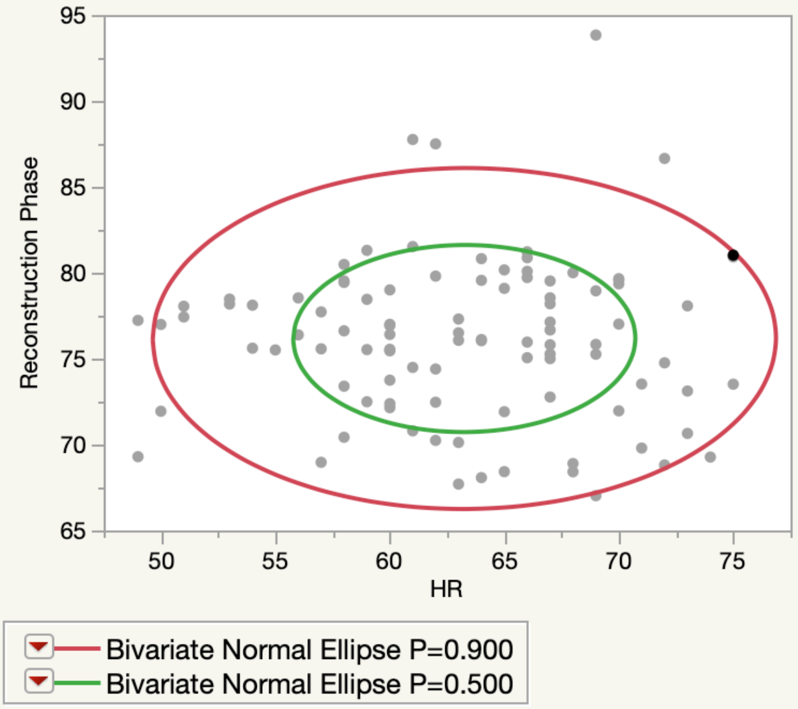


Figure 12 Comparison of R-R interval with Reconstruction phase.
(R-R = Blue; Reconstruction Phase = Red)

As the heart rate increases the reconstruction phase moves to QT instead of PR. However, the rules are very scattered for high heart rate patients as the reconstruction phase can even be observed in PR interval.

Bivariate Fit of Reconstruction Phase By HR



Bivariate Normal Ellipse P=0.900

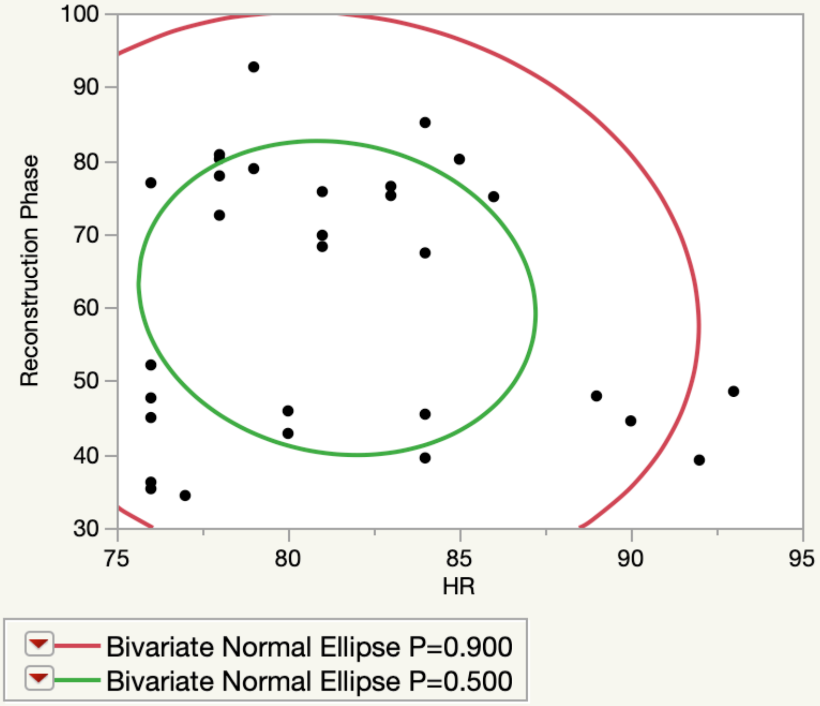
Variable	Mean	Std Dev	Correlation	Signif. Prob	Number
HR	63.2551	6.342966	0.005009	0.9610	98
Reconstruction Phase	76.17021	4.624309			

Bivariate Normal Ellipse P=0.500

Variable	Mean	Std Dev	Correlation	Signif. Prob	Number
HR	63.2551	6.342966	0.005009	0.9610	98
Reconstruction Phase	76.17021	4.624309			

Figure 13 Bivariate Fit of Reconstruction Phase by Heart Rate for the patients who have heart rate ≤ 75 beats per minute.

Bivariate Fit of Reconstruction Phase By HR



Bivariate Normal Ellipse P=0.900

Variable	Mean	Std Dev	Correlation	Signif. Prob	Number
HR	81.43333	4.917831	-0.09903	0.6026	30
Reconstruction Phase	61.25397	18.14525			

Bivariate Normal Ellipse P=0.500

Variable	Mean	Std Dev	Correlation	Signif. Prob	Number
HR	81.43333	4.917831	-0.09903	0.6026	30
Reconstruction Phase	61.25397	18.14525			

Figure 14 Bivariate Fit of Reconstruction Phase by Heart Rate for the patients who have heart rate ≥ 75 beats per minute.

The above two figures show that the density ellipsoid is more circular when the heart rate is ≥ 75 beats per minute meaning that there is less correlation between the variables in higher heart rates. (Figure 13 and 14).

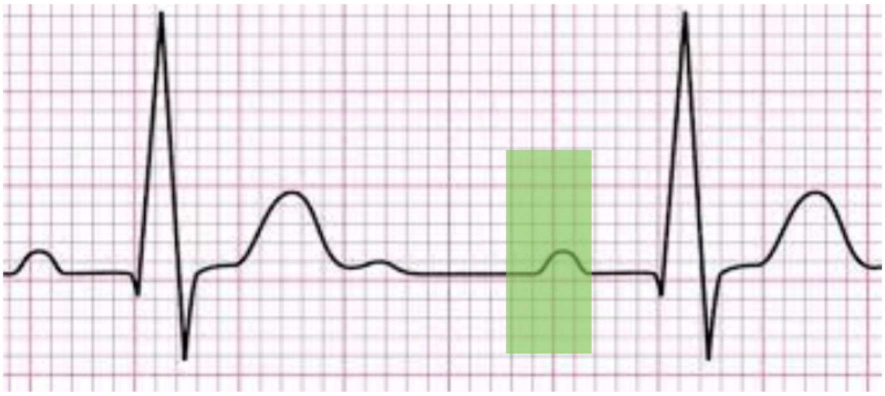


Figure 15 Suitable zone of getting the reconstruction phase for patients with HR ≤ 75 beats per minute.

After analyzing the data, it is assumed that the most frequent location of getting the best image is around the P wave if the heart rates are ≤ 75 beats per minute. This is a small portion of the whole cardiac cycle which is actually responsible for necessary image formation in most of the cases. (Figure 15).

CHAPTER 5 RESULT

Among the 128 patients 98 were men and 30 women, age 67± 12 years (mean ± standard deviation)]. Age range: 30–87 years and their mean HR during the examination was 67 beats/min (range: 49–93 beats/min).

Our result shows that when the heart rate is ≤ 75 beats/min the best reconstruction phase is found at PR (66% to 82% of the R-R interval) which is the diastolic phase of the cardiac cycle. But if the heart rate is > 75 beats/min then the reconstruction phase is found irregularly at QT of the ECG wave. In detail, for the first group of patients the optimum quality image was found before P wave in 63% cases, over P wave at 19% cases, after the P wave at 9% cases and end of the T wave is at 9% cases. Prospective scan affirms diagnostic phase if the heart rate is lower. Therefore, the optimal necessary image for making the diagnosis was found at PR for the patients having heart rate ≤ 75 beats/min and on QT for the patients having HR > 75 beats/min.

CHAPTER 6 DISCUSSION

Detection of Reconstruction phase in real time can provide the exact cardiac phase [67]. And visibility of the coronary vessels highly depends on heart rate [88]. Another study revealed that there is a relation of the reconstruction phase when the HR is slower and for getting the best image quality the maximum heart rate should have to be 65 beats/min [42], [88]. Due to the advancement of the faster scanners it became possible to extend the limit of this range. This study revealed that when the heart rate is ≤ 75 beats/min the reconstruction phase is observed at the diastolic phase with FIRST which was similar to some other studies except their highest range of heart beat was lower [17], [42], [58], [88], [105]. P. A. Araoz *et al*. divided the two groups of patients at 70 beats per minute level [60]. But due to use of faster scanner limit could be raised. Therefore, the heart rate range is raised from 65 to 75 beats/min. And we found that the faster scanners are capable to give similar findings among this patient group with relatively higher heart rates [19], [103]. Therefore, this study extended it up to 75 beats/min. This finding is similar to another study using dual source CT angiography except their maximum heart rate range was below than our study [88], [104].

ECG gating with a 64 Slice CT scanner provided useful phase detection for a wide range of heart rates [59]. And ECG gating increases the image quality even in the pediatric patients [20], [131]. This study included a 320 Slice scanner with ECG gating which helped to increase the range. The collected data on the ECG graph (R-R mean) were tabulated with the reconstruction phase along with the diagnostic phase. And it revealed a regular correlation stated in charts above. In 62 patients the best reconstruction phase was seen to be placed just before the P wave, in 19 patients reconstruction phase was just over the P wave, in 8 patients it was observed after the P wave and in another 8 patients the best image was formed at the end of the T wave who have relatively higher heart rates.

P. A. Araoz *et al*. found that for low heart rate patients the best image sharpness is observed at 65% to 70% of the reconstruction phase and for high heart rate patients the range is 35% to 45% [60]. However, in this study the range is 63% to 83% for the patients having heart rate less than 75 beats per minute. And for the high heart rate patients there is no specific range found rather the best quality image was observed at different ranges which could not be bracketed by a specific range. The above group also studied on 4 vessles including the right coronary artery (RCA), left main (LM), left anterior decending (LAD) and circumflex (Cx) arteries but this study evaluated every segment of all of the coronary vessels. The study also excluded phases below 25% and above 75% for reconstruction, however, our study included the full range for getting the best phase for quality image. The study also made a score system of their own to classify image quality, however, our study attempted for the best one rather than making gradation for low category images.

The reconstruction phase data for the 98 patients who have heart rate ≤ 75 beats/min were plotted over a chart and the distribution appears homogenous. But the second group of 30 patients who have heart rate higher than 75 beats/min didn't show similar findings, rather they are located at Q-T of the cardiac cycle. Some of the cases followed the reconstruction phase with end-systolic and early-diastolic intervals in patients having high heart rate though they used lower slice CT scanner equipment [58], [59]. The software used in different studies for reconstruction was sometime different [59]. However, the expected image quality could be achieved through reconstruction though the phase location varies in patients with high heart rates [19]. This findings is similar to another study where their projection was above 65 beats/min [130]. So, it could be concluded that when the heart rate is higher the reconstruction phase location can be scattered though most of them are at the systolic phases. However, high-pitch dual-source CT angiogram may be performed for patients having heart rate less than 70 beats/min for optimum image quality [103]. The R-R mean is also compared with the reconstruction phase and the diagnostic phase. It appears that they are proportionate to each-other. The lower the heart rate the higher the R-R mean as well as the diagnostic and reconstruction phase.

In-stent restenosis by CT angiography has modest diagnostic accuracy [66]. Reconstruction phase in patients having coronary stents revealed similar findings in respect of heart rate irrespective of restenosis.

It is known that Iterative Reconstruction markedly improves image quality and does not affect radiation dose [20], [35], [131], [132]. And FIRST can reduce the radiation does significantly [34], [38], [61], [132], [133]. Also the FIRST method improves the detection of coronary plaque [134], [135]. So it is was the method of choice as an upgraded solution for this study though adaptive statistical iterative reconstruction method could balance image quality with other radiation parameters [136], [137].

There was some limitation of the study from the ECG software side. The ‘ECG Viewer’ software is a special software that can measure the various aspects of the ECG wave as well as x ray exposure and detection of the location of the reconstruction phase. However, it does not save the time of scan of the CT scanner machine, rather it saves its own time. So, we had to keep the time records manually for every patient. This problem could not be solved as the ECG viewer is not a part of the CT scan machine and the software companies for the CT scan and ECG viewer are different. We also excluded patients who performed helical scan. And radiation doses were not measured in this study.

CHAPTER 7 CONCLUSION

There is a positive correlation of the reconstruction phase with the specific cardiac phase in patients having heart rate ≤ 75 beats per minute in an advanced setting irrespective of R-R mean. The optimally necessary images were obtained at P-R or the diastolic phase of the cardiac cycle in patients with HR ≤ 75 beats/min or from 66% to 82% of the R-R interval. And if the HR is more than 75 beats/min, the reconstruction phase shifts to QT or at the late systolic phase of the cardiac cycle. We can set a protocol targeting this specific portion of the cardiac cycle that would reduce the radiation dose further. We also can set an auto-reconstruction mode in future CT console software that could narrow down the radiation dose, reduce the radiologist's effort as well as the diagnosis time.

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