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Evaluating the Accuracy of 128-Section Multi-Detector Computed Tomography (MDCT) in Detecting Coronary Artery Stenosis

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Thesis Approval

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Dedication

This Research is Dedicated to

My Dear Parents, beloved wife, Instructors, and Colleagues

Declaration

I certify that this thesis submitted for the degree of Master is the result of my research, except where otherwise acknowledged, and that this study (or any part of the same) has not been submitted for a higher degree to any other university or Institution.

Mutasem Mohammad Rafiq Kmail

Signed:

Date: 2nd/06/2022

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Mutasem Mohammad Rafiq Kmail

Abstract

Coronary Artery Disease (CAD) is the main cause of death around the world. Many techniques are used for diagnosing and detecting the disease which are classified into invasive and non-invasive techniques. One of the most popular non-invasive techniques is Multi-detector Computed Tomography (MDCT) which has been employed in aiding the analysis of coronary illness. Although MDCT is used as an alternative for invasive coronary angiography to reduce possible risks, there is a debate about its accuracy in diagnosing the existence or absence of the disease. Therefore is a need to evaluate the accuracy of MDCT in CAD detection. So, this study aims to evaluate the accuracy of 128-section MDCT in comparison with Catheter-Based Coronary Angiography (CCA) as a standard reference in the identification of significant CAD. In order to achieve this goal, 128-section MDCT and CCA reports are collected for 65 patients in order to be compared in which CCA reports play the role of the gold standard. The produced results showed that 128-section MDCT has high diagnostic accuracy for both per-patient and per-artery analysis. For per-patient analysis sensitivity, specificity, PPV and NPV values were 96.8%, 97%, 96.8%, 97% respectively. In addition, the research results were compared with the results of previous studies and showed that accuracy measures except PPV nearly the same on per-patient basis. The false-negative results appeared due to poor opacification or motion blur. Accordingly, this research concludes that 128-section MDCT could replace invasive coronary angiography particularly for patients who couldn't do surgeries or have coagulation disorders and expanded vessels.

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Abbreviations

Abbreviation	Definition
CT	Computed Tomography
CAD	Coronary Artery Disease
MDCT	Multi-Detector Computed Tomography
CCA	Catheter-Based Coronary Angiography
ECG	Electrocardiogram
PPV	Positive Predictive Value
NPV	Negative Predictive Value
CCS	Chronic Coronary Syndrome
ACS	Acute Coronary Syndrome
NSTEMI	Non-St Elevation Myocardial Infarction
STEMI	St-Elevation Myocardial Infarction
UAP	Unstable Angina Pectoris
MI	Myocardial Infarction
ICA	Invasive Coronary Angiography
ESC	European Society Of Cardiology
MRI	Magnetic Resonance Image
CTA	Computed Tomographic Angiography
PET	Positron Emission Tomography
mAs	Milliampere-Seconds
kVp	Peak Kilovoltage
mm	Millimeter
S	Seconds
CV	Cardiovascular
PTP	Pre-Test Probability
DLP	Dose Length Product

CTDIvol	Volume Computed Tomography Dose Index
LMCA	Left Main Coronary Artery
CX	Circumflex Artery
LAD	Left Anterior Descending Artery
RCA	Right Coronary Artery
No	Number

Chapter 1

Introduction

1.1 Background of the Study

Coronary Artery Disease (CAD) is one of the most popular diseases around the world. It is also called coronary heart disease or ischemic heart disease [1]. It is accompanied by an atherosclerotic narrowing of the coronary arteries, which can cause a supply-demand mismatch in myocardial blood perfusion [2]. CAD is caused by plaque buildup in the walls of coronary arteries that supply the heart. In this context, plaque means the deposits of cholesterol and other materials in the arteries leading to what is called atherosclerosis which is terminology that is used for describing the narrowing down of arteries leading to blood flow blocking [3].

The CAD has many symptoms including chest pain, discomfort, and Angina. Angina happens when arteries become very narrow due to too much buildup of plaque-causing to block blood flow to the heart [4]. CAD is considered a leading cause of death around the world [5]. Accordingly, optimal diagnosis and detection techniques are invented. These techniques are classified into invasive and non-invasive techniques. On one hand, an invasive procedure means surgery, which means that skin is broken. Although some see this as a demerit, others consider this technique is good as it produces long-term results. On the other hand, non-invasive means that skin will not be broken and scars are not left. The non-invasive technique can be used for CAD detection using different methods including Multi-Detector Computed Tomography (MDCT). Non-invasive is popular nowadays, due to the fact that it is good for in operative patient [6].

As for invasive technique, for a very long-time catheter angiography has been the highest quality level of coronary angiography. However, it may cause risks for patients with coagulation disorders and expanded vessel delicacy and it is contraindicated in a few patients [7]. Thus, there was a need for finding a sheltered and dependable screening methodology for the assessment of coronary supply routes [8, 9]. Accordingly, MDCT (non-invasive technique) has been employed in aiding the analysis of coronary illness which means that there is a need for evaluating to what extent MDCT can replace CCA (invasive technique) for patients who can't undergo surgeries, and who suffer from coagulation disorder and expanded vessel delicacy. This can be done by evaluating the accuracy of MDCT against CCA as standard reference as proposed in this thesis.

Image acquisition in MDCT can be done as either sequential imaging or spiral imaging [10]. In sequential imaging, the Electrocardiogram (ECG) trace initiates the CT scan after a specific amount of time determined by the operator after the R-wave. While in spiral imaging, the CT data and ECG trace is captured together at the same time. After acquiring the CT images, motion artifacts are decreased to enhance the image quality even for patients with quick heartbeats [10, 11]. Cardiac MDCT imaging can be done using 64-slice MDCT and above [12, 13]. Many studies have compared these technologies. For example, Chua, S.K., et al approved that the 256-slice MDCT is more accurate and has a shorter scanning time than 64-slice MDCT. On the other hand, Madhok et al. assessed 128-slice MDCT and concluded that it is a good method for detecting coronary artery anomalies. In addition, they revealed that it is good in capturing modality for patients who avoid doing invasive angiography such as patients with equivocal stress test results [14].

Given previous scenario this dissertation focuses on evaluating the accuracy of 128-slice MDCT in comparison with CCA as a gold standard for patients with suspected CAD from Palestine.

1.2 Problem Statement

Due to the ongoing debate on which is better to go for Cardiac catheterization and coronary angiography or Multi Detector Computed Tomography (MDCT) in order to detect CAD, many researchers have assessed both modalities and they found that the diagnostics capabilities of the two exams are equivalent [9, 12]. However, there is still a need for more research work that explores to what extent MDCT (particularly 128-MDCT) could replace CCA, particularly for patients who prefer MDCT over CCA for CAD scanning as it is a non-invasive technique. In addition, there is a need to create a comparative analysis between the results previous studies that evaluated the accuracy of MDCT in CAD detection.

Although Cardiac catheterization and coronary angiography are generally considered to be safe procedures, they have some risks associated with the following: (1) hematoma which is generated due to bleeding under the skin at the wound site, (2) bruising which usually lasts for a few weeks in arms or groin, (3) damage at the artery in the arm or groin where the tube of cardiac catheterization is inserted, (4) heart attack where heart blood supply is blocked, (5) stroke where blood flow to the brain is blocked, (6) tissue damage if x-ray radiation is prolonged (7) death [15]. According to the above-mentioned risks of CCA, MDCT is considered a gatekeeper and first-line test for patients who couldn't undergo CCA or who don't prefer invasive diagnostic of CAD. Therefore, there is a need to investigate their ability to diagnose CAD using MDCT instead of using CCA. This will be done by evaluating the accuracy of 128-MDCT in CAD detection for patients in Palestine as a case study which will help in improving the detection accuracy of CAD and consequently will improve health care for Palestinians in general.

1.3 Justification

Coronary Artery Disease (CAD) is the main cause of death and morbidity around the world [5]. Each year CAD causes an estimated 17 million deaths worldwide, accounting for one-third of all deaths worldwide. More than one-third of these deaths occur in middle-aged adults[16]. The coronary artery may lead to ischemic heart disease, also it may cause luminal stenosis [7]. CAD can be detected using various methods including MDCT and coronary angiography. MDCT is a very fast type of CT scan. Also, MDCT creates images of the healthy and diseased parts of the heart. These images can be viewed from any angle and can help doctors find problems in patient's heart structure and in how the heart pumps blood.

Many researchers have assessed both methods and found that the diagnostics capabilities of the two exams are equivalent [9]. However, there is still a need for more research work that explores to which extent MDCT (particularly 128-MDCT) can replace CCA, particularly for patients who prefer MDCT over CCA for CAD scanning as it is a non-invasive technique.

Accordingly, this research focuses on evaluating 128-slice MDCT in comparison with CCA as a standard reference in two similar populations for patients from Palestine in order to enhance the diagnostic performance in the detection of obstructive coronary artery disease. Motivated by the fact that CAD constitutes the leading cause of death in the world, posing significant challenges.

1.4 Study Aim and Objectives

This research aims to evaluate the accuracy of 128-section MDCT in comparison with CCA as a standard reference in the identification of significant CAD. This can help in improving the detection accuracy of CAD and consequently helps in providing better health care for Palestinian patients who are living with resources under occupation. To meet this aim the following objectives are pursued:

1- Investigate to what extent 128-section MDCT could replace CCA in significant CAD detection
2- Compare our produced accuracy measures for 128-slice MDCT with accuracy measures of previous studies

1.5 Study Question

To what extent can the non-invasive 128-section MDCT be an alternative for CCA in CAD detection?

Chapter 2

Literature Review

This chapter aims to provide a state-of-the-art survey that covers several topics including previous studies related to this study, coronary artery disease (CAD) and methods used for diagnosing CAD including invasive and non-invasive techniques. It starts with viewing and describing previous studies related to this study. Section 2.2 views a background about CAD. Section 2.3 describes in detail the methods used for detecting and diagnosing CAD including CCA (invasive technique), MRI, PET, and CT (non-invasive techniques).

2.1 Previous studies related to this work

Many studies have evaluated the diagnostic accuracy of 128- section multi detector computed tomography (MDCT) in comparison with invasive conventional coronary angiography (CCA) in coronary artery disease (CAD) detection [14, 18-20]. For example, the diagnostic accuracy of 128-multi detector row computed tomography coronary angiography (MDCTCA) in CAD detection is compared with invasive conventional coronary angiography (CCA) [18]. The researchers collected data about 42 patients who did both MDCTCA and CCA and the results were compared by experts. 128-slice MDCT (Brilliance 128, Philips Healthcare, Netherland) using prospective or retrospective electrocardiographic (ECG) gating was used for CT coronary angiography with the following parameters: 128 x 0.6 collimation, 0.3 sec rotation time, 120 kV tube voltage and 185 reference mAs [18]. The results showed that MDCTCA is excellent in CAD detection with high sensitivity of 100%, specificity of 93% and positive and negative predictive values of 87%, 100% respectively [18].

Moreover, the diagnostic accuracy of 128-slice MDCT was compared with CCA in CAD detection and the results showed that it is possible to assess CAD without invasive techniques using 128-slice MDCT [14]. The researches collected the data for 40 patients suffering from chest paint and suspecting having CAD. Beyond both CT coronary angiography and CCA are done for patients and their results were compared [14]. The CT coronary angiography was done for patients using SIEMENS 128-slice Dual Source Flash

Definition CT Scanner under either Retrospective or Prospective mode depending on the heart rate of the patient. The results showed high accuracy of 128-slice MDCT with sensitivity of 95.26%, specificity of 95.12%, positive predictive value of 88.46% and negative predictive value of 98.08% [14].

In [21], the authors have evaluated the accuracy of 128-slice MDCT for patients having ischemic heart disease. 128 slice CT coronary angiography was performed in 53 patients prior to conventional coronary angiography. The used device for scanning is 128 slice cardiac CT, SOMATOM definition as+ from Siemens. The results showed sensitivity of 95.45 %, Specificity of 91.66 %, Positive predictive value of 91.30 %, Negative predictive value of 95.65%.

Other studies have evaluated the accuracy of 64-slice MDCT [19, 20, 22]. For example, the diagnostic accuracy of 64-slice MDCT was evaluated in comparison with CCA [20]. The research included CT cardiac angiography for 70 patients suffering from chest pain. 64-slice MDCT scanner was used with the following characteristics: Sensation 64 Cardiac, Siemens Medical Systems, Forchheim, Germany [20]. The results of this study showed sensitivity of 90%, specificity of 95%, positive predictive value of 93% and negative predictive value of 93% [20] .

The diagnostic accuracy of 64-slice MDCT is also evaluated in [22] using a 64-slice MDCT-scanner (Sensation 64, Siemens Medical Solutions, Forchheim, Germany) with the following scanning parameters: slice collimation 32×0.6 mm, rotation time 0.33 ms, tube voltage 120 kV, tube current (effective mAs) 900 mA, and pitch 0.2 (3.84 mm table feed per tube rotation). The produced results showed high diagnostic accuracy with sensitivity of 96%, specificity of 69%, PPV of 92% and NPV of 82%.

Only 128 slice studies are summarized in Table 2.1 as follows.

TABLE 2.1. COMAPARATIVE ANALYSIS BETWEEN DIFFERENT SYSTEMS EVALUATED THE ACCURECY OF MDCT

Authors	Type of MDCT device	Accuracy measures
Chaosuwannakit, N., S. Kiatchoosakun, and P. Makarawate [18]	Brilliance 128, Philips Healthcare, Netherland	Sensitivity 100% Specificity 93% PPV 87% NPV 100%

Madhok, R. and A. Aggarwal. [14]	SIEMENS 128-slice Dual Source Flash Definition CT Scanner	Sensitivity 95.26% Specificity 95.12% PPV 88.46% NPV 98.08%
Sakthivel, D. [21]	128 slice cardiac CT, SOMATOM definition as+ from Siemens	Sensitivity 96%, specificity 69% PPV 92% NPV 82%

2.2 Coronary Artery Disease

CAD is one of the diseases that may cause death around the world. It is accompanied by an atherosclerotic narrowing of the coronary arteries, which can cause a supply-demand mismatch in myocardial blood perfusion [2]. Different clinical presentations can appear as a result of CAD, these presentations can be classified clinically as either chronic coronary syndrome (CCS) or acute coronary syndrome (ACS). In the CCS, an inadequate oxygen supply can lead to myocardial ischemia, which is typically recognized as chest discomfort.

The ACS is usually caused by thrombus formation due to erosion or rupture of an atherosclerotic plaque and is often presenting with chest discomfort or chest pain. The ACS is clinically classified as non-ST elevation myocardial infarction (NSTEMI), ST-elevation myocardial infarction (STEMI), and unstable angina pectoris (UAP) [12, 13].

"A myocardial infarction (MI) is either a STEMI or NSTEMI and is defined as the presence of acute myocardial injury detected by significantly increased cardiac biomarkers, preferably troponins, in the setting of typical symptoms and/or evidence of acute myocardial ischemia (12). While both a STEMI and NSTEMI diagnosis require elevated troponin, the conditions are being distinguished based on electrocardiogram (ECG) characteristics, since a STEMI presents with a persistent ST-segment elevation, while an NSTEMI may or may not have other ECG characteristics indicative of ischemia" [12, 23].

A UAP event is considered to be present in patients with ACS symptoms, with or without ECG changes indicative of ischemia, but without elevated troponin over the decision limit. Thus, an NSTEMI and a UAP differ primarily in if the myocardial ischemia is severe enough to result in elevated troponins [13, 24].

A CCS is associated with recurrent symptoms indicative of ischemia, and such a diagnosis may be based on typical patient history, assessment of cardiovascular risk factors, and physical examination. If a CCS diagnosis needs to be verified, pre-test probability (PTP) models can be applied. Such models estimate the PTP of obstructive CAD, thereby supporting the clinical decision whether to proceed with further non-invasive imaging or invasive coronary angiography (ICA). Guidelines from the European Society of Cardiology (ESC) recommend the PTP model to be based on age, sex, and nature of symptoms [25], whereas U.S. guidelines use more than one PTP model. While the ACS is caused by an epicardial arterial obstruction mechanism, some CCS may be caused by microvascular disease, which can be difficult and complex to diagnose with conventional methods [26]. The manifestations of CAD may be stable for long periods, such as in CCS, but a plaque rupture or erosion may provoke an acute presentation such as in an ACS. Therefore, CAD is to be considered a dynamic process, which may cause various clinical presentations over time [27].

The CAD can result in different clinical presentations and is clinically categorized as either CCS or acute ACS [28]. For many people, the first clue that they have CAD is a heart attack. Symptoms of a heart attack include chest pain or discomfort (angina), light-headedness, weakness, feeling sick to your stomach, or a cold sweat, pain or discomfort in the arms or shoulder and shortness of breath.

2.3 CAD Diagnostic Methods.

CAD can be diagnosed using various tests including ECG or EKG, Echocardiogram, Exercise stress test, Chest X-ray, Cardiac catheterization, Coronary angiogram, Coronary artery calcium scan, Magnetic Resonance Imaging (MRI), and Multi-detector computed tomography (MDCT).

Many studies have compared the use of these tests. For example, ECG is used for measuring characteristics of heartbeat such as rate, regularity, and electrical activity [29].

Although this test is safe, most of the time it is normal or nearly normal with coronary artery disease. An echocardiogram, a image of the heart based on ultrasound waves is created using a handheld wand placed on the patient's chest [30]. This test is also safe, but if contrast injection is used, complications may happen such as an allergic reaction to the contrast [31]. Exercise stress test measures how well your heart works when it needs to pump more blood by measuring heart rate while the patient walking on a treadmill. This test has some rare risks such as chest pain, collapsing, and fainting. Chest X-ray is used for creating a image of the heart and other organs in the chest region. Although it is painless and non-invasive, it has a small risk due to using a small amount of radiation [32]. Cardiac catheterization is used for checking the blockage of arteries based on inserting a tube to reach the patient's heart. This method has many risks such as bleeding, infection, bruising at the catheter insertion site, and heart attack [33]. In a Coronary angiogram test, blood flow blockage is monitored using an x-ray that detects dye injected via cardiac catheterization. This procedure has risks associated with radiation exposure, heart attack, infection, and excessive bleeding. Regarding Coronary artery calcium scan, it looks for calcium and plaque buildup using CT. As this method depends on a CT scan, it suffers from the risk of radiation exposure. MRI can also be used for detecting CAD. MRI is one of the emerging techniques in CAD detection. As no radiation is used in MRI, there is no risk of radiation exposure, but it can't be performed with patients having implanted pacemakers, intracranial aneurysm clips, or having metallic objects such as bullets, shrapnel, and surgical clips [34]. As for MDCT, it is also an emerging technique in CAD detection where computer software quantifies calcium in the coronary artery and calculates its score [9]. The calcium score of zero suggests a low chance of developing a heart attack in the future, while the higher calcium score suggests the higher risk of having CAD.

MDCT is considered a significant tool in CAD detection due to the fact that it helps in diagnosing the existence of CAD with high accuracy (around 90%) [9]. MDCT has several types including 16-section MDCT, 64-section MDC, 128-section MDCT, and others. 128-section MDCT provides a good temporal resolution, high scanning speed, and high resolution. Thus, in this dissertation, the accuracy of 128-section MDCT will be evaluated in comparison with CCA which is a procedure to detect heart problems. Cardiac MDCT imaging can be done using two basic modes of operation for image acquisition: prospective triggering and retrospective gating [8]. For sequential imaging, a prospective trigger is derived from the ECG trace to initiate the CT scan with user selected delay after the R-wave. In spiral imaging, the ECG trace is recorded simultaneously with collected CT data. Retrospective gating can be then used to select the spiral data for image reconstruction relative to a selected heart phase. When images are obtained in the diastolic cardiac phase motion artifacts are minimized, even in patients with faster heart rates [8].

2.3.1 Invasive Testing for CAD

Catheter angiography uses a catheter, x-ray imaging guidance, and an injection of contrast material to examine blood vessels in key areas of the body for abnormalities such as aneurysms and diseases such as atherosclerosis (plaque). Using catheter has the advantage of combining treatment and diagnosis in one operation together. Besides, it has other advantages summarized by its ability to produce clear, detailed and precise images of vessels that helps in identifying possible treatment. In order to create a catheter angiography for patients, a catheter is inserted into blood vessel through a small incision in the skin. The catheter then is guided to the area being examined, and after that the technician injects a contrast material through the catheter and captures images using a small dose of ionizing radiation (x-rays) [35].

Before doing CCA, patients need to be guided with different instructions including the following: (i) determination the type of food and drink during the last 24 hours before the procedure; (ii) patients to should be fasting last 6-8 hours before the procedure; (iii) patients should tell their doctors about their medical history and if they take any medicine; (iv) some medical tests are needed to be done before doing the operation including blood pressure [15].

However, this technique is invasive, expensive, and not without risks; it is associated with a major complication rate of 1.7% [36]. Up to 20% of diagnostic CCAs fail to show obstructive lesions, while only one-third are associated with a concurrent intervention [37]. In addition, patients with impaired kidney function, especially those who also have diabetes, are at a higher risk of complications.

2.3.2 Non-Invasive Testing for CAD

2.3.2.1 Magnetic resonance imaging (MRI)

MRI is a medical imaging technique used to form images of the anatomy and some physiological processes of the body [38]. This technique produces precise images of the internal organs of human's body by using special radio waves and large magnets. Special type of MRI is called Cardiac MRI which deals with diagnosing heart problems and ascertains that the cardiac system has no problems and working properly [34].

One of the main characteristics of MRI doesn't use radiation; hence it is painless for patients, and doesn't produce side effects on the long term. The obvious merits of MRI over current conventional nuclear-based cardiac-imaging techniques, such as positron emission tomography (PET) or myocardial scintigraphy, comprise its high spatial resolution and lack of exposure of the patient to ionizing radiation[38]. Also, quantification of cardiac morphology and function by MRI is more accurate and image quality is more reproducible than in echocardiography, However, MRI has some disadvantages such as the time needed for MRI is longer than that needed for CT. Besides, MRI is more expensive than CT. Also, MRI is usually less likely to be immediately available than CT. Thus, CT may be better in emergencies, such as serious injuries and stroke [34].

2.3.2.2 Positron Emission Tomography

A positron emission tomography is considered a strong test for heart muscle and is used for CAD detection. This is due to its ability to precisely measure blood flow between the heart muscle and coronary arteries [39]. Cardiac PET scan is done using the following process. At first, Rubidium-82 or Ammonia N-13 tracer, a small quantity of radioactive tracer is inserted to a vein. using The test is created while the patient at rest. After that, the PET scanner produces images by detecting the radiation of the tracer. During the test, an ECG is placed on the chest of the patient [40].

In order to do the test for patients, the patient should be fasting before the examination for 4-6 hours . Also caffeine should not present on their blood for 24 hours before the test. In PET scanning, the radiation is generally low and doesn't stays for long in the patient body. Pregnant and breastfeeding should tell their doctors before doing the test, Also . Babies and infants are more sensitive to the radiation of the test as they are in a adult patients . Some people are affected by the PET test by having redness at the site of the injection, or some of them have pain [40].

2.3.2.3 Computed tomography (CT)

Computed tomography (CT) is usually described as a breakthrough medical imaging technique in medicine since its launch in the early 1970s. CT involves a rotating X-ray tube and detectors in conjunction with a computer that processes the internal organs and structures and creates cross-sectional and three-dimensional images. In comparison to X-ray radiography, it provides a high-quality image, contrast, and more details that can cover wide regions of the patient's body. The cost of the CT examination is fair the procedure is simple and easy to execute [41]. The CT scan is extremely helpful, as several various kinds of tissue such as lungs, heart, bones, soft tissues, muscles, and blood vessels can be viewed simultaneously [42]. With constant and wide enhancements in efficiency, resolution, accuracy, and speed the number of CT scanners is growing drastically. However, there is a growing concern and anxiety regarding the dangers of such radiation exposure. Radiation-induced cancer is a probabilistic (stochastic) effect. CT is correlated with high radiation exposure increasing the risk of developing cancer, although even lower doses of radiation might cause carcinogenesis [42].

Computed tomographic angiography (CTA) is a general expression exploited to refer to noninvasive imaging of the arteries with various types of CT machines, such as Multi Slice CT (MSCT), Multi Detector CT (MDCT), and dual-source CT (DSCT). The use of CTA has increased over the years due to advances in technology and the rapid diffusion of machines outside the hospital settings[34]. The initial single slice CT machines produced poor-quality images. In the late 1990s, 4 slice CT machines were introduced, with 16 slice and 64 slices CT machines following shortly afterward. Image quality and performance reportedly enlarged with each model. However, inquiries remain on the indications for use. A particular focus has been the use of CTA for the evaluation of the coronary arteries in patients with chest pain. People against CTA have declared that cardiac CTA may decrease the need for invasive coronary angiography for specific patients. Critics have pointed out the lack of evidence on outcomes and the limitations to the technology including uninterpretable/unassessable segments and the health risks from the considerable radiation exposure [43].

CTA procedure can starts with injecting a special dye through Intravenous (IV) in the arm or hand. The injected material is called contrast material as it lights up the blood vessel and tissue. Then, a CT scan which is a type of X-ray using computer is done. Cross-sectional images are produced and processed for diagnosis by the computer [43].

Chapter 3

Materials and Methods

This chapter introduces the methods, study design and implementation details of the approach for evaluating 128-Section Multi Detector Computed Tomography (MDCT) in detecting the Coronary Artery Stenosis. Different statistical measures are used for assessing accuracy including sensitivity, specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) . Section 3.1 introduces the study design and image acquisition. The details of analyzing 128- section MDCT and CCA image are described in section 3.2, in addition to the implemented statistical measures for analyzing data.

3.1 Study Design and Image Acquisition

3.1.1 Ethical approval

The study proposal was submitted to Al-Quds University research Ethics Committee to obtain approval and permission to conduct the study. The approval was obtained on 16/2/2021 under the number 170/REC/2021 as shown in Appendix 1. The Research Ethics Committee confirmed that this research is in accordance with the research ethics guidelines at Al-Quds University.

3.1.2 Study population

The population of this retrospective study consists of 65 patients with suspected CAD having the following symptoms (chest pain, abnormal stress test, multiple cardiovascular risk factors including diabetes mellitus (DM). These patients presented to Istishari Arab Hospital a private medium size Hospital between 2017and 2022 because of suspected CAD. In order to get the required data, an ethical approval was obtained and approved by ethics committee at Al-Quds University as detailed in the previous section.

3.1.3 Study sample size

The 65 patients including (55 male and 10 female) were evaluated. The average age is 56.2 years old. The youngest patient was 27 years old and oldest was 82 years old.

3.1.4 Data Collection

Data about the Patient's age, radiologists' reports, and MDCT images were extracted from the patient files for each participant in the study.

3.1.5 Inclusion and exclusion criteria

Inclusion criteria for patients included both male and female suffering from mild to intermediate symptoms of CAD , all ages also were included . All patients underwent both CTA and CCA were included

Exclusion criteria for MDCT included the presence of multiple ectopic beats, atrial fibrillation, pregnancy, renal failure, and a history of allergic reaction to iodine-containing contrast agents.

3.1.6 Study device and instruments

Philips 128-slice Single Source Ingenuity Core CT device is used in this study. The scanning parameters are shown in Table 3.1. Dose modulation was attained with electrocardiographic gating for a maximum gantry delivery between 40% and 80% during the R-R interval. A bolus of 70-80 ml of contrast madia (Omnipaque™ (iohexol) 350 mg/ml) was administered intravenously at flow rate 5 ml/sec, followed by 20 ml of saline injected at the same infusion rate. The scan was initiated according to the bolus-tracking technique. Image data sets were analyzed using multi-planar reconstruction on retro-processing workstations (CardioQ3 package, Advantage Workstation version 4.2, GE Healthcare, Milwaukee, WI). Oral/ intravenous Beta-blockers were used wherever required. After the scan, the system generates the best systolic, diastolic, and 0 to 100% of the cardiac cycle for ejection fraction. This data was transferred to the Syngovia workstation for PostProcessing.

Regarding the devices used for creating CCA, two devices are used: Philips Allura Centron and Philips Allura Clarity.

TABLE 3.1 PROTOCOL PARAMETERS IN THE HOSPITAL

Protocol parameter	Value
Scan mode	Helical
Thickness	0.8 mm
kVp	120
Gap	0.4
mAs	55
Rotation time	0.4 second
Collimation	Auto
Pitch	0.32
DLP	56.2mGy*cm
CTDIvol	3.7mGy

3.2 Data Analysis

3.2.1 128-MDCT image analysis

All 128-slice MDCT images were analyzed by four experienced radiologists with more than 10 years of experience and they were blinded to the results of CCA.

3.2.2 Conventional Coronary Angiography (CCA)

All patients did CCA according to the ordinary and standard techniques. Images were evaluated by experienced cardiologists blinded to 128-MDCT images.

3.2.3 Statistical Analysis

For the statistical manipulation of our data; simple descriptive statistics such as count, maximum, minimum, percentages and means were used to provide summary about study population. In addition, Chai square test is used to measure statistical significance between the results of 128-MDCT and CCA. The statistical analysis was carried out using Microsoft Excel and SPSS.

In addition, the CCA was used as a standard reference (gold standard) for evaluating the diagnostic accuracy of 128-slice MDCT based on four statistical measures including sensitivity, specificity, NPV, PPV. These calculations are calculated using SPSS software version 28.0.1.1.

Diagnostic performance was evaluated on per-patient basis and on per-artery basis. For per-patient analysis, a true positive was defined as having one positive result (>=50% lumen diameter narrowing) in both CT coronary angiography report and Cath report regardless of location [44].

For per-artery analysis, the results were classified as normal artery or not normal for each of the following arteries: Left Main coronary artery (LM), Circumflex artery (CX), Left Anterior Descending artery (LAD), and Right Coronary Artery (RCA). A true positive is defined as having “not normal” result in both CT coronary angiography report and Cath report.

The following statistical measures "sensitivity", "specificity", "PPV" and "NPV" are used in analyzing the collected data in order to extract final statistical calculations and results.

Sensitivity: it refers to the proportion of patients who received a positive result on a test (128-section MDCT) out of those who have the condition (CAD).

Sensitivity=TP/(TP+FN)

Where TP: True Positive, FN: False Negative

Specificity: it refers to the proportion of patients who received a negative result on a test (128-section MDCT) out of those who do not have the condition (CAD).

Specificity=TN/(TN+FP)

Where TN: True Negative, FP: False Positive

PPV: the positive predictive value is the probability that following a positive test (128-section MDCT) result, that individual will truly have that specific disease (CAD).

Positive Predictive Value(PPV)=TP/(TP+FP)

NPV: the negative predictive value is the probability that following a negative test (128-section MDCT) result, that individual will truly not have that specific disease (CAD).

Negative Predictive Value (NPV)=TN/(FN+TN)

Chi square test: is used to compare two variables and see whether distribution of categorical variables differ from each other.

One-Sample t-test: the one-sample t-test compares the mean of a single sample to a predetermined value to determine if the sample mean is significantly greater or less than that value.

Chapter 4

Results and Discussion

This chapter shows the produced results from this study work that aimed to evaluate the accuracy of 128-MDCT in significant CAD detection for patients in Palestine. Besides, it compares the produced results with results of previous studies. In addition, it discusses to what extent 128-section Multi Detector Computed Tomography (MDCT) could replace CCA in CAD detection.

A total of 65 patients including (55 male and 10 female) were considered in the study. The youngest patient was 27 years old and the oldest was 82 years old. The mean age of the study population was 56.2 years.

A total of 65 patients , 15 patients (23%) had a calcium score of more than 400 with the highest value was 2983. The mean CT coronary calcium score was 345.1 Agatston units.

4.1 Accuracy of 128-section MDCT in Significant CAD Detection

Accuracy measures for the detection of significant CAD disease is evaluated on per-patient analysis and on per-artery analysis as detailed below.

4.1.1 Accuracy measures for per-patient analysis

Table 4.1 shows accuracy measures of per-patient analysis; in 31 patients 128-MDCT correctly identified the presence of CAD (True positive), in 32 patients also 128-MDCT correctly identified the absence of CAD (True negative). However, the result of 128 MDCT revealed the absence of CAD in 1 patient, while in reality according to CCA result he had CAD (False negative). Moreover, the result of 128 MDCT revealed the presence of CAD in 1 patient, while in reality according to CCA result; he had not CAD (False positive).

Accordingly the sensitivity value is 96.8% (31/(31+1)), Specificity is 97% (32/(32+1)), positive predictive values (PPV) is 96.8% (31/(31+1)) and negative predictive value (NPV) is 97% (32/(32+1)).

TABLE 4.1. ACCURECY MEASURES FOR PATIENT-BASED ANALYSIS

Accuracy measure	Value
Sensitivity	96.8%
Specificity	97%
PPV	96.8%
NPV	97%

An example of a study sample where 128-section MDCT incorrectly identified the presence of CAD for a patient while he is in reality doesn't have the disease (False positive) is depicted in Figures 4.1 and 4.2. The MDCT report in Figure 4.1 shows that the patient has severe stenosis in LAD which means he has stenosis in conclusion. While in the CCA report as shown in Figure 4.2, the patient does not have severe stenosis.

Radiology result report 04/03/2022 12:33 AM

Patient information :

Patient id	43617	Patient name	[redacted]		
National id	[redacted]	Birth date	[redacted]	Gender	Male

Encounter information :

Facility	Istishari Arab Hospital	Enc. date	04/20/2019	Physician	Nizar Shakhshir

Order information :

Activity code	129370	Activity name	DUAL CORONARY ANGIOGRAPHY CT SCAN (INCLUDING CALVIUM SCORING , WITHOUT AND WITH CONTRAST)
Radiologist notes		Examination Date	4/22/2019 1:04:09 PM

CORONARY ARTERY CT SCAN

Calcium Score: Total calcium score 51 lying within the 70 % percentile.

Dominance of the coronary artery: Right.

Left main coronary artery:
Anomaly: None.
Plaque: calcific plaque at the ostium.
Stenosis: None.

Left anterior descending artery (LAD):
Anomaly: None.
Plaque: calcific plaques in the proximal portion.
Stenosis: There are areas of severe stenosis of LAD.

Left circumflex artery (CX):
Anomaly: None.
Plaque: none.
Stenosis: None.

Right coronary artery (RCA-PDA)
Anomaly: None.
Plaque: none.
Stenosis: None.

Cardiac morphology: Normal.
Pericardial Effusion: None.
Thoracic aorta: Normal.
Hiatus hernia is incidentally seen.

FIGURE 4.1. 128 MDCT REPORT THAT INCORRECTLY IDENTIFIED THE PRESENCE OF CAD WHEN COMPARED WITH CATH REPORT

Cath Report

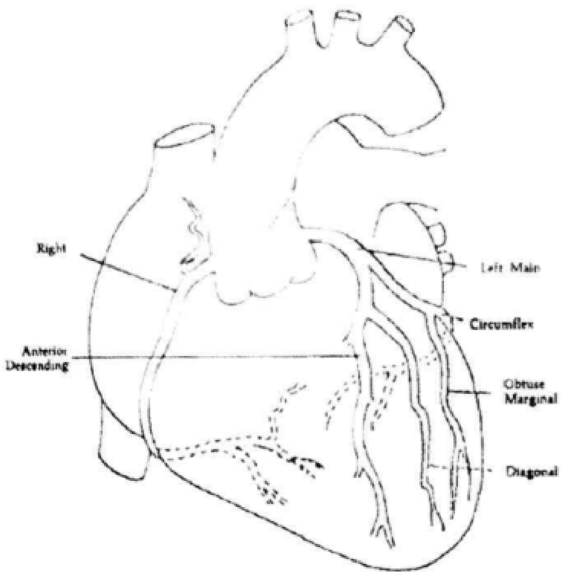
Patient information

Patient Name: [redacted] **Patient ID** 43617 **Patient Age** 56

Department Medium Care Unit MCU Department **Gender** Male

CD No: **Date:** 27/04/2019

Dr nizar shakhshir **Procedure:** CORONARY ANGIOGRAPHY



Comments & Recommendations:

aspirin 100 mg *1
crestor 10 mg *1

LM	Normal
LAD	Normal
CX	Normal
RCA	Normal
LV	

FIGURE 4.2 CATH REPORT THAT REVEALS THE ABSCENCE OF CAD

One popular limitation of CT coronary angiography is heavy calcification of vessel walls leading to overestimation of the stenosis degree in the lesion due to calcium blooming and blurring of the vessel lumen. This may be the main reason for false negative or false positive in some cases, in addition to the low quality or obesity of the produced CT images.

However, in most patients CT correctly identified the absence or existence of CAD disease in comparison with CCA as depicted in Figure 4.3 and Figure 4.4.

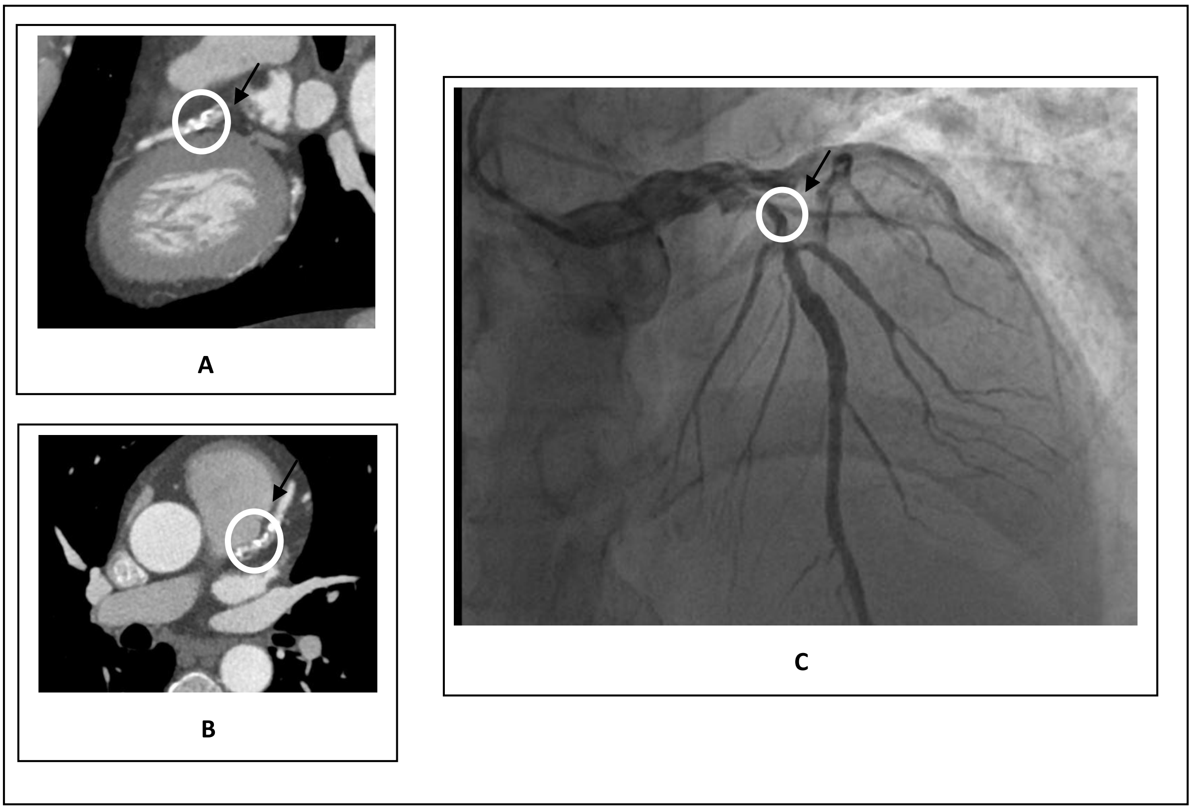


FIGURE 4.3 COMPARING RESULTS OF CCA AND 128- MDCT FOR 50 YEARS OLD MAN WITH CHEST PAIN OVER THE LAST 2 WEEKS

A. A coronary calcium scan shows calcification in Left Anterior Descending (LAD) coronary artery.
B. An axial image of LAD shows severe calcification in the artery which indicates the accurate detection and localization of stenosis.
C. The conventional coronary angiography confirms stenosis in LAD with 70% reduction in size.

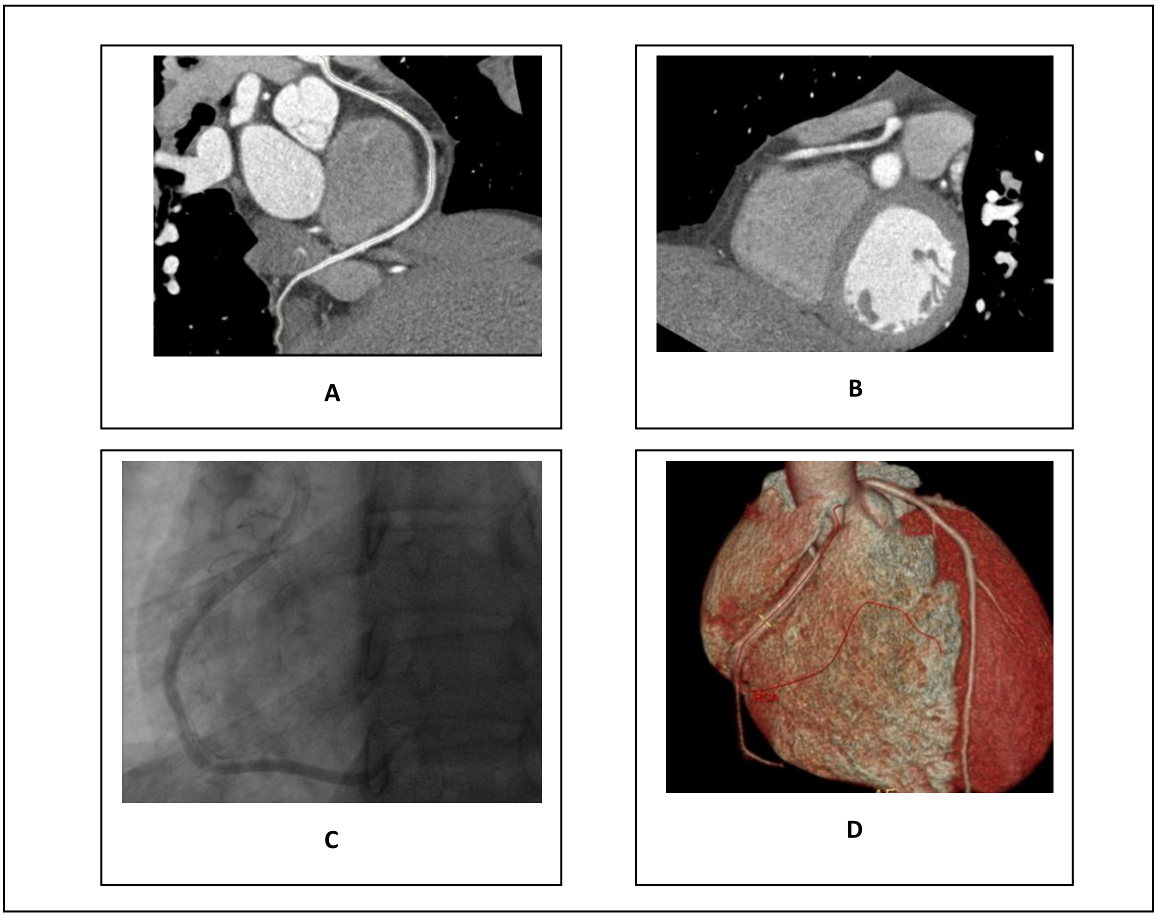


FIGURE 4.4 26 YEARS OLD MAN WITH CHEST PAIN OVER THE LAST 2 WEEKS

A. The Sagittal section of RCA shows that the patient has no stenosis with zero calcium score.
B. The axial section of CT scan shows no stenosis in RCA.
C. The conventional coronary angiography (CCA) confirms the absence of stenosis in RCA
D. Volume rendered image shows no calcification in Right Coronary Artery (RCA)

As shown in Figure 4.2, a 26 years old patient did both 128-section MDCT and CCA for diagnosing the presence or absence of CAD. The results of both tests confirm the absence of disease. This means that the patient did an invasive procedure, exposed to x-rays and paid for doing the CCA in the hospital without gaining any extra benefit. In such cases, it is obvious that MDCT could replace CCA and this leads to avoid its side effects.

4.1.2 Accuracy measures for artery-based analysis

This section describes in details accuracy measures for the Left Main Coronary Artery (LM), Left Anterior Descending (LAD), Circumflex artery (CX), Right Coronary Artery (RCA).

TABLE 4.2 ACCURECY MEASURES FOR ARTERY-BASED ANALYSIS

Artery / Measure	**LM**	**LAD**	**CX**	**RCA**
Sensitivity	100%	90.6%	61.1%	73.70%
Specificity	98.40%	97%	100%	97.8%
PPV	75%	96.6%	100%	93.3%
NPV	100%	91.4%	87%	90%

As shown in table 4.2, 128- section MDCT for LM had an overall sensitivity of 100%, specificity of 98.4%, a positive predictive value of 75%, and a negative predictive value of 100% with invasive catheter angiography as the gold standard. High sensitivity value indicates that 128-slice MDCT is capable of correctly identifying those individuals who have the disease in LM, that is, true positives. Lower specifity and the positive predictive value indicate that 128-slice MDCT is less capable of correctly identifying those individuals who don’t have the disease in LM, that is, true negative.

Regarding Left Anterior Descending (LAD) Coronary Artery, it has high specificity and positive predictive values (97%, 96.6) respectively. 97% Specificity means that 128-section MDCT was capable to give negative test results for 32 people of 33 people who don't have the disease in LAD. While the result of measuring PPV means that all people who have positive test results truly had the disease in LAD with 96.6% probability. Sensitivity and NPV measures are nearly the same. As shown in table 4.2, 90.6% of patients got positive test results and they truly had CAD disease in LAD. While 91.4% of patients got negative test results and they truly had not the CAD disease in LAD.

As for CX Coronary Artery, it has high specificity and positive predictive values (100%), which mean that 128-section MDCT was capable to give negative test results for all people who don't have the disease in CX. Sensitivity and NPV measures are 61.1%, 87% respectively. Sensitivity result means that more than half of patients got positive test results and they truly had CAD disease in CX according to the gold standard (angiography). While NPV means that 87% of people got negative test results and they truly had not the CAD disease in CX.

As shown in Table 4.2, the highest accuracy measures in Right Coronary Artery are specificity and positive predictive values. 97.8% Specificity means that 128-section MDCT was capable to give negative test results for most patients who don't have the disease in RCA. While the result of measuring PPV means that the majority of patients (93.3%) who have positive test results truly had the disease in RCA.

Based on the above-mentioned results, it is concluded that 128-slice MDCT is best suitable for detecting the existence (True positives) of CAD disease in LM. While it is best used for identifying people who don't have the disease in CX.

4.2 Could 128-section MDCT replace CCA in CAD Detection?

This section answers the following question: "to what extent 128-section MDCT could replace CCA in significant CAD detection?"

Based on using SPSS, Chi square test is used to determine whether there is statistically significant association between the results of CCA and MDCT through comparing the p-value to the significance level (α or alpha= 0.05 works well).

If P-value ≤ α: The variables have a statistically significant association (Reject the null hypothesis and conclude that there is a statistically significant association between the variables). The result of Chi square test is shown below.

TABLE 4.3. CHI-SQUARE TESTS

	Value	Df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	57.244[a]	1	**P-value <.001**		
Continuity Correction[b]	53.551	1	<.001		
Likelihood Ratio	72.231	1	<.001		
Fisher's Exact Test				<.001	<.001

N of Valid Cases	65				
a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 15.75.					

The Chi square test result showed $p<0.001$ which means that there is strong association between CCA results and MDCT results. This means that 128-section MDCT could replace invasive coronary angiography for patients who couldn't do surgeries or have coagulation disorders, and expanded vessel. However, it will not replace CCA as a reference tool but it can be considered as a reliable alternative.

4.3 Comparing results with previous studies

This section compares our produced results with the results of previous researches that assessed the diagnostic accuracy of 128 MDCT coronary angiography in comparison with invasive coronary angiography. This study uses larger study population size than other studies as shown in table 4.3, which provides smaller margin of error and increases the validity.

Per-patient accuracy measures are shown in Table 4.5. It is obvious that accuracy measures in all of them are high. High sensitivity and specifity values indicate the excellent ability of 128 MDCT coronary angiography of detecting true positive (people got positive test results and they truly had CAD disease) and true negative cases (people got negative test results and they truly had not CAD disease).

PPV in this study (96.8%) is higher than others (87%, 88.46%). This means all people who have positive test results in this study truly had the disease with 96.8% probability.

In order to compare accuracy measures of this study with previous studies, one sample t-test is used. It compares the means of sensitivity, specificity, PPV and NPV of previous studies with this research results. The significance refers to p-value. Assuming that alpha is 0.05, then sensitivity, NPV, specificity are greater than it. This means that sensitivity, specifity and NPV are not statistically significant different from this research results.

On the other hand, PPV is less than alpha which means that it is statistically significant different from this research PPV value.

TABLE 4.4 T-TEST SCORES USED FOR COMPARING ACCURACY MEASURES

Measure	T	df	Significance		Mean Difference	95% Confidence Interval of the Difference	
			One-Sided p	Two-Sided p		Lower	Upper
Sensitivity	.655	2	.290	.580	.010000000	-.05572411-	.07572411
Specificity	-2.646-	2	.059	.118	-.023333333-	-.06127916-	.01461250
PPV	-4.583-	2	.022	.044	-.070000000-	-.13572411-	-.00427589-
NPV	-.644-	2	.293	.586	-.036666667-	-.28174587-	.20841254

TABLE 4.5 COMPARING ACCURECY MEASURES AMONG DIFFERENT RESEARCHES

Research	Study population size	Sensitivity	Specificity	PPV	NPV
Narumol Chaosuwannakit , Songsak Kiatchoosakun [18]	42	100%	93%	87%	100%
Madhok, R., & Aggarwal, A. [14]	40	95.26%	95.12%	88.46%	98.08%
Sakthivel, D. [21]	46	96%,	69%	92%	82%
This research	65	96.8%	97%	96.8%	97%

Chapter 5

This chapter shows the conclusion of the study, limitations, recommendations, and future work.

5.1 Conclusion

This dissertation aimed to evaluate the accuracy of 128-section MDCT in significant CAD detection in comparison with CCA. In order to achieve this aim, a literature review related to 128-section MDCT and CCA is conducted. Then, the required data for evaluating the accuracy of 128-section MDCT are collected. These data include CCA and 128-section MDCT reports for 65 patients with suspected CAD. After that, the collected data are analyzed and compared. CCA reports are used as the gold standard to determine if patients have CAD or not. A spreadsheet summarizing all the results is created using Excel and SPSS in order to summarize the results and accomplish statistical calculations including sensitivity, specificity, PPV, and NP.

The results of per-patient analysis showed that 128-slice MDCT is excellent in detecting the existence of significant CAD. The research showed high overall accuracy measures represented by sensitivity 96.8%, specificity 97%, PPV 96.8%, and NPV 97% which mean that 128-section MDCT could replace invasive coronary angiography particularly for patients who couldn't do surgeries or have coagulation disorders, and expanded vessel.

In addition, based on artery based analysis, it is conclude that 128-slice MDCT is best suitable for detecting the existence (True positives) of CAD disease in LM. While it is best used for identifying people who don’t have the disease in CX (True negatives).

5.2 Limitations

Although our research work showed promising results in evaluating the accuracy of 128-section MDCT in CAD detection, it has limitations associated with the number of patients (65 individuals) used in the evaluation process. It was a challenge to get data for a larger number of patients who should have done both MDCT and CCA. In addition, the rules and policies in hospitals are complex which requires a long time and sequence of agreements and consents from different parties until having the required data for the research.

5.3 Recommendations

Based on our produced results, it is recommended to use 128-section MDCT as a first test in CAD detection as it shows promising results in detecting the existence and absence of disease due to the high accuracy measures. In addition, it is recommend to give continuous training for radiographers about how to do correct and accurate 128-MDCT scanning in order to reduce errors that may be generated in the result of the test due to poor opacification or motion blur.

5.4 Future work

Though the accomplished evaluation of 128-section MDCT in detecting CAD showed promising results in terms of identifying the absence or existence of the disease, other remaining challenges and research areas could be explored in the future as outlined below:

1. Repeat the calculation of accuracy measures for a larger number of patients who did both 128-section MDCT and CCA.

2. Evaluate the accuracy of 256-section MDCT and compare the produced results with the produced results of evaluating the accuracy of 128-section MDCT in detecting CAD.

الملخص باللغة العربية

تعتبر أمراض الشرايين التاجية من الأمراض الرئيسية المسببة للوفاة في جميع أنحاء العالم. يتم استخدام العديد من التقنيات لتشخيصهم واكتشافهم بما في ذلك التقنيات التداخلية وغير التداخلية (الجراحية وغير الجراحية).

الطريقة التداخلية (القسطرة): هي عملية جراحية تعتمد على شق جراحي من الجلد يتم عن طريقه الوصول الى الشرايين التاجية. تعد هذه الطريقة المعيار الذهبي في تشخيص أمراض الشرايين التاجية. على الجهة المقابلة، تتسبب القسطرة في آثار جانبية متعددة للمرضى والتي يجب محاولة تجنبها خصيصاً عند من يعانون من اضطرابات في التخثر واضطرابات في الأوعية الدموية. بناءً على ذلك، هناك ضرورة ملحة لإيجاد طرق ذات أضرار جانبية أقل في الوقت الذي يمكن الاعتماد عليها في تقييم أمراض الشرايين التاجية .

يعد التصويرالمقطعي المحوسب متعدد الكاشفات المكون من 128 قسمًا (128- slice MultiDetector CT scan) أحد أهم الطرق غير الجراحية وأكثرها شيوعًا، حيث يساعد في تقييم حالة الشرايين التاجية.

هناك حاجة ملحّة لتقييم مدى دقة التصوير المقطعي في اكتشاف أية تغيرات مرضية في الشرايين التاجية من أجل إحلال التصوير المقطعي كبديل عن تصوير الأوعية التاجية بالطريقة التداخلية لتجنب المخاطر المحتملة. لذلك، تهدف هذه الدراسة إلى تقييم دقة التصوير المقطعي في اكتشاف أمراض الشرايين التاجية، ولتحقيق ذلك، تم جمع تقارير التصوير المقطعي و تقارير عمليات القسطرة الشريانية لـ 65 مريض من أجل دراستهم ومقارنة نتائجهم.

قمنا باستخدام مقاييس إحصائية مختلفة لحساب دقة جهاز التصوير المقطعي مثل: حساسية المعيار والنوعية للمعيار والقيمة الإيجابية المتوقعة والقيمة السلبية المتوقعة للمعيار.

أظهرت النتائج التي تم الحصول عليها أن التصوير المقطعي يتمتع بدقة عالية مع قيم عالية لكل من الحساسية والنوعية وقيمة التنبؤية الايجابي وقيمة التنبؤية السلبية. بعض النتائج اظهرت ان نتيجة القسطرة مغايرة لنتيجة التصوير المقطعي المحوسب متعدد الكاشفات المكون من 128 قسمًا لعدة اسباب منها: ضعف التعتيم (الماده الملونه) أو ضبابية الحركة(حركة النبض).

نستنتج أن التصوير المقطعي المحوسب متعدد الكاشفات المكون من 128 قسمًا يمكن أن يحل محل القسطرة خاصة للمرضى الذين لا يستطيعون إجراء العمليات الجراحية التداخلية أو الذين يعانون من اضطرابات في التخثر أو الأوعية الموسعة المشوهة.

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Appendix 1. Ethical Approval

Al-Quds University
Jerusalem
Deanship of Scientific Research

بسم الله الرحمن الرحيم

جامعة القدس
القدس
عمادة البحث العلمي

Research Ethics Committee
Committee's Decision Letter

Date: February 16, 2021
Ref No: 170/REC/2021

Dear Dr. Mohammad Hjoj,

Thank you for submitting your application for research ethics approval. After reviewing your application entitled "Assessing 128-Section Multi Detector Computer Tomography (MDCT) Angiography in Detecting the Coronary Artery Stenosis", the Research Ethics Committee confirms that your application is in accordance with the research ethics guidelines at Al-Quds University.
We would appreciate receiving a copy of your final research report/ publication.
Thank you again and wish you a productive research that serves the best interests of your subjects.

PS: This letter will be valid for two years.

Sincerely,

Suheir Ereqat, PhD
Associate Professor of Molecular Biology

Research Ethics Committee Chair

Cc. Prof. Imad Abu Kishek - President
Cc. Members of the committee
Cc. file