INTRODUCTION

In the evaluation of patients with suspected coronary artery disease (CAD), the role of non-invasive imaging has increased exponentially over the past decades, particularly in patients with an intermediate likelihood of CAD.

Non-invasive imaging plays an important role in risk stratification and selection of further treatment strategies [(1)].

Traditionally, the detection of CAD by non-invasive imaging was based on assessment of the hemodynamic significance of the stenosis through visualization of inducible ischemia. For this purpose, myocardial perfusion imaging (MPI) with gated single-photon emission computed tomography (SPECT) has been used extensively [(2)].

More recently, multi-slice computed tomography (MSCT) has been proposed as an alternative imaging modality for evaluation of patients with suspected CAD.

With the recently introduced 64-slice MSCT, high sensitivity and specificity for the detection of significant (>50% luminal narrowing) stenosis have been reported [(3)].

However, because MSCT visualizes coronary artery stenosis directly, rather than the hemodynamic significance of the lesions, it is important to recognize that, unlike MPI, the technique identifies atherosclerosis rather than ischemia [(4)].

Recent advances in multi-detector-row computed tomography (MDCT) technology have continuously improved the quality of non-invasive coronary artery imaging. As a result, various studies have demonstrated a high accuracy of coronary angiography with 64-slice CT for the diagnosis of CAD.

In particular, the high negative predictive value with an overall sensitivity of 96.4% and specificity of 97.5% for the detection of significant coronary stenosis has made noninvasive coronary angiography using 64-slice CT a modality that allows significant coronary stenosis to be reliably excluded [5].

Consequently, the Task Force on the Management of Stable Angina Pectoris of the European Society of Cardiology has recently recommended in their guidelines that CT coronary angiography should be performed in patients with stable angina who have a low pre-test probability of CAD, and an inconclusive exercise electrocardiogram (ECG) or stress imaging test [6].

Conventional invasive coronary angiography (ICA) has been the "gold standard" for the diagnosis of coronary artery disease. However, CAG shows only luminal stenosis and the extent of coronary atherosclerosis. It does not provide information on plaque composition. Non-invasive coronary MDCT can visualize the coronary artery lumen, artery wall, and atherosclerotic plaque; even the lipid pool can be visualized, which is fibrous, calcified, and heavily laden with cholesterol [7].

In two studies, it was confirmed that contrast-enhanced MDCT permits accurate identification of coronary plaques, and that CT density values within plaques reflect echogenicity and plaque composition [8, 9].

The value of MSCT in guiding Interventional Cardiologists about the Stent Length & Diameter is still unclear with no available data [10].

AIM OF THE WORK

To assess the accuracy of determining the medina classification, angle measurement and plaque composition and their effect on choosing the appropriate intervention technique based on multislice CT coronary angiography in comparison to invasive coronary angiography in bifurcational lesions intervention.

Chapter 1:

CT OVERVIEW

Computed tomography (CT) was introduced in the early 1970s and has revolutionized not only diagnostic radiology, but also the entire practice of medicine. In 1979, G. Hounsfield and A.M. Cormack received the Nobel Prize for their significant contributions to the development of computed axial tomography. Using computer reconstruction techniques, Hounsfield demonstrated that the internal structures of an object could be reconstructed based on the attenuation pattern of an X-ray beam that had passed through the object at different angles. In 1971, Hounsfield had constructed the first CT scanner that could image the brain [(11)].

The basic principle of CT is that a fan-shaped, thin X-ray beam passes through the body at many angles to allow for cross-sectional images. The corresponding X-ray transmission measurements are collected by a detector array. Information entering the detector array are used to produce thin sections. The data recorded by the detectors are digitized into picture elements (pixels) with known dimensions. The gray-scale information contained in each individual pixel is reconstructed according to the attenuation of the X-ray beam along its path using a standardized technique termed "filtered back projection". Gray-scale values for pixels within the reconstructed tomogram are

defined with reference to the value for water and are called "Hounsfield units", or simply "CT numbers"[12].

Since CT uses X-ray absorption to create images, the differences in the image brightness at any point will depend on physical density and the presence of atoms with different atomic numbers. The absorption of the X-ray beam by different atoms will cause differences in CT brightness on the resulting image. Blood and soft tissue (in the absence of vascular contrast enhancement) have similar density as they consist of similar proportions of the same atoms (hydrogen, oxygen, carbon). Bone has an abundance of calcium. Fat has an abundance of hydrogen. Lung contains air which is of extremely low physical density. The higher the density, the brighter the structure on CT [13].

Calcium is bright white, air is black, and muscle or blood is gray. Computed tomography, therefore, can distinguish blood from air, fat and bone but not readily from muscle or other soft tissue. The densities of blood, myocardium, thrombus, and fibrous tissues are so similar in their CT number that non enhanced CT cannot distinguish these structures [14].

The distinction of blood and soft tissue (such as the left ventricle, where there is no air or fat to act as a natural contrast agent) requires injection of contrast with CT. Similarly, distinguishing the lumen and wall of the coronary artery also requires contrast enhancement. The accentuated absorption of X-rays by elements of high atomic number like calcium and iodine

allows excellent visualization of small amounts of coronary calcium as well as the contrast-enhanced lumina of medium-size coronary arteries [15].

In the early 1990s, the introduction of spiral CT constituted a further evolutionary step in the development and ongoing refinement of CT imaging techniques [16].

Strategies to achieve more substantial volume coverage with improved longitudinal resolution have necessitated the simultaneous acquisition of more than one slice at a time and a reduction of the gantry rotation time. Interestingly, the very first medical CT scanners were 2-slice systems, such as the EMI head scanner, introduced in 1972, or the Siemens SIRETOM, introduced in 1974. With the advent of whole body fan-beam CT systems for general radiology, 2-slice acquisition was no longer used [17].

In 1998, all major CT manufacturers introduced MSCT systems, which typically offered simultaneous acquisition of 4 slices at a rotation time of down to 0.5 s. This was a considerable improvement in scan speed and longitudinal resolution and offered better utilization of the available X-ray power [18].

The race for more slices is on-going. In 2004, all major CT manufacturers introduced the next generation of multi-slice CT systems, with 32, 40, and even 64 simultaneously acquired slices, which brought about a further leap in volume coverage speed.

Whereas most of the scanners increase the number of acquired slices by increasing the number of the detector rows, some of the new scanners use additional refined z-sampling techniques with a periodic motion of the focal spot in the zdirection (z-flying focal spot). This so-called "double z" sampling technique can further enhance longitudinal resolution and image quality in clinical routine [19].

These developments were quickly recognized as revolutionary improvements that would eventually enable users to do real isotropic 3D imaging. Consequently, all vendors pushed towards more and more slices, turning the number of slices into the most important performance characteristic of a CT scanner. Interestingly, analogous to "Moore's Law" in the computer industry, the increase in the number of slices has been exponential, approximately doubling every 18 months [20].

In 2008, ten years after the introduction of the 4-slice scanner, Toshiba has declared its most recent multi-slice CT scanner with the ability to acquire 320 slices with one gantry rotation.

The development of basic multi-slice cardiac CT scan reconstruction techniques and the first clinical evaluation of multi-slice CT angiography of the heart and coronary arteries involved the use of 4-slice CT scanners with a fastest rotation time of 0.5 s. Several studies demonstrated the feasibility of 4-slice CT scanners to non-invasively image the cardiac

morphology and the coronary arteries but the performance of 4slice CT scanners in terms of spatial resolution, temporal resolution, and breath hold times was shown to be too limited for regular clinical use [21].

The availability of 8- to 10-slices per rotation with submillimeter collimation and a fastest rotation time of less than 0.5 s represent the minimum CT performance requirements for contrast-enhanced imaging of the heart and the coronary arteries. However, several studies demonstrated a substantial improvement of clinical robustness for cardiac and coronary artery diagnosis when using 16-slice CT technology with submillimeter collimation and rotation time of less than 0.4 s [22].

The clinical robustness and diagnostic accuracy of CT angiography of the heart and coronary arteries benefits significantly from the further enhanced spatial resolution, temporal resolution, and reduced breath-hold times in 32- to 64slice CT scanners.

Furthermore, a 32- to 64-slice CT scanner is usually a prerequisite for imaging of coronary stents and analysis of coronary plaque [23].

Indications of CT coronary angiography:

Once the physician determines the presence of symptoms that may represent obstructive CAD (ischemic equivalent present), the pretest probability of CAD should be assessed [24].

There are a number of risk algorithms available that can be used to calculate this probability. Clinicians should become familiar with those that pertain to the populations they encounter most often. In scoring the indications, the following probabilities as calculated from any of the various available algorithms should be applied:

- Low pretest probability: less than 10% pretest probability of CAD.
- Intermediate pretest probability: Between 10% and 90% pretest probability of CAD.
- High pretest probability: more than 90% pretest probability of CAD.

Pretest probability of CAD by age, sex, & symptoms ***(Taylor et al., 2010)***.

Pretest probability of coronary artery disease

Age	Gender	Typical angina	Atypical/ probable angina	Non-anginal CP	Chest pain
< 39	M	Intermediate	Intermediate	Low	Very low
	F	Intermediate	Very low	Very low	Very low
40-49	M	High	Intermediate	Intermediate.	Low
	F	Intermediate	Low	Very low	Very low
50-59	M	High	Intermediate	Intermediate	Low
	F	Intermediate	Intermediate	Low	Very low
> 60	M	High	Intermediate	Intermediate	Low
	F	High	Intermediate	Intermediate	Low

Figure (1): Pretest probability of CAD by age, sex, & symptoms

Appropriate clinical indications for the use of computed tomography coronary angiography [25] figures (2, 3, and 4).

Detection of CAD with prior test results-evaluation of chest pain syndrome (use of CT angiogram)
• Uninterpretable or equivocal stress test (exercise, perfusion, or stress echo)
• Intermediate pre-test probability of CAD
ECG uninterpretable or unable to exercise
Detection of CAD: symptomatic-acute chest pain (use of CT angiogram)
• Intermediate pre-test probability of CAD
No ECG changes and serial enzymes negative
Detection of CAD: symptomatic-evaluation of intra-cardiac structures (use of CT angiogram)
• Evaluation of suspected coronary anomalies
Structure and function-morphology (use of CT angiogram)
• Assessment of complex congenital heart disease including anomalies of coronary circulation, great vessels, and cardiac chambers and valves
• Evaluation of coronary arteries in patients with new onset heart failure to assess aetiology
Structure and function-evaluation of intra- and extra-cardiac structures (use of cardiac CT)
• Evaluation of cardiac mass (suspected tumour or thrombus)
Patients with technically limited images from echocardiogram, MRI, or TEE
• Evaluation of pericardial conditions (pericardial mass, constrictive pericarditis, or complications of cardiac surgery)
Patients with technically limited images from echocardiogram, MRI, or TEE
• Evaluation of pulmonary vein anatomy prior to invasive radiofrequency ablation for atrial fibrillation
• Non-invasive coronary vein mapping prior to placement of biventricular pacemaker
• Non-invasive coronary arterial mapping, including internal mammary artery prior to repeat cardiac surgical revascularization
Structure and function-evaluation of aortic and pulmonary disease (use of CT angiogram[a])
• Evaluation of suspected aortic dissection or thoracic aortic aneurysm
• Evaluation of suspected pulmonary embolism

Figure (2): Appropriate clinical indications for the use of computed tomography coronary angiography

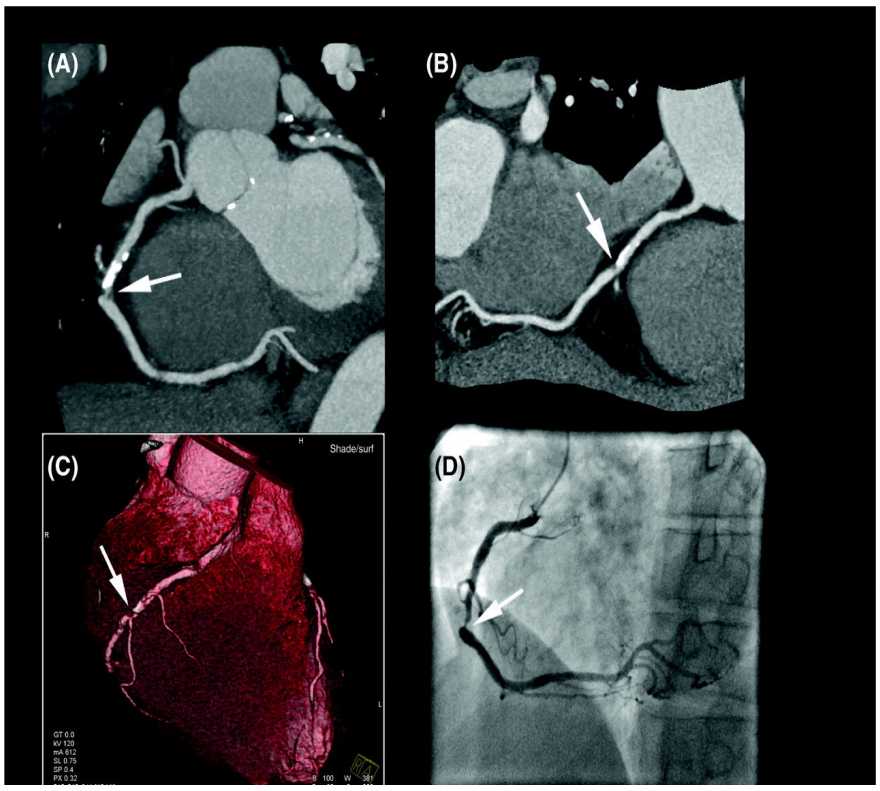

Figure (3): Coronary artery stenosis detection with multi-detector row computed tomography.

High-grade stenosis of the mid-right coronary artery in a 55-year-old man with atypical chest pain. (*A*) A maximum intensity projection, with a high-grade luminal reduction distal to a calcified segment. (*B*) A curved multiplanar reconstruction. (*C*) A three-dimensional rendering of the heart and right coronary artery. (*D*) Shows the corresponding coronary angiogram. [26]

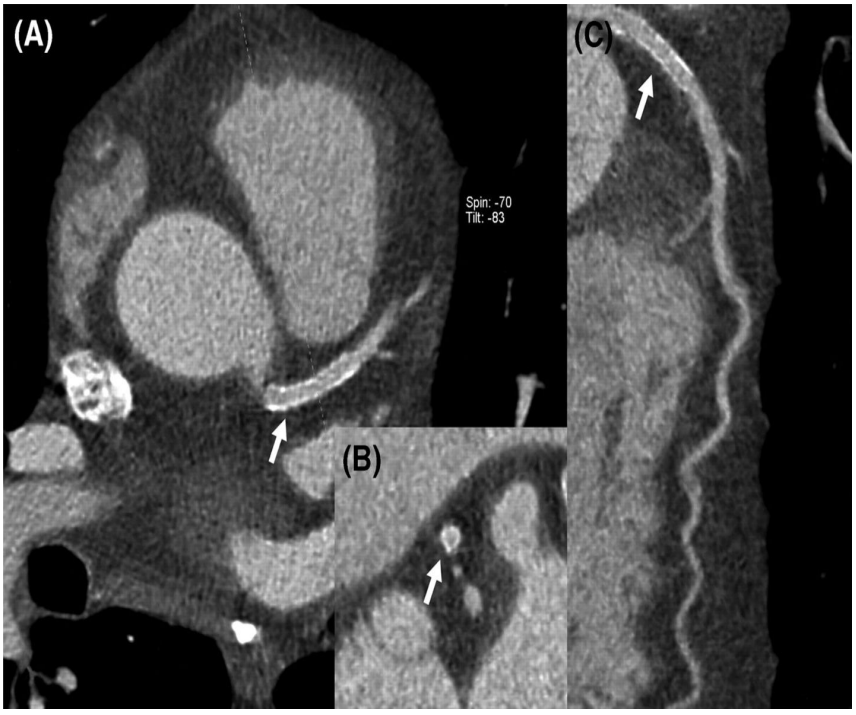

Figure (4): Assessment of coronary artery stents by multi-detector row computed tomography angiography

Assessment of coronary artery stents by multi-detector row computed tomography angiography. Example of a stent placed in the proximal part of the left anterior descending coronary artery. Image quality is good and the coronary artery lumen within the stent can be assessed. multi-detector row computed tomography shows absence of significant in-stent-stenosis. (*A*) Longitudinal view; (*B*) axial orientation; (*C*) curved multiplanar reconstruction[27].

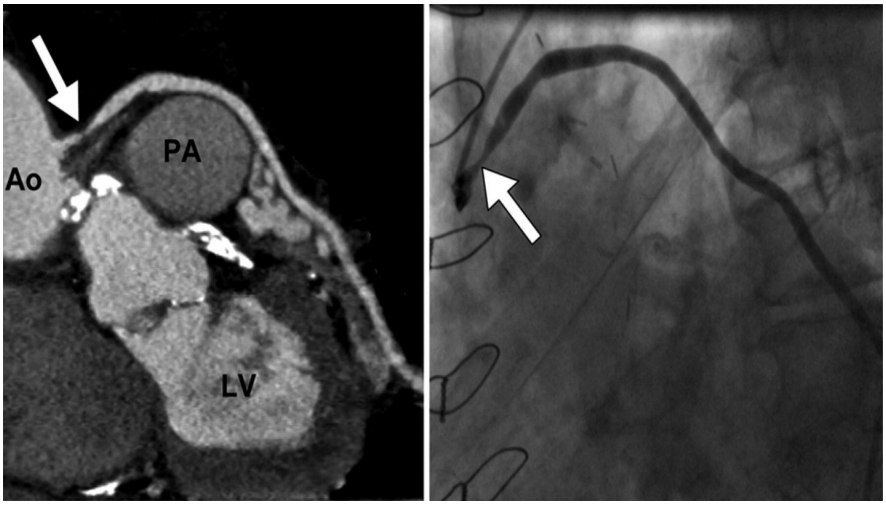

Figure (5): Coronary artery bypass graft imaging with multi-detector row computed tomography.

Cardiac computed tomography evaluation of the heart in an 82-year-old man 9 years after coronary artery bypass surgery. The curved multiplanar reconstruction (left panel) of the venous graft to the first obtuse marginal branch demonstrates a significant lesion in the proximal part (arrow), which is confirmed by invasive angiography (right panel) [28].

Chapter 2:

CORONARY PLAQUE IMAGING

Calcium scoring:

Coronary calcium is a surrogate marker for the presence and amount of coronary atherosclerotic plaque[29].

MDCT permits accurate detection and quantification of coronary artery calcium, The so-called 'Agatston Score', which takes into account the area and the CT density of calcified lesions, is most frequently used to quantify the amount of coronary calcium in CT, and large population reference databases are available. With the exception of patients with renal failure, calcifications occur exclusively in the context of atherosclerotic lesions [30].

The amount of coronary calcium correlates moderately closely to the overall atherosclerotic plaque burden, on the other hand, not every atherosclerotic coronary plaque is calcified, and calcification is a sign of neither stability nor instability of an individual plaque [31].

In several trials, the absence of coronary calcium ruled out the presence of significant coronary artery stenoses with high predictive value. However, even pronounced coronary calcification is not necessarily associated with