

# **Plaque characterization by optical coherence tomography and correlation with clinical presentation**

Thesis submitted for partial fulfillment of Master Degree in  
Cardiovascular Medicine

By **Mina Sami Halim Fawzy Youssef**

M.B.B.Ch.

Supervised by

**Prof. Dr. Mohammed Mahmoud Abdel Ghany, MD**

Professor of Cardiovascular medicine

Cairo University

**Dr. Amr Abdel Aziz ElFaramawy, MD**

Assistant Professor of Cardiovascular medicine

Cairo University

**Dr. Khaled Abdel Azim Shokry, MD**

Director Manager of Kobry el kobba military hospital

Faculty of Medicine

Cairo University

2015

# **Acknowledgments**

I owe my deepest gratitude to my dear professors; Dr. Mohamed Abdel Ghany, Professor of Cardiology, Dr. Amr Al Faramawy, Assistant professor of Cardiology and Dr. Khaled Abdel Azim Shokry, Head of Heart Hospital at Kobry el Kobbah Military hospital who were abundantly helpful and offered invaluable assistance, support and guidance.

I also wish to express my love and gratitude to my beloved family and friends; for their understanding & endless love.

Mina Samy

## Table of Contents

List of abbreviations .....	I
List of tables.....	V
List of figures.....	VI
Abstract.....	X
Introduction.....	1
Aim of work.....	3
Review of literature.....	4
Chapter 1: Overview of Coronary artery disease.....	4
Chapter 2: Imaging modalities for coronary artery disease .....	18
Chapter 3: Optical coherence tomography .....	34
Patients and methods.....	61
Results .....	67
Discussion.....	81
Conclusion .....	92
Summary.....	93
References .....	94

## List of abbreviations

ACC	American College of Cardiology
ACCF	American College of cardiology foundation
ACS	Acute Coronary syndrome
AHA	American Heart Association
AMI	Acute Myocardial Infarction
ATP	Adenosine Tri-Phosphate
BMS	Bare Metal Stent
BVS	Bioresorbable Vascular Scaffold
CABG	Coronary Artery Bypass Graft
CAD	Coronary Artery Disease
CCS	Canadian cardiovascular society
CI	Confidence Interval
CK-MB	Creatine Kinase myocardial band
CMR	Cardiac Magnetic Resonance
CRP	C - Reactive Protein
CT	Computed Tomography
CTA	Computed Tomography Angiography
DES	Drug Eluting Stent
ECG	Electro-Cardio Gram
ESC	European Society of Cardiology

## List of abbreviations

FD-OCT	Fourier Domain Optical Coherence Tomography
FFR	Fractional Flow Reserve
FPS	Frame per second
HR	Hazard Ratio
ICA	Invasive Coronary Angiography
ICT	Intracoronary Thermography
IC	Intracoronary
IVOCT	Intra Vascular Optical Coherence Tomography
IVUS	Intra-Vascular Ultra-Sonography
IV	Intra-Venous
LAD	Left Anterior Descending Artery
LBBS	Left Bundle Branch Block
LCX	Left Circumflex
LDL	Low Density Lipoprotein
LMCA	Left Main Coronary Artery
LV	Left Ventricle
LVEDV	Left Ventricular End Diastolic Volume
LVEDP	Left Ventricular End Diastolic Pressure
LVEF	Left Ventricular Ejection Fraction
MD-CT	Multi-Detector Computed Tomography
MI	Myocardial Infarction
MIT	Massachusetts Institute of Technology
MLA	Minimum Luminal Area
MPI	Myocardial Perfusion Imaging

## List of abbreviations

MMP	Matrix Metallo-Proteinases
MR	Magnetic Resonance
MRA	Magnetic Resonance Angiography
NPV	Negative Predictive Value
NSTEMI	Non-ST segment Elevation Myocardial Infarction
OCDR	Optical Coherence Domain Reflectometry
OCT	Optical Coherence Tomography
PCI	Percutaneous Coronary Intervention
PIT	Pathological Intimal Thickening
PPV	Positive Predictive Value
PTCA	Percutaneous Trans-luminal Coronary Angioplasty
PTP	Pre-Test Probability
RCA	Right Coronary Artery
SAP	Stable Angina Pectoris
SCAD	Stable Coronary Artery Disease
SD	Standard Deviation
SERCA	Sarco-Endoplasmic Reticulum Calcium ATPase
SMCs	Smooth Muscle Cells
STEMI	ST-Elevation Myocardial Infarction
TCFA	Thin Cap Fibro-Atheroma
TD-OCT	Time Domain Optical Coherence Tomography

## List of abbreviations

UA                      Unstable Angina

VH-IVUS              Virtual Histology Intra-Vascular Ultra-Sonography

## List of tables

<b>Table number</b>	<b>Table title</b>	<b>Page</b>
1	Canadian Cardiovascular Society classification of angina pectoris	6
2	Braunwald Classification of Unstable Angina	7
3	ECG criteria for diagnosis of STEMI in setting of LBBB	11
4	Comparison of Necrotic Core Size, Number of Cholesterol Clefts, Macrophage Infiltration, Number of Vasa Vasorum, and Hemosiderin-Laden Macrophages in Culprit Plaques	12
5	Accuracy of 64-Section CT and Dual-Source CT for Detection of Coronary Stenosis in Comparison with Conventional Coronary Angiography	22
6	Use of coronary computed tomography angiography for the diagnosis of stable coronary artery disease	24
7	Studies Comparing Angiographic Versus IVUS Guidance for Percutaneous Coronary Intervention with Drug-Eluting Stents	27
8	Summary of Published Human Thermography Studies	32
9	Technical Characteristics of Intravascular Ultrasound and Frequency-domain Optical Coherence Tomography	37
10	Baseline characteristics	68
11	LV EF and ECG data	69
12	OCT Findings of Underlying Plaque Characteristics	70
13	OCT based Quantitative Analysis for Plaques in Native Vessel	72
14	OCT Data Analysis for Patients with previous PCI	73
15	Treatment modality	73
16	Inter-Observer variability	74



## List of figures

<b>Figure number</b>	<b>Figure title</b>	<b>Page</b>
1	Typical Morphological Traits Associated With Rupture-Prone Plaques	12
2	Curved multi-planar reformat of the circumflex coronary artery from CT coronary angiography	20
3	Non-calcified plaque confirmed at conventional coronary angiography	20
4	Images in 57-year-old man with persistent chest pain despite negative prior conventional angiography findings by CT	23
5	Real-time intravascular-ultrasonography	28
6	Images of a coronary plaque before and after disruption	29
7	Angioscopic classification of coronary plaques	30
8	Light path through a Michelson interferometer	38
9	Schematic of Optical Coherence Tomography Imaging System	38
10	Dragon fly catheter	41
11	IVOCT images displayed using different look up tables	43
12	Optical coherence tomography shows the three layer appearance of normal vessel wall	44
13	Example of intimal thickening revealed by optical coherence tomography	45
14	Optical coherence tomography showing calcific plaque	45
15	Optical coherence tomography showing lipid pole	46
16	OCT showing lipid pole with thin cap fibro-atheroma.	47
17	Intracoronary thrombi, the left picture shows white thrombus while that on the right shows red thrombus	50

## List of figures

18	Macrophage infiltration of fibrous cap	50
19	Neo-vessels seen at 7 o'clock by OCT	50
20	Study flow chart	67
21	Coronary risk factors among the two groups	68
22	Plaque type in recruited patients	71
23	Culprit pathology in ACS	71
24	Flow charts showing classification of patients according Culprit Lesion	72
25	Treatment Modality	74
26	<ul style="list-style-type: none"> <li>a) Cross section of analyzable frame showing normal coronary vessel.</li> <li>b) The same patient with zoom in, showing the three layers of normal coronary vessel by OCT</li> </ul>	75
27	Blood artifact impairs the analysis of the lumen border, thus, this cross section cannot be included in analysis	75
28	Fibrous plaque	75
29	Lipid pool	75
30	Calcium plaque (arrow)	75
31	Measurement of fibrous cap at non-ruptured	76
32	Measurement of fibrous cap at ruptured site	76
33	Thin cap fibro-atheroma	76
34	TCFA in patient with rupture plaque	76
35	Macrophages (arrow)	76
36	Neovascularization at 6 o'clock	76
37	Plaque Erosions	77

## List of figures

38	Plaque rupture with thrombus	77
39	Intracoronary thrombus (mural)	77
40	Intracoronary thrombus (luminal)	77
41	a) Minimum luminal cross sectional area b) Reference luminal cross sectional area (arrow)	77
42	Stent and Lumen CSA	78
43	Neointimal hyperplasia CSA	78
44	Homogenous NIH	78
45	Heterogenous NIH	78
46	Fibrolipidic plaque	78
47	Cholesterol crystals	78
48	a) Silent plaque rupture in a patient with SCAD b) Silent plaque rupture in same patient	79
49	Well deployed BVS	79
50	Site of overlap of two BVS	79
51	a) Coronary angiography showing spontaneous dissection (black arrow) b) OCT imaging for the same patient showing the dissection in the cut section (red arrows) in the upper part of the figure and in the longitudinal section (blue arrow) in the lower part of the figure	79
52	a) Coronary angiography showing proximal LAD lesion b) OCT imaging for the same patient showing fibro-lipidic plaque at the site of the lesion (upper part of the figure), and longitudinal section of the LAD with the red arrow pointing to the site of the lesion	80
53	a) Coronary angiography showing mid LAD lesion b) OCT imaging for the same patient showing fibro-lipidic plaque at the site of the lesion (upper part of the figure), and longitudinal section of the LAD with the red arrow pointing to the site of the lesion	80

## List of figures

54	a) Coronary angiography showing mid LCX b) Imaging for the same patient showing evidence of rupture plaque at the site of the lesion	80
----	--	----

# Abstract

**Background** Optical coherence tomography is a new intravascular imaging method with high resolution. This may allow us to assess the vulnerable plaques in detail in vivo.

**Objectives** The aim of the present study was to evaluate the ability of optical coherence tomography (OCT) for assessment of plaque characteristics and vulnerability in patients with acute coronary syndrome compared to stable angina patients.

**Methods and results** Patients undergoing cardiac catheterization were enrolled and categorized according to their clinical presentation: recent acute coronary syndrome (ACS), or stable coronary artery disease (SCAD). OCT imaging was obtained using the commercially available Frequency Domain-OCT C7XR system and the Dragonfly catheter (St Jude Medical system, Lightlab Imaging Inc., Westford, Massachusetts). Two observers independently analyzed the images using the previously validated criteria for plaque characterization. Of 48 patients enrolled, 27 with ACS, and 21 with SCAD. In the ACS, and SCAD groups, lipid-rich plaque (was observed in 96.3%, and 66.7%, respectively ( $P=0.015$ ). The median value of the minimum thickness of the fibrous cap was 70, and 100  $\mu\text{m}$ , respectively ( $P=0.064$ ). The frequency of thin-cap fibroatheroma (defined by lipid-rich plaque with cap thickness  $\leq 65 \mu\text{m}$ ) was 33.3%% in the ACS group, and 14.3% in the SCAD group ( $P=0.185$ ). No procedure-related complications occurred.

**Conclusion** The current FD-OCT study demonstrated the differences of the culprit lesion morphologies between ACS and stable CAD. There was a trend toward a higher frequency of TCFAs in patients with ACS compared to SAP patients. The morphological feature of lipid rich plaque content, plaque rupture and the intracoronary thrombus could relate to the clinical presentation in patients with acute coronary disease. Plaque erosion was a frequent finding in patients with ACS not in SCAD patients. This is consistent with previous pathological studies.

**Keywords:** OCT, ACS, SCAD, vulnerable plaques, TCFAs.

# Introduction

Cardiovascular disease has long been the leading cause of death in developed countries, and it is rapidly becoming the number one killer in the developing countries<sup>1</sup>.

It is accepted that clinical evaluation of luminal stenosis in coronary arteries, even using invasive angiography, is unable to predict the future development of ACS. Accordingly, a detailed understanding of the tissue characteristics of coronary atherosclerotic plaques is essential for identifying potentially vulnerable coronary plaques and then establishing strategies to prevent the progression and deterioration of coronary artery disease (CAD)<sup>2</sup>.

Because many of the determinants of plaque vulnerability are structural abnormalities, a high-resolution imaging technique may offer promise as a method of detecting vulnerable plaques. Presently, however, a reliable method of identifying such plaques is not available<sup>3</sup>.

Based on this clinical perspective, several groups have tried to elucidate the features of vulnerable coronary plaques by using intravascular ultrasound (IVUS), virtual histology-IVUS, angioscopy, and non-invasive multidetector computed tomography<sup>4 5 6 7</sup>.

However, even IVUS studies have not clearly identified the specific changes in the fine morphological characteristics of plaque components or the arterial wall, or which changes predict future plaque progression and the development of ACS. This may be due partly to the limited spatial resolution (as low as 100µm) of the IVUS technique.

Since intravascular ultrasound was introduced in the early 1990s,<sup>8 9</sup> it has been used not only as adjunctive device to percutaneous coronary interventions (PCI), but also as research tool to evaluate vessel structure in detail. Although IVUS helped broaden our understanding of coronary artery structure, its limited spatial resolution doesn't allow for assessment of microstructures, which is important for identification of vulnerable plaques. Optical coherence tomography (OCT) is analogous to ultrasound, except that it generates images by measuring the echo time delay and magnitude of back scattered light instead of sound<sup>10</sup>.

## Introduction

The recent introduction of optical coherence tomography (OCT) into the catheterization laboratory was received with great expectation, as this light based imaging modality offers 10 times higher resolution and 40 times faster imaging acquisition compared with other modalities such as IVUS<sup>11</sup>.

Different studies have shown that OCT can assess coronary plaque morphology and identify thrombus, intimal rupture, lipid-laden plaques, and determine accurately the thickness of the fibrous cap. Thus, it has been applied for the assessment of culprit lesion morphologies and understanding the thrombosis-prone vulnerable plaques in patients with acute coronary syndrome (ACS)<sup>12 13</sup>.

Despite the increasing rate of atherosclerotic coronary artery disease particularly ACS in Egypt, there are no data about the prevalence of different underlying pathogenesis for ACS in Egyptian population.