Preface

Over the last century there was a global increase in cardiovascular disease, and today, it is regarded as the leading cause of death in the developed world. This has been attributed to the raised proportion of older adults, as well as to the modern life style and type of diet. Among the cardiovascular causes of death, coronary artery disease is the main cause of mortality, and accounts for one in five deaths in men and women in Europe. To address this major problem, over the last year, a great effort was made in developing new effective treatments which will reduce the mortality and morbidity, and improve the quality of life of the patients who are known to have coronary atherosclerosis. Recent advances in coronary artery bypass surgery (CABG) (e.g. minimally invasive CABG), and especially in interventional cardiology (e.g. drug eluting stents, rotablator, aspiration devices), have made feasible the revascularization of high risk patients.

The augmented number of the available devices and treatment options has also created a need for a better and more detailed imaging of coronary artery pathology. Medical imaging has made a substantial progress over the last years, and nowadays, there are a multitude of imaging modalities available for the evaluation of the extent and the severity of coronary artery disease. New developments of signal processing have enabled non-invasive imaging modalities (e.g. computed tomographic coronary angiography [CTCA], magnetic resonance imaging [MRI] coronary angiography) to be used to study the coronary anatomy and detect the presence of atherosclerotic lesions. CTCA nowadays constitutes a useful alternative for the identification of luminal stenosis and the characterization of the type of the plaque, but on the other hand it has limited capability in quantifying the plaque burden especially in small caliper and stented coronaries and thus quite often adjunctive coronary angiography is required to assess the severity of a lesion and plan treatment. Similarly, MRI is not able yet to examine with accuracy the coronary pathology as its poor resolution limits coronary visualization, and hence, further development is required before being implemented in clinical and research arena.

The limitations of the non-invasive imaging modalities have been successfully addressed by invasive imaging. X-ray angiography continues to constitute the most popular imaging modality for evaluating the severity of coronary artery disease and planning treatment as it is able to provide a holistic visualization of vessel silhouette and geometry and allows direct assessment of luminal lesions. However, coronary angiography does not give information regarding the plaque composition and burden, while often it is unable to estimate accurately the severity of a stenosis as it has limited resolution. These drawbacks were overcome by intravascular imaging. Recently, the miniaturization of medical devices and advances in signal processing have allowed the development of numerous alternative invasive imaging modalities, which permit detailed imaging of coronary artery morphology from inside. The breakthrough in intravascular imaging started approximately 20 years ago with the introduction of intravascular ultrasound
IVUS has the unique ability to provide high resolution cross sectional images that portray the luminal morphology, as well as the type of the plaque and its burden. Initially, IVUS had limited utility, mainly in research in the study of the effect of invasive and non-invasive treatments on atherosclerotic process. However, as the complexity of interventions increased there was an increased interest towards the clinical applications of IVUS and today it constitutes a valuable tool in clinical practice.

Another clinically useful intravascular modality is optical coherence tomography (OCT), which, similar to IVUS, provides cross sectional images of the coronary artery. OCT has evolved over the last decade and is based on the analysis of reflected light. A unique advantage of OCT is its increased axial resolution that permits visualization of intra-coronary features which are unseen by IVUS (e.g. thrombus) and reliable detection of the vulnerable plaque. The third intravascular imaging modality, which also allows visualization of the lumen, is angioscopy. This uses illumination fibers to assess vessel wall morphology. Another relatively new invasive imaging modality is near infrared spectroscopy (NIRS), which, in contrast to the previous techniques, cannot portray morphological features of the studied vessel, but uses infrared light to detect the type of the plaque. Finally, thermography is the last intracoronary imaging modality, which was introduced to measure the vessel wall temperature. This information has been proven useful in the detection of the plaques which are prone to rupture and cause acute coronary events as in these there is increased inflammation, and thus, they tend to have higher temperatures comparing to the stable plaques.

Intracardiac echocardiography (ICE) is the last invasive imaging technique, recently introduced to visualize in great detail the cardiac chambers and the major blood vessels. It is similar to intravascular ultrasound, and in contrast to transesophageal echocardiography, it does not requires intubation. This advantage, as well as its unique ability to provide high quality diagnostic images in real time, has rendered it a unique tool in structural interventions and in electrophysiology.

Though the abovementioned imaging modalities only emerged over the last two decades, they already have a recognized role in research and clinical arena. They have been used to understand the atherosclerotic process, to assess the extent and severity of the coronary artery disease, to evaluate the effect of pharmacological and invasive treatments, to estimate prognosis, and guide complex percutaneous coronary and structural intervention. The augmented use of these techniques and the increased amount of the diagnostic information provided has created the need for the development of automated methodologies which will allow fast and accurate analysis of the acquired data. Furthermore, advances in image processing and miniaturization devices have permitted the combination of the information given by two or more different imaging techniques. These data fusion methodologies provide hybrid models that allow a more thorough representation of vessel anatomy and pathology, and have an already established value in clinical practice and research. However, although there is a real revolution in invasive cardiac imaging, many doctors insist on using the traditional and old-fashioned diagnostic tools to assess coronary pathology and guide treatment. This is at least partially due to the fact that many medical doctors are not familiar with the newly developed intravascular modalities and ignore the data which support their clinical and research utility.

This objective of this book is to inform the readers and give a thorough and complete description of all the available intravascular imaging modalities. More specifically, it presents the technical aspects of each methodology aiming to demonstrate their advantages and indigenous limitations. A major scope of this manuscript is to familiarize the clinicians with these new intravascular modalities and provide guidance about the interpretation of the obtained data. This book also summarizes the applications of the available imaging modalities, reviews the literature, and informs the readers about how to use these
methodologies in clinical practice and research. It also includes a complete and detailed description of the existing processing methodologies and systems currently used to analyze the provided data. Finally, it aims to address future trends in intravascular imaging and discuss their potential value.

This book is intended to a broad spectrum of scientists working in the field of cardiovascular imaging. Cardiologists and interventional radiologists can greatly benefit from this as it provides valuable clinical information. It also refers to biomedical engineers and researchers as it presents an overview of the available knowledge in the field of image processing, which provides not only the background for further research, but also highlights the current limitations that need to be addressed in the future. Finally, the book can be used as a textbook in graduate courses for medical schools or engineering schools focusing on biomedical aspects.

This book is an edited volume, which received contributions from many scientists and researchers in the field. Part of the work, as well as its organization, has been performed within the framework of the ARTREAT project (ARTREAT: Multi-level patient-specific artery and atherogenesis model for outcome prediction, decision support treatment, and virtual hand-on training, FP7-224297), whose aim was to integrate different imaging modalities in order to provide reliable and comprehensive coronary representation and study the effect of blood flow on the atherosclerotic evolution. The contributors kindly offered their knowledge, and the editors assigned them different parts of this book. All chapters passed through a review process and they have been resubmitted in their final form.

The book is organized in ten sections. The first six present the available intravascular imaging techniques, namely: IVUS, angioscopy, thermography, OCT, NIRS, and ICE. The other four are divided as follows: section seven focuses on the current applications of invasive and non-invasive imaging, which rapidly evolves and nowadays challenges intravascular imaging, section eight on the hybrid cardiovascular imaging; section nine highlights the role of intravascular imaging in the understanding of the impact of rheology on plaque development, and the book finishes with section ten, which presents the future trends in cardiovascular imaging.

Section one is devoted to IVUS and includes six chapters. The first chapter describes the basic principles of IVUS image acquisition. Issues like the physical phenomena behind IVUS are discussed, as well as the artifacts that can affect IVUS image quality. Chapter two focuses on the interpretation and limitations of IVUS images, while chapter three presents the available image processing methodologies. This provides an overview of the methods developed for the segmentation of the IVUS sequence and the identification of the type of the plaque in grayscale IVUS frames, and presents the commercially available systems that incorporate these algorithms. Chapter four describes the plaque characterization techniques that are based on the analysis of the IVUS radiofrequency backscatter signal, while the last two chapters review the literature and present the current clinical and research applications of IVUS.

Section two focuses on the clinical and research utility of angioscopy. Initially, we present the historic evolution of this imaging technique and its limitations. In the main part of the section we stress the value of angioscopy in the study of the atherosclerotic evolution, discuss its role in the understanding of the mechanism of action of different interventional devices (e.g. stent, atherectomy, laser, etc.), and compare this modality with other invasive imaging techniques.

Section three is devoted to thermography and is divided in two chapters. In the fist we analyze the basic principles of thermography, discuss its limitations, and present the available devices used to measure in vivo the temperature of the coronary atherosclerotic plaques. This chapter is completed with the description of microwave radiometry, an alternative technique that provides non-invasive measurements of the heating of the plaque, and is currently under clinical evaluation. In the second chapter we
review the literature and present data from *in vitro* and *in vivo* studies that implemented thermography to measure the coronary wall temperature. These studies have improved our knowledge about the association between arterial wall inflammation and plaque vulnerability helped us to identify morphological characteristics associated with high risk plaques, and allowed us to assess their prevalence in different populations and the anti-inflammatory efficacy of various pharmacological treatments.

Section four deals with OCT and is divided in four chapters. The first chapter describes the engineering behind OCT image acquisition, while the second chapter focuses on the interpretation of OCT images and presents the available techniques developed for automated OCT processing. The third and the fourth chapter discuss the utility of this imaging technique in the current clinical practice and research arena.

NIRS is described in section five. Initially, we present the physical principles of NIRS and highlight its advantages in analyzing coronary wall tissue. In the main focus of the chapter we describe the NIRS system and present the results of the most important *in vitro* and *in vivo* validation studies. Finally, we discuss the clinical value of NIRS in assessing outcome after pharmaceutical or percutaneous coronary interventions and in detecting high risk patients who would be benefit by aggressive medical treatment.

Section six focuses on ICE. It describes the available devices and presents an overview of the typical images obtained during ICE examination. In addition, it discusses the current clinical applications of ICE in electrophysiology and structural interventional cardiology, and concludes with its limitations.

Section seven summarizes the current status of cardiovascular imaging. The first chapter of this section is devoted to the intravascular imaging techniques and particularly, IVUS and OCT, which are mainly used in clinical settings. The book focuses on their value in the assessment of the extent and the severity of coronary atherosclerosis and their utility in treatment planning during complex percutaneous coronary interventions. The second chapter deals with the non invasive imaging. It presents the current applications of non invasive imaging in portraying and assessing coronary atherosclerosis discusses its potentialities in the detection of vulnerable plaques and concludes with its current limitations.

Hybrid imaging is based on the integration of data provided by different imaging techniques and provides models which allow a more comprehensive and complete representation of coronary artery morphology. Today there are numerous data fusion methodologies with an evidenced based role in the diagnosis of coronary artery disease and have enriched our understanding about the atherosclerotic evolution. In section eight the available data fusion techniques are reviewed, and their clinical and research potentialities are discussed.

Blood flow haemodynamics appear to play a significant role in plaque development and destabilization. The current developments in intravascular imaging have allowed reliable representation of vessel’s morphology and geometry and permitted *in vivo* study of the role of local haemodynamics in the atherosclerotic evolution. Section nine provides the definition regarding the haemodynamic forces and flow patterns, reviews the literature, and cites the evidence concerning the effect of blood flow on atherosclerotic process.

Finally, the last section is devoted to the future trends in cardiovascular imaging. In the first chapter we analyze the necessity in developing new invasive imaging techniques, which will allow more accurate assessment of the anatomical and histopathological characteristics associated with increased plaque vulnerability. The second chapter discusses the potentialities of non invasive imaging modalities, and particularly, of multi slice computed tomography. It summarizes the current clinical utility of this promising imaging technique and attempts to foresee its future clinical and research applications. The last chapter is devoted to imaging techniques applied not to assess coronary morphology and anatomy but mainly to detect other features associated with increased vulnerability, such as the biomechanical profile
of the plaque, or the presence of inflammation and increased neo-vascularization, and aims to highlight the variety of the imaging options and the need to invest in the early detection of vulnerable plaques.

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