

## Optical Mapping of Cardiac Excitation and Arrhythmias

Edited by David S. Rosenbaum and José Jalife.  
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In the field of biomedical science, conceptual contributions and technological advances are closely related. The availability of new investigative instruments makes it possible to answer, from new points of view, the numerous questions that arise in the course of advancing science, and affects the questions that are asked in the process. The development of techniques for recording cardiac electrical activity has resulted in the study of rhythm disorders. The use of the capillary electrometer at the end of the 19<sup>th</sup> century and the cord galvanometer (electrocardiography) increased our ability to study the activation process and cardiac arrhythmias at the beginning of the 20<sup>th</sup> century, and enabled progress in the study of the mechanisms surrounding the appearance, perpetuation, or cessation of rhythm disorders. Two questions raised by initial studies of cardiac electrical phenomena were the identification of the temporary sequence of events involved in both normal and disease-related cardiac excitation, and the firm establishment of the location in which the phenomena being studied were occurring. The combination of chronological and spatial information is what we know as mapping, or cartography, of cardiac electrical activity where the resolution of the measures (time and distance) determines the precision of the analysis performed. In studies on activation and cardiac arrhythmias performed by pioneers of electrocardiography such as Lewis; by investigators belonging to the Holland school such as Durrer; or by members of the Mexican school, such as Sodi Pallarés, sequential cartography was performed to identify the moment of activation in areas where the recording electrodes were located during successive cycles. This cartographic technique requires a certain degree of stability and repetition of the phenomenon studied, as the temporal information obtained during successive cycles and the resulting spatial information (the activation «map») is completed by analyzing the process in various cycles whose number depends on the number of simultaneous recordings made (the number of cycles needed to complete the activation map equals the number of points being analyzed or number of electrodes used, or both). The ability to simultaneously record activation in multiple sites has made it possible to better analyze both the repetitive processes (improving spatial resolution and decreasing the time needed to collect information) and those changing processes in which the activation process constantly varies. The development of multiple electrodes, therefore, and the techno-

logy capable of processing and locating in space large amounts of information generated by the recordings from each electrode in the multiple electrode matrix has opened new doors to the study of cardiac electrical phenomena and has allowed better understanding of the activation process during complex arrhythmias such as atrial fibrillation, as was performed by Allesie in experimental models. Along with the development and perfecting of cartographic systems based on the use of multiple extracellular electrodes, another type of cartographic system has recently been developed that is based on optical procedures that do not require the use of electrodes and that increases the spatial resolution of cartography, as well as providing information on the myocardial repolarization process. This phenomena is optic mapping or cartography, whose principals are based on the use of colorants sensitive to changes in voltage and fluorescence directly resulting from transmembrane voltage of cardiac cells, so that information directly related to action potentials can be obtained and, therefore, information on the chronology and characteristics of the depolarization and repolarization processes of cardiac cells can be obtained. The light emitted by the fluorescent colorant is detected by photo detectors that, with video cameras or other imaging systems, permit mapping of the activation process. Depending on the type of photo detectors used, the temporal resolution of the cartography system varies, so that those based on the use of video cameras with great spatial resolution but less temporal resolution, depending on the frequency of the camera images.

The book *Optical Mapping of Cardiac Excitation and Arrhythmias*, edited by Drs. David Rosenbaum and José Jalife, explores in clear detail what optical cartography is and what its applications and principal contributions are to the study of cardiac activation and cardiac arrhythmias. The book begins with a preface written by Dr. Josephson that points out the advantages of optical mapping in relation to other techniques such as the great spatial resolution, the capacity to study phenomena occurring immediately after defibrillation, the capacity to evaluate propagation on a microscopic scale or the capacity to simultaneously analyze activation, excitation, and recuperation. He also points out some of the limitations of the technique, such as the use of drugs or procedures to avoid mechanical activity, as analysis of the recordings is difficult, or those related to the technique's inability to obtain direct information on intramural activation.

The book is divided into 4 sections. The first concerns basic principles, the second discusses the usefulness of the technique for analyzing microscopic propagation, the third deals with the study of cardiac arrhythmias, and the fourth discusses cardiac defibrillation. Each section is divided into several chapters written by authors who have worked directly in the fields discussed, and is preceded by an introduction written by the editors that summarizes the contribu-

tions of the technique. Similarly, with the exception of the first section, the sections end with a review written by Drs. Waldo, Packer, or Zipes that discusses the relevance of the clinical applications of the topic discussed.

The first section, entitled «Basic Principles», begins with an introduction by Dr. Rosenbaum that reviews the principles and components of the optical cartography system. This is followed by 5 chapters: the first explains the fundamentals of the technique and the history of its development; the second, the mechanisms and principles of fluorescence sensitive to voltage changes; the third, the optical properties of cardiac tissues and the factors that affect the transmission of light in tissues; the fourth chapter describes the optical systems and detectors used for optical cartography; and the fifth chapter discusses the filtration and signal processing systems used to achieve optimal visualization.

The second section is called «Microscopic Propagation», and also begins with an introduction written by Dr. Rosenbaum that highlights the role of optical cartography in providing information on temporal variations of transmembrane potentials and repolarization, without using electrodes. The section comprises 6 chapters. The 6<sup>th</sup> chapter deals with the propagation of impulses within cardiac myocytes, and the 7<sup>th</sup> with propagation among the myocytes; in chapter 8 recent discoveries on the basic mechanisms of discontinuous conduction are reviewed, analyzing the role of cell coupling, structural discontinuity, and tissue anisotropy, as well as the mechanisms underlying unidirectional blocking and micro-re-entrance. The subject of both chapters 9 and 10 is the propagation of impulses in the atrioventricular node analyzed by optical cartography. The section ends with chapter 11, in which Dr. Waldo reviews the significance of the clinical applications of the information provided by optical cartography on the activation of myocardial fibers.

The third section of the book is entitled «Cardiac Arrhythmias», and begins with an introduction by Dr. Jalife that stresses the relevant role of optical cartography in the study of the dynamics and mechanisms of arrhythmias. It consists of 6 chapters, the first 2 of which (chapters 12 and 13) are about aspects of repolarization such as its dispersion or the wavelength of the activation process. With regard to the dispersion of repolarization, the role of spatial heterogeneity of restitution kinetics and of repolarization gradients is discussed, indicating the dynamic characteristics of the electrophysiological substrates that make re-entrance activation possible. With relation to the activation wavelength, the contributions of the technique in determining this parameter and for the analysis of turning point conduction are discussed. Its dynamic characteristics are also analyzed, including factors such as stimulation frequency or early stimuli, and their relationship to other parameters such as the window of excitability and its pharmacological modulation. Chapter 14 is about the contributions of optical cartography using video images on the study of fibrillatory processes. In this chapter, subjects such as signal processing and the acquisition of isochrone and phase maps are analyzed, and topics such as the 3-dimensional nature of the atrial activation process are

discussed. Chapter 15 deals with the usefulness of the technique for recording fixed or moving spiral waves and analyzes its role in both monomorphic and polymorphic ventricular tachycardia. The chapter provides information obtained from the study of activation wave propagation in a transgenic model of hypertrophic cardiomyopathy, and the section ends with the chapter written by Dr. Packer that reviews the development of cartographic techniques and their usefulness in clinical practice, which has resulted in better knowledge of cardiac electrophysiology, the mechanisms explaining the source and perpetuation of arrhythmias, and the action of anti-arrhythmia medications. Lastly, Dr. Packer discusses the current limitations of the technique that prevent its clinical use such as the absence of optical windows, the presence of artifacts and noise related to movement, and the potential toxicity of the colorants when they are utilized *in vivo*.

The fourth section is entitled «Cardiac Defibrillation» and consists of 6 chapters. The introduction is written by Dr. Jalife and concerns the unique role of optical cartography in the study of cardiac defibrillation and the relationship that exists between the distribution of extracellular electrical gradients and transmembrane potentials. Chapter 18 deals with the analysis of cardiac myocyte response to electrical fields, discusses concepts such as the virtual electrode, and describes the cellular response in areas that are close to and far from the electrode, as well as the optical recording of individual cells. Chapter 19 analyzes new electrophysiological perspectives on the bi-dominion model, which assumes that cardiac syncytia can be represented by a 3-dimensional, non-linear, continuous cable that incorporates the effects of intracellular unions on intracellular conductivity. The role of the model in the study of cardiac fibrillation is also analyzed. In chapters 20, 21, and 22, the mechanisms of defibrillation are discussed; in chapter 22, the primary influence of fiber structures on tissue response to electrical stimulation is discussed and data is provided different stimulation modes, such as one point unipolar or linear unipolar modes. In the next chapter, the applications of laser sweep technology in the analysis of defibrillation is discussed, and chapter 22 is about the relationship between the success or failure of defibrillation and the wave fronts induced by virtual electrodes, as well as the role of phase singularities. In the last chapter of the book, Dr. Zipes reviews the clinical relevance and applications of the analysis of defibrillation with optical procedures, and discusses the hypotheses that exist on the mechanisms of ventricular defibrillation. The chapter ends with a reflection on the challenge presented by identifying people at risk for successive arrhythmias or sudden death and the prevention of these events, which underscores the need for increasing our knowledge about the mechanisms that cause ventricular fibrillation.

There are 174 figures and 3 tables in the book. The figures are uniformly distributed, well-edited, and are illustrative of the principles and phenomena described in the text. Each chapter is accompanied by a sufficient number of references citing the studies by chapter authors and other inves-

tigators, and allows further research on the subjects discussed in the book, which in and of itself is enough to obtain clear and up-to-date knowledge of optical cartography in the study of cardiac electrical phenomena.

In summary, and borrowing the comments made by Dr. Josephson in the preface, the book edited by Drs. David S. Rosenbaum and José Jalife provides the opportunity for bringing basic studies to the clinic, and augments understanding of the basis of cardiac electrophysiology, providing current information on the technique of optical cartography, the mechanisms of cardiac arrhythmias, the effects of anti-arrhythmia drugs, and the effects of electrical cardiac defibrillation.

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