Cardiac Mapping
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Third Edition

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This book is dedicated to those who paved the “roads of cardiac mapping” and to all who taught us: our mentors, colleagues, students and patients. We also dedicate this book to our wives, children, and parents for their continuous lifetime support and love.
CD-ROM

A companion CD-ROM is included at the front of the book.

The CD includes:

A database of video clips
A search function
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Preface to the Third Edition

Since the publication of the second edition of *Cardiac Mapping*, which stood as the only comprehensive textbook in the field, substantial achievements and breakthroughs have been made in the fields of interventional electrophysiology and imaging technologies. Today, mapping technology is no longer an investigational research tool; rather, it is an essential part of the clinical electrophysiology laboratory. The mapping of complex arrhythmias such as atrial and ventricular fibrillation introduces a new era in the management of these arrhythmias.

We are privileged that leading experts have accepted our invitation and provided a contemporary state-of-the-art reference work in the field. The third edition is somewhat different from its preceding editions in that it is focused on new developments in fields such as mapping of complex arrhythmias, stereotaxis, image integration, and future directions in cardiac mapping and imaging.

We hope that this new edition will remain a useful source for basic scientists and clinical electrophysiologists to understand mechanisms and improve patient outcomes by more accurate and safer mapping. In the introduction to the first edition we stated that cardiac mapping is an integral part of cardiac electrophysiology, which remains true; however, at this point, cardiac mapping and imaging are integrated, and we focus on the impact of new imaging technology and mapping.

The last chapter of this edition discusses new developments and future trends in cardiac mapping. A special chapter is also devoted to the limitations of each mapping technology. Paradoxically, in the recent AHA/ACC/ESC updated guidelines on clinical cardiac electrophysiology and ablation, very little was mentioned about mapping procedures: In view of the impressive progress in mapping techniques, a comprehensive review of the latest results is warranted.

As the field of interventional electrophysiology continues to evolve, cardiac mapping will remain an integral part of the science and practice of complex rhythm management.

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Preface to the Second Edition

The first edition of *Cardiac Mapping* stood out as the only textbook in the field with outstanding contributions from world-renowned authors. The book was well received and indeed sold out. Since the release of the first edition, there have been areas of significant progress and even major breakthroughs in the field of cardiac mapping and catheter ablation of arrhythmias. In particular, the technical advancements in noncontact and nonfluoroscopic mapping improved our understanding of the mechanism and thus the appropriate treatment of many arrhythmias, particularly atrial and ventricular fibrillation. The second edition offers a unique source for the latest developments in cardiac mapping of arrhythmias.

This new edition of *Cardiac Mapping* provides an important resource of the interventional electrophysiologist, rhythmologist, and those who are interested in understanding the mechanism of cardiac arrhythmias.

As the field of interventional electrophysiology continues to evolve, cardiac mapping will remain an integral part of the science and practice of electrophysiology.

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Cardiac mapping has always been an integral part of both experimental and clinical electrophysiology. Indeed, Sir Thomas Lewis systematically investigated the activation of the dog ventricle as early as 1915. The detailed activation map from that experiment is shown in Figure 1. Since then, cardiac mapping has evolved from single sequential probe mapping to very sophisticated computerized three-dimensional mapping. By the time cardiac mapping began being used in the surgical management of ventricular as well as supraventricular tachycardias, a large body of literature had already been collected.

Despite this significant progress, a collective textbook that attempted to discuss all aspects of cardiac mapping did not exist. When we first considered working on such a project, we were not sure if our friends and colleagues who have paved the road to this point would think it necessary to join us in this effort, especially in the era of implantable devices. We were surprised and encouraged by their unanimous positive support to go ahead with this text. (Many of the contributors have already asked about the second revised edition!) The contributors unanimously agreed to prepare manuscripts that discussed their latest work and that would subsequently be published in this, the only comprehensive book to present the state of the art on all aspects of cardiac mapping from computer simulation to online clinical application. Thus, we would like to thank all the contributors for presenting their best work here. Without them, this book would not have been possible.

A unique feature of this book is that the chapters are followed by critical editorial comments by the pioneer of that specific area, so that the state of the art is discussed. We hope this book will serve as an impetus to stimulate new ideas for cardiac mapping in the future.

The Editors
The Merriam-Webster online dictionary defines a map as “a representation . . . of the whole or a part of an area.” Indeed, reading maps is the fundamental process by which one navigates uncharted or unknown regions. The goal of such navigation may be simply to get from one point to another using the location of major structures such as mountains and rivers. For example, Lewis and Clark in 1803–4 explored the uncharted western United States, which allowed subsequent settlers to travel the same geography more easily, safely, and quickly. Maps can also be used to understand the composition of the underlying terrain, such as geologic maps of the earth’s crust. Finally, maps can be employed to comprehend functional changes superimposed on the various fixed structures, such as weather and geothermal maps. To be used effectively, the functional map must be interpreted in light of the topography and composition.

Fundamental to all maps is the ability to create an image. Lewis and Clark imaged the Missouri River through the Rocky Mountains to the Pacific Ocean. Later maps represented the composition of the soil, while still later maps, the functional terrain. And this is the general development of maps and their corresponding images, from noting fixed structures, to drilling down (literally and figuratively) into the fixed structures, to understanding functional events unfolding on top of, and within, the structures.

Mapping in medicine has followed the same general concepts. Initially, anatomists such as Virchow and Rokitansky noted the gross anatomy, while Purkinje, His, Tawara, and Watson and Crick, explored the cellular and subcellular composition. Starling, Harvey, and Einthoven composed functional maps of muscle contraction, blood flow, and electrical activation.

In fact, mapping and image generation have reached unprecedented importance in modern medicine. Molecular and autonomic imaging, cardiac CT, MRI, echo, electrocardiographic and electrophysiologic imaging, PET, along with image integration to superimpose functional images on stationery ones, have revolutionized our tools and capabilities to diagnose and treat in unparalleled ways. While satellite mapping confers precise images of the earth’s terrain, its composition, and functional events, so, too, the advances in medical imaging explore the body’s every nook and cranny. Joe Louis (world heavyweight boxing champion, 1937–49) said, when facing a title bout against Billy Conn in 1941, “He can run, but he can’t hide.” There is no longer any hiding in medicine.

The present book admirably captures the latest electrophysiologic advances in cardiac mapping and imaging, transporting the reader from the structure (e.g., left ventricular anatomy), to composition (e.g., areas of scar), to functional interplay on and within its surface (e.g., activation sequence of ventricular tachycardia). In today’s world, such knowledge is fundamental to delivering the latest diagnostic and therapeutic advances to our patients and makes reading this book mandatory.

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PART I

Historical Perspectives
CHAPTER 1
Cardiac Activation Mapping: The Amsterdam Years

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Summary
Starting in the late fifties of the last century professor Durrer and his cardiology group in Amsterdam developed a very strong base to expand our knowledge of electrocardiography and electrophysiology. It resulted in major accomplishments such as the unraveling of the complete excitation of the isolated perfused human heart and the introduction of programmed stimulation of the heart to induce and study clinically occurring cardiac arrhythmias.

Deciding factors in these advances were the presence of a brilliant leader, an interested and motivated group of coworkers, and the constant support from the department of medical physics.

Introduction
Essential for our understanding of cardiac function in health and disease is knowledge about the way, and in what sequence, the muscle cells of the different parts of the heart are activated. We require insight into the time course and instantaneous distribution of the excitatory process of the heart, and how this is represented in the electrocardiogram (ECG), which is a global representation of the activation process.

Already in 1918, Boden and Neukirch understood that in order to obtain data about total excitation of the heart the beating isolated heart should be studied [1]. It would take 50 more years, however, before epicardial and transmural activation of the isolated intact human heart would be accomplished by Dirk Durrer and colleagues in Amsterdam.

In the 1950s, Durrer, a cardiologist, started to study the cardiac activation process in the mammalian heart. He recognized from the beginning the necessity, especially in the ventricle, to study not only the activation process on the epicardium but also intramurally, in order to clearly delineate cardiac excitation and to correlate this excitation with the ECG.

Together with the physicist Henk van der Tweel, head of the department of medical physics at the University of Amsterdam, instrumentation was developed to study the activation in the ventricular wall. Needles were constructed allowing accurate measurements of transmural activation (Figure 1.1). Essential in this process was demonstration of the physico-mechanical basis of the intrinsic deflection of the electrogram indicating the timing of myocardial activation at the recording electrode. The outcomes of these 2D and 3D studies were published in four articles in the American Heart Journal in 1953–1955 [2–4].
Total Excitation of the Isolated Human Heart

The observations discussed above were made in the dog heart. But Durrer wanted to know how global electrical activation takes place in the intact human heart to help us understand its relation to the ECG. He assembled a group of investigators experienced in keeping the heart beating after being removed from the body, recording from multiple intramural terminals, and careful offline measurements of the recorded signals. Apart from Durrer, the group consisted of Rudolf van Dam, Gerrit Freud, Michiel Janse, Frits Meijler, and an American engineer, Robert Arzbacher.

After control experiments in canine hearts had shown that isolation and perfusion of the heart outside the body did not affect mode and speed of excitation as measured in situ, human hearts were studied. With informed consent of family members, hearts were obtained from individuals who had died from various cerebral conditions without a previous history of heart disease. This was at a time before cardiac transplantation! ECGs taken several hours before death showed no evidence of cardiac disease. The hearts were removed within 30 min after death, the criterion being cessation of cardiac activity.

The aorta was cannulated and attached to a Langendorff perfusion apparatus. The hearts were perfused with an oxygenated, heparinized, modified Tyrode solution, with washed bovine erythrocytes. Most hearts resumed beating spontaneously within the first 5 min of perfusion; in a few cases electrical defibrillation was needed because of ventricular fibrillation. The hearts continued beating in a spontaneous sinus rhythm for periods ranging from 4 to 6 hr.

The electrical activity of the heart was recorded from epicardial (hand-held) and intramural (needle) electrodes. Unipolar and bipolar leads were recorded on a 14-channel Ampex tape recorder. Data quality was controlled online using a 14-channel Elema inkwriter. For measuring activation times the tapes were played on the Elema inkwriter at a paper speed of 960 mm/sec, giving a time resolution of better than 1 msec.

All activation times were expressed in milliseconds following the onset of left ventricular depolarization. Measurements were made from as many as 870 intramural terminals. Figures 1.2 and 1.3 are from the publication in Circulation [6] showing both a 2D and 3D isochronic representation of ventricular activation of an isolated human heart using epicardial and intramural activation times. The figures beautifully illustrate early activation at the exits of the bundle branches and the spread of activation thereafter.

The Wolff–Parkinson–White syndrome

Starting in the 1930s, Holzman and Scherf [7] and Wolfeth and Wood [8] postulated that in patients with the Wolff–Parkinson–White (WPW) syndrome, two connections between atrium and ventricle were present, and that they could be incorporated in a tachycardia circuit with the impulse going from atrium to ventricle over one connection and from ventricle to atrium over the other.
Figure 1.2 Isochronic representation of ventricular activation of an isolated human heart, using measurements at 870 intramural electrode terminals. Each color represents a 5-msec interval.
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Figure 1.3 Three-dimensional isochronic representation of the activation of the same heart as in Figure 1.2. Color scheme identical to the one in Figure 1.2.

The author remembers discussions in Amsterdam in the early 1960s about this possibility, especially during visits from Howard Burchell of the United States. Around that time, a unique opportunity presented itself to obtain more information. In 1966, at Leiden University Hospital, A. G. Brom was scheduled to operate on a 21-year-old woman with an atrial septal defect of the secundum type. But the patient also had ECG changes that met the criteria for a diagnosis of WPW syndrome, and Brom consented to an epicardial map in the patient during sinus rhythm. So, Durrer and Jan Roos travelled to Leiden to map the epicardium of the heart prior to surgery.

Figure 1.4 shows the 12-lead ECG of the patient before the operation. Figure 1.5 shows the ventricular epicardial map during sinus rhythm. It is clear that in this patient, in contrast to epicardial, ventricular activation in a person with a normal ECG did not start in the area pretrabecularis, close to the descending left coronary artery. The earliest epicardial activation was found in the anterolateral part of the right ventricle very close to the tricuspid annulus [9].

Figure 1.4 The electrocardiogram of the patient whose epicardial activation map is shown in Figure 1.5. At that time it was called WPW type B. Now we would say that the patient has a right free wall accessory AV pathway located anterolaterally.
That observation clearly demonstrated an abnormal ventricular activation pattern that was very suggestive of a connection between the right atrium and the right ventricle. Then the question arose of how to prove that such a connection could play a role in the tachycardias that are so often present in the WPW patient. Again, an important contribution came from the department of medical physics.

Already in the early 1950s, experiments had been performed to study cardiac excitability in dogs. This required a special stimulator. This stimulator, and several more versatile ones thereafter, was developed in close collaboration with van der Tweel and his group. To study WPW patients, however, a stimulator was required not only able to synchronize to the patient’s rhythm and to give timed premature beats, but also able to perform basic pacing and induce premature stimuli at selected intervals.

Such a device was built by a young engineer, Leo Schoo, after long discussions between the medical physicists van der Tweel and Strackee, and the cardiologists Durrer and Reinier Schuilenburg. With this stimulator, stimuli with a regular rhythm could be produced by two basic pulse generators. The cycle length of these pulses could be varied with an accuracy of 1 msec from 9999 to 100 msec. Instantaneous changes in driving rate could be achieved by switching from one stimulator to the other. Two (in a later version, three) independent test pulses could be delivered during the spontaneous rhythm or during regular driving, with a selected interval accurate to 1 msec. The basic pulses and the two (or three) test pulses could be applied to one pair of stimulating electrodes or to separate pairs in any desired combination (Figure 1.6).

In the fall of 1966, this versatile stimulator was used in a patient with WPW syndrome. With catheters in the right atrium and right ventricle it was shown for the first time that by giving accurately timed stimuli, the properties of the two connections between atrium and ventricle differed, resulting in the initiation of a circus movement tachycardia using one connection for atrioventricular and the other one for ventriculo-atrial conduction. It was also demonstrated that these tachycardias could be terminated from atrium and ventricle by giving appropriately timed stimuli [10]. A registration from such a study is shown in Figure 1.7.

These observations, also the one by Coumel et al. [11], rapidly led on both sides of the Atlantic to the use of programmed electrical stimulation of the heart to study patients suffering from supraventricular tachycardias [12]. By placing catheters at
Figure 1.6 Photo of the sophisticated stimulation and registration equipment used in Amsterdam during the early studies in patients with tachycardias.

Figure 1.7 Example of the initiation and termination of a circus movement tachycardia by high right atrial stimuli. The intracardiac catheter is located in the coronary sinus. RK = retrograde Kent; sa = stimulus artefact.
different sites in the atrium, the ventricle, and the coronary sinus it soon became possible to map the site of origin or pathway of the tachycardia. This opened the door to new therapies for supraventricular tachycardias. The reproducible initiation and termination of ventricular tachycardia by programmed stimulation followed rapidly thereafter [13]. It took a while, however, before Mark Josephson and colleagues showed the importance of cardiac mapping in those patients [14].

In retrospect the advances made in Amsterdam were based on the presence of a brilliant, inspiring leader, a hard-working, motivated, interested group of coworkers, and the constant support from the department of medical physics. The Amsterdam years will always be remembered as an exciting journey into a new discovered land!

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