This book is accompanied by a website:
www.wiley.com/go/shenasa/cardiacmapping
The website includes:
• 47 video clips showing procedures described in the book
• All video clips are referenced in the text where you see this logo

Cardiac Mapping is the cardiac electrophysiologist’s GPS. It will guide you to new places in the heart and help you find the old places more easily… a valuable addition to your bookshelf
Douglas P. Zipes, from the Foreword.

Over the course of three previous editions, this book has become the acknowledged gold standard reference on the electro-anatomical mapping of the heart. This new edition features greatly expanded coverage—the number of chapters have doubled to 80 with 39 new chapters—on leading edge science, new clinical applications and future frontiers, authored by a who’s-who of global electrophysiology.
This unique text offers truly comprehensive coverage of all areas of cardiac mapping, from core scientific principles to methodological and technical considerations, to the latest data that you can put to work caring for patients. In addition, the all new 4th edition adds essential content on:
- mapping in experimental models of arrhythmias
- mapping supraventricular and ventricular tachyarrhythmias
- new catheter-based techniques
- also featuring a companion website with video clips illustrating essential techniques described in the text

The only state-of-the-art, stand-alone text on this dynamic subject, Cardiac Mapping is an essential resource for basic scientists, clinical electrophysiologists, cardiologists and all physicians who care for patients with cardiac arrhythmias.
Cardiac Mapping
We dedicate this book to those who have paved the “roads of cardiac mapping” and to all who have 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.

Companion website

This book is accompanied by a website:

www.wiley.com/go/shenasa/cardiacmapping

The website includes:

- 47 video clips showing procedures described in the book
- All video clips are referenced in the text where you see this logo
Contents

List of Contributors, ix
Preface to the Fourth Edition, xv
Preface to the First Edition, xvi
Foreword by Douglas P. Zipes, xvii
European Perspective by A. John Camm, xix
Acknowledgements, xx

Part I Methodological and Technical Considerations

1 Evolution of Cardiac Mapping: From Direct Analog to Digital Multi-Dimensional Recording, 3
   Jacques M. T. de Bakker and Marc A. Vos

2 Image Acquisition and Processing in New Technologies, 12
   Clinton Schneider and Srijoy Mahapatra

3 Microelectrode Arrays in Cardiac Mapping, 18
   Thomas Meyer, Elke Guenther and Udo Kraushaar

4 Cardiac Morphology Relevant to Mapping, 28
   Siew Yen Ho, Josè Angel Cabrera and Damian Sánchez-Quintana

5 Comparison of Mapping Technologies for Cardiac Electrophysiology, 36
   Ross J. Hunter and Richard J. Schilling

6 Interpretation of Electrograms and Complex Maps of Different Mapping Technologies, 46
   Kyoko Soejima and Seiji Fukamizu

7 Cardiac Mapping: Approach and Troubleshooting for the Electrophysiologist, 53
   Matthew J. Swale and Samuel J. Asirvatham

Part II Mapping in Experimental Models of Cardiac Arrhythmias

8 Optical Mapping: Its Impact on Understanding Arrhythmia Mechanisms, 71
   Jan Némec, Jong Kim and Guy Salama

9 Optical Mapping of the Sinoatrial Node and Atrioventricular Node, 79
   Ajit H. Janardhan, Di Lang and Igor R. Efimov

10 Panoramic Optical Imaging of Cardiac Arrhythmias, 90
    Crystal M. Ripplinger

11 Optical Imaging of Arrhythmias in Cardiomyocyte Monolayer Culture, 98
    Herman D. Himel IV, Gil Bub and Nabil El-Sherif

12 Mapping of Rotors in Atrial Fibrillation: From Animal Models to Humans, 108
    Omer Berenfeld, David Filgueiras-Rama and Felipe Atienza

13 Multiple Mechanisms Causing Ventricular Tachycardia, 119
    Andrew L. Wit and Mark E. Josephson

14 Modeling of Atrial Fibrillation, 131
    Nathalie Virag, Vincent Jacquemet and Lukas Kappenberger

15 Modeling of Ventricular Arrhythmias, 140
    Natalia A. Trayanova

16 Personalized Electrophysiological Modeling of the Human Atrium, 150
    Olaf Dössel, Martin W. Krüger and Gunnar Seemann

17 Mapping of the Atrial Neural Network: Autonomic Mechanisms Underlying Complex Fractionated Atrial Electrograms and the Substrate for Atrial Fibrillation, 159
    Youqi Fan, Benjamin J. Scherlag, Yu Liu, Heng Cai, Lilei Yu, Eric Hepler, Shailesh Male, Warren M. Jackman and Sunny S. Po

18 Mapping of Atrial Repolarization Changes and Tachyarrhythmia Sites of Origin During Activation of Mediastinal Nerve Inputs to the Intrinsic Cardiac Nervous System, 172
    René Cardinal and Pierre Pagé
Contents

19 How to Map Autonomic Activity, 179  
Eue-Keun Choi, Mark J. Shen, Shien-Fong Lin, Michael C. Fishbein, Lan S. Chen and Peng-Sheng Chen

Part III  Mapping of Supraventricular Tachyarrhythmias

20 Mapping of Human Atrial Flutter and Its Variants, 191  
Navinder S. Sawhney, Wayne Whitwam and Gregory K. Feld

21 New Insights into Reentry Circuits from Mapping and Ablation of Atrioventricular Nodal Reentrant Tachycardia, 213  
Tomos Walters and Jonathan M. Kalman

22 Atrioventricular Nodal Reentrant Tachycardia: Current Understanding and Controversies, 224  
Mohammad-Reza Jazayeri, Edward T. Keelan and Mohammad-Ali Jazayeri

23 Mapping of Typical Preexcitation Syndromes, 249  
Pradyot Saklani, Peter Leong-Sit, Lorre J. Gula, Allan C. Skanes, Andrew D. Krahn, Raymond Yee and George J. Klein

24 Cardiac Mapping in Variants of the Ventricular Preexcitation Syndrome, 262  
Eduardo Back Sternick, Yash Lokhandwala and Hein J. J. Wellens

25 Three-Dimensional Post-Pacing Interval Mapping of Left Atrial Tachycardia, 299  
Philipp Sommer and Christopher Piorkowski

26 Recent Observations in Mapping of Complex Fractionated Atrial Electrograms in Atrial Fibrillation, 306  
Koonlawee Nademanee and Montawatt Amnueypol

27 Monophasic Action Potential Recordings in Atrial Fibrillation and Role of Repolarization Alternans, 317  
Michael R. Franz, Sameer M. Jamal and Sanjiv Narayan

28 Mapping of the Atrial Electrogram in Sinus Rhythm and Different Atrial Fibrillation Substrates, 328  
Yenn-Jiang Lin, Shih-Lin Chang, Li-Wei Lo and Shih-Ann Chen

29 Management of Atrial Tachycardias Arising in the Context of Atrial Fibrillation Ablation, 341  
Amir S. Jadidi, Ashok J. Shah, Meleze Hocini, Michel Haïssaguerre and Pierre Jaïs

30 Stepwise Approach to Management of Atrial Arrhythmias after Catheter Ablation of Atrial Fibrillation, 351  
Borislav Dinov, Arash Arya and Gerhard Hindricks

31 Mapping of Persistent Atrial Fibrillation: How Many Sites, How Many Lines?, 358  
Claude S. Elayi, Luigi Di Biase, Gustavo Morales, Jenks Thompson and Andrea Natale

32 Mapping of Focal Right Atrial and Coronary Sinus Tachycardias, 367  
Nitish Badhwar, Byron K. Lee, Melvin M. Scheinman and Jeffrey E. Olgin

33 Is There a Role For Mapping of Dominant Frequency in Human Atrial Fibrillation?, 380  
Hakan Oral and Fred Morady

34 Do Mapping Strategies Influence the Outcome in AF Ablation?, 391  
Laura Vitali Serdoz and Riccardo Cappato

35 Mapping of Atrial Fibrillation: Comparing Complex Fractionated Atrial Electrograms, Voltage Maps, Dominant Frequency Maps and Ganglionic Plexi, 400  
Amin Al-Ahmad and John A. Schoenhard

36 Mapping Strategies in Failed and Redo Ablation of Atrial Arrhythmias, 410  
Stephen B. Wilton, Shinsuke Miyazaki and Michel Haïssaguerre

37 The Use of Multi-electrode Catheters for Electroanatomical Mapping of Atrial Fibrillation, 418  
Moussa Mansour and Jeremy N. Ruskin

Part IV  Mapping of Ventricular Tachyarrhythmias

38 Mapping of VT in Structurally Normal Hearts, 425  
Amit J. Thosani, Martin L. Bernier and Mark E. Josephson

39 Advances in Mapping and Catheter Ablation of Ventricular Arrhythmias in Ischemic and Scar-related Substrates, 439  
Ransford S. Brenya, Deepak Bhakta and John M. Miller

40 Mapping of Ventricular Tachycardias in Rare Cardiomyopathies, 450  
Lars Eckardt, Dirk Dechering, Stephan Zellerhoff, Günter Breithardt and Kristina Wasmer

41 Advances in Mapping of Ventricular Fibrillation and Defibrillation: Role of the Purkinje System, 459  
Derek J. Dosdall, Paul B. Tabereaux and Raymond E. Ideker

42 Phase Mapping of Cardiac Fibrillation: Applications in Studying Human Ventricular Fibrillation, 467  
Karthikeyan Umapathy, Stéphane Massé and Kumaraswamy Nanthakumar
## Contents

43 Myocardial Substrate Mapping in Non-ischemic Cardiomyopathy Ventricular Tachycardia, 477
   Michifumi Tokuda and William G. Stevenson

44 Epicardial Mapping: Technique, Indication and Results, 484
   Jeffrey R. Winterfield, Alexander Green, Peter Santucci, Smit Vasaiwala and David J. Wilber

45 Combined Endocardial and Epicardial Mapping of Ventricular Tachycardia, 500
   Mathew D. Hutchinson and Francis E. Marchlinski

46 Localization of the Arrhythmogenic Substrate in Non-ischemic Cardiomyopathy: Combined Endocardial and Epicardial Mapping and Ablation, 514
   Nilesh S. Mathuria, Roderick Tung and Kalyanam Shivkumar

47 Is Resetting and Entrainment Mapping Still Useful with New Technologies?, 524
   David J. Callans

48 Should We Map and Ablate the Triggers, Substrates, Ventricular Tachycardia Circuit or All?, 537
   Daniel Steven, Jakob Lüker, Arian Sultan, Imke Drewitz, Boris Hoffmann, Helge Servatius and Stephan Willems

49 Mapping of Ventricular Arrhythmias Originating from Aortic and Pulmonic Valves, 544
   Erik Wissner, Andreas Metzner, Roland Richard Tilz, Feifan Ouyang and Karl-Heinz Kuck

50 Do Mapping Strategies Influence Outcomes in Ventricular Tachycardia Ablation?, 551
   Pasquale Vergara, Nicola Trevisi and Paolo Della Bella

---

### Part V Future Directions and Technologies in Cardiac Mapping and Imaging of Cardiac Arrhythmias

   Thomas Gaspar and Christopher Piorkowski

52 Role of Remote Navigation in Mapping and Ablation of Complex Arrhythmias, 566
   Sabine Ernst

53 Diffusion Tensor Magnetic Resonance Imaging-Derived Myocardial Fiber Disarray in Hypertensive Left Ventricular Hypertrophy: Visualization, Quantification and the Effect on Mechanical Function, 574
   Archontis Giannakidis, Damien Rohmer, Alexander I. Veress and Grant T. Gullberg

54 Imaging Fiber Orientation with Optical Coherence Tomography and Diffusion-Tensor Magnetic Resonance Imaging and its Role in Arrhythmogenesis, 589
   Rachel C. Myles and Crystal M. Ripplinger

55 Novel Imaging Strategies for Cardiac Arrhythmias, 598
   Abhishek Deshmukh, Jagat Narula and Partho P. Sengupta

56 Role of Magnetic Resonance Imaging in Mapping the Architecture of the Arrhythmia Substrate in Patients with Ischemic and Non-ischemic Cardiomyopathy, 612
   Frank Bogun and Gisela Mueller

57 New Image Integration Technologies for Optimization of Cardiac Resynchronization Therapy, 620
   Charlotte Eitel and Christopher Piorkowski

58 Role of Mapping and Imaging in Brugada Syndrome, 627
   Sergio Richter and Pedro Brugada

59 Role of Mapping and Ablation in Genetic Diseases: Long QT Syndrome and Catecholaminergic Polymorphic Ventricular Tachycardia, 644
   Steven J. Fowler, Larry A. Chinitz and Silvia G. Priori

60 Role of Late Gadolinium-Enhanced Magnetic Resonance Imaging in Detection and Quantification of Atrial Fibrosis, 656
   Alexis Ramirez and Nassir F. Marrouche

61 Hypertrophic Cardiomyopathy: Risk Stratification and Management of Arrhythmia, 664
   Pier D. Lambiase and William J. McKenna

62 Role of Magnetic Resonance Imaging in Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy, 678
   Aditya Bhonsale, Hugh Calkins and Harikrishna Tandri

63 Role of Cardiac Computed Tomography Imaging to Guide Catheter Ablation of Arrhythmias in Complex Cardiac Morphologies, 686
   Farhood Saremi

64 Multi-modality and Multi-dimensional Mapping: How Far Do We Need To Go?, 705
   Nikolaos Kanagkinis, Arash Arya and Gerhard Hindricks

65 Advances in Non-invasive Electrocardiographic Imaging: Examples of Atrial Arrhythmias, 712
   Yoram Rudy, Phillip S. Cuculich and Ramya Vijayakumar

66 ST Segment Mapping in Ventricular Tachycardia, 722
   Levent Sahiner and Ali Oto
<table>
<thead>
<tr>
<th>Chapter</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>67</td>
<td>Microvolt T-wave Alternans</td>
<td>726</td>
</tr>
<tr>
<td></td>
<td><em>Levent Sahiner and Ali Oto</em></td>
<td></td>
</tr>
<tr>
<td>68</td>
<td>Electrophysiological Implications of Myocardial Cell and Gene Therapy Strategies</td>
<td>732</td>
</tr>
<tr>
<td></td>
<td><em>Leonid Maizels and Lior Gepstein</em></td>
<td></td>
</tr>
<tr>
<td>69</td>
<td>Towards Non-invasive Mapping and Imaging of Cardiac Arrhythmias</td>
<td>742</td>
</tr>
<tr>
<td></td>
<td><em>Victoria Delgado, Matteo Bertini and Jeroen J. Bax</em></td>
<td></td>
</tr>
<tr>
<td>70</td>
<td>Mapping and Ablation of Ventricular Arrhythmias in Patients with Congenital Heart Disease</td>
<td>756</td>
</tr>
<tr>
<td></td>
<td><em>Edward P. Walsh</em></td>
<td></td>
</tr>
<tr>
<td>71</td>
<td>Mapping and Imaging of Supraventricular Arrhythmias in Adult Complex Congenital Heart Disease</td>
<td>771</td>
</tr>
<tr>
<td></td>
<td><em>Paul Khairy</em></td>
<td></td>
</tr>
<tr>
<td>72</td>
<td>Remodeling and Reverse Remodeling: Mapping/Imaging Findings</td>
<td>788</td>
</tr>
<tr>
<td></td>
<td><em>Philippe Comtois and Stanley Nattel</em></td>
<td></td>
</tr>
<tr>
<td>73</td>
<td>Epicardial Mapping of Longstanding Persistent Atrial Fibrillation</td>
<td>797</td>
</tr>
<tr>
<td></td>
<td><em>Natasja de Groot and Maurits A. Allessie</em></td>
<td></td>
</tr>
<tr>
<td>74</td>
<td>Use of Intracardiac Echocardiography to Guide Ablation of Atrial and Ventricular Arrhythmias</td>
<td>809</td>
</tr>
<tr>
<td></td>
<td><em>Jason T. Jacobson and Bradley P. Knight</em></td>
<td></td>
</tr>
<tr>
<td>75</td>
<td>Role of Magnetic Resonance Imaging in Electrophysiology</td>
<td>819</td>
</tr>
<tr>
<td></td>
<td><em>Anita Wokhu and Douglas L. Packer</em></td>
<td></td>
</tr>
<tr>
<td>76</td>
<td>Magnetic Resonance Phase Mapping for Myocardial Structural Abnormalities Relevant to Arrhythmias</td>
<td>828</td>
</tr>
<tr>
<td></td>
<td><em>Daniela Föll, Thomas Faber, Michael Markl, Christoph Bode and Bernd Jung</em></td>
<td></td>
</tr>
<tr>
<td>77</td>
<td>Three-Dimensional Mapping to Guide Optimal Catheter Position in Cardiac Resynchronization Therapy</td>
<td>836</td>
</tr>
<tr>
<td></td>
<td><em>David Spragg, Fady Dawoud and Albert C. Lardo</em></td>
<td></td>
</tr>
<tr>
<td>78</td>
<td>Array Tomography for Cardiovascular Imaging: Description of Technique and Potential Applications</td>
<td>847</td>
</tr>
<tr>
<td></td>
<td><em>Sanaz Saatchi, Stephen J. Smith and Kristina D. Micheva</em></td>
<td></td>
</tr>
<tr>
<td>79</td>
<td>Optimizing Patient Safety and Image Quality with Cardiac Mapping and Imaging Tools During Catheter Ablation</td>
<td>857</td>
</tr>
<tr>
<td></td>
<td><em>Monica Jiddou and David E. Haines</em></td>
<td></td>
</tr>
<tr>
<td>80</td>
<td>The Future of Cardiac Mapping: Dawn of a New Decade</td>
<td>867</td>
</tr>
<tr>
<td></td>
<td><em>Mohammad Shenasa, Shahriar Heidary, Javad Rahimian and Gerhard Hindricks</em></td>
<td></td>
</tr>
</tbody>
</table>

**Companion website**

This book is accompanied by a website:  
[www.wiley.com/go/shenasa/cardiacmapping](http://www.wiley.com/go/shenasa/cardiacmapping)

The website includes:  
- 47 video clips showing procedures described in the book  
- All video clips are referenced in the text where you see this logo
List of Contributors

Amin Al-Ahmad MD
Stanford University Medical Center, Stanford, CA, USA

Maurits Allessie MD
Department of Physiology, Cardiovascular Research Institute Maastricht, Maastricht University, The Netherlands

Montawatt Amnueypol MD
Pacific Rim Electrophysiology Research Institute at White Memorial Hospital, Los Angeles, CA, USA; Bangkok Medical Center, Bangkok, Thailand

Arash Arya MD
Department of Electrophysiology, University of Leipzig, Heart Center, Leipzig, Germany

Samuel J. Asirvatham MD
Division of Cardiovascular Diseases, Department of Pediatrics and Adolescent Medicine, Mayo Clinic, Rochester, MN, USA

Felipe Atienza MD, PhD
Electrophysiology Laboratory, Cardiology Department, Hospital General Universitario Gregorio Marañón and Universidad Complutense de Madrid, Madrid, Spain

Nitish Badhwar MD
Cardiac Electrophysiology, Division of Cardiology, Department of Medicine, University of California San Francisco, CA, USA

Jacques M. T. de Bakker PhD
Department of Medical Physiology and the Division of Heart and Lungs, University Medical Center, Utrecht, the Netherlands; The Center of Heart Failure Research, Department of Experimental Cardiology, Academic Medical Center, Amsterdam, the Netherlands; Interuniversity Cardiology Institute of the Netherlands, Utrecht, the Netherlands

Jeroen J. Bax MD, PhD
Department of Cardiology, Leiden University Medical Center, Leiden, the Netherlands

Omer Berenfeld PhD
Center for Arrhythmia Research, Departments of Internal Medicine and of Biomedical Engineering, University of Michigan, Ann Arbor, Michigan, MI, USA

Martin L. Bernier MD
Division of Cardiac Electrophysiology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA

Matteo Bertini MD, PhD
Department of Cardiology, S. Anna University Hospital, Cona-Ferrara, Italy

Deepak Bhakta MD
Indiana University School of Medicine, Indianapolis, IN, USA

Aditya Bhonsale MD
The Johns Hopkins Hospital, Baltimore, MD, USA

Christoph Bode, MD
Cardiology and Angiology I, Heart Center Freiburg University, Freiburg, Germany

Frank Bogun MD
Department of Internal Medicine, Division of Cardiology, University of Michigan, Ann Arbor, MI, USA

Martin Borggreve MD
Department of Angiology and Pneumology, University Medical Center, University of Heidelberg Mannheim, Germany

Günter Breithardt MD
Department of Cardiology and Angiology, Hospital of the University of Münster, Münster, Germany

Ransford S. Brenya MD
Indiana University School of Medicine, Indianapolis, IN, USA

Pedro Brugada MD, PhD
Heart Rhythm Management Center, Cardiovascular Center, Free University of Brussels, Brussels, Belgium

Gil Bub PhD
Department of Physiology, Anatomy and Genetics, University of Oxford, Oxford, UK

José Angel Cabrera MD, PhD
Hospital Quirón, Madrid, Spain

Heng Cai MD
TianJin Medical University General Hospital, TianJin, China

Hugh Calkins MD
The Johns Hopkins Hospital, Baltimore, MD, USA

David J. Callans MD
Cardiovascular Division, Department of Medicine, University of Pittsburgh, Pittsburgh, PA, USA

A. John Camm MD
British Heart Foundation, St. George’s, University of London, London, UK

Riccardo Cappato MD
Arrhythmias and Electrophysiology Center, IRCCS, Policlinico San Donato, Milan, Italy

René Cardinal PhD
Centre de recherche, Hôpital du Sacré-Cœur de Montréal, QC, Canada; Department of Pharmacology, Faculty of Medicine, Université de Montréal, Montréal, QC, Canada

Shih-Lin Chang MD, PhD
School of Medicine, National Yang-Ming University, Taipei, Taiwan; Division of Cardiology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan

Lan S. Chen MD
Department of Neurology, Indiana University School of Medicine, Indianapolis, IN, USA

Peng-Sheng Chen MD
Kranert Institute of Cardiology, Division of Cardiology, Department of Medicine, Indiana University School of Medicine, Indianapolis, IN, USA
List of Contributors

David E. Haines MD
Department of Cardiovascular Medicine, Oakland University William Beaumont School of Medicine and Beaumont Health System, Royal Oak, MI, USA

Michel Haïssaguerre MD
Service de Rhythmologie, Hôpital Cardiologique du Haut Lévêque, Université Bordeaux II, Pessac, France

Shahriar Heidary MD
Division of Cardiovascular Medicine, Stanford University School of Medicine, Stanford, CA, USA; Department of Cardiovascular Services, O’Connor Hospital, San Jose, CA, USA

Eric Hepler BA
St. Jude Medical, Atrial Fibrillation Division, Minnetonka, MN, USA

Herman D. Himel IV PhD
Department of Biomedical Engineering, Duke University, Durham, NC, USA

Gerhard Hindricks MD, PhD
Department of Electrophysiology, University Leipzig, Heart Center, Leipzig, Germany

Siew Yen Ho PhD
Cardiac Morphology Unit, Royal Brompton Hospital, London, UK

Meleze Hocini MD
Hôpital Cardiologique du Haut-Lévêque and Université Bordeaux II, Bordeaux, France

Boris Hoffmann MD
University Heart Center, Hamburg, Germany

Ross J. Hunter MRCP
Department of Cardiology, St. Bartholomew’s Hospital, Barts Health NHS Trust and QMUL, London, UK

Mathew D. Hutchinson MD
Cardiovascular Division, Department of Medicine; University of Pennsylvania Perelman School of Medicine; Philadelphia, PA, USA

Raymond E. Ideker MD, PhD
Departments of Cardiovascular Disease, Physiology and Bioengineering, University of Alabama at Birmingham, Birmingham, AL, USA

Warren M. Jackman MD
Heart Rhythm Institute at the University of Oklahoma, Health Sciences Center, Oklahoma City, OK, USA

Jason T. Jacobson MD
Columbia University Division of Cardiology at Mount Sinai Medical Center, Miami Beach, FL, USA

Vincent Jacquet MD
Department of Physiology, University of Montreal and Centre de Recherche, Hôpital du Sacré-Coeur, Montréal, QC, Canada

Amir S. Jadidi MD
Hôpital Cardiologique du Haut-Lévêque and Université Bordeaux II, Bordeaux, France

Pierre Jaïs MD
Hôpital Cardiologique du Haut-Lévêque and Université Bordeaux II, Bordeaux, France

Sameer M. Jamal MD
Veteran Affairs Medical Center and Washington Hospital Center, Washington, DC, USA

Ajit H. Janardhan MD, PhD
Department of Medicine, Division of Cardiology, Washington University School of Medicine, St. Louis, MO, USA

Mohammad-Ali Jazayeri BS
Medical College of Wisconsin, Milwaukee, WI, USA

Mohammad-Reza Jazayeri MD
Bellin Health Hospital Center, Green Bay, WI, USA

Monica Jiddou MD
Department of Cardiovascular Medicine, Oakland University William Beaumont School of Medicine and Beaumont Health System, Royal Oak, MI, USA

Mark E. Josephson MD
Cardiovascular Medicine Division, Harvard–Thorndike Electrophysiology Institute and Arrhythmia Service, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA

Bernd Jung PhD
Department of Radiology, Medical Physics, University Medical Center Freiburg, Freiburg, Germany

Jonathan M. Kalman MD
Department of Cardiology, Royal Melbourne Hospital and the Department of Medicine, University of Melbourne, Melbourne, Australia

Nikolaos Kanagkinis MD
Department of Electrophysiology, University of Leipzig, Heart Center, Leipzig, Germany

Lukas Kappenberger MD
Lausanne Heart Group, Lausanne, Switzerland

Edward T. Keelan MD
Mater Private Healthcare, Dublin, Ireland

Paul Khairy MD, PhD
Adult Congenital Heart Center and Electrophysiology Service, Montreal Heart Institute, University of Montreal, Montreal, QC, Canada

Jong Kim PhD
Department of Medicine, Cardiovascular Institute, University of Pittsburgh, Pittsburgh, PA, USA

George J. Klein MD
Cardiac Electrophysiology, Division of Cardiology, Western University, ON, Canada

Bradley P. Knight MD
Department of Internal Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

Andrew D. Krahn MD
Cardiac Electrophysiology, Division of Cardiology, Western University, London, ON, Canada

Udo Kraushaar PhD
Natural and Medical Sciences Institute at the University of Tuebingen, Reutlingen, Germany

Martin W. Krüger PhD
Institute of Biomedical Engineering, Karlsruhe Institute of Technology (KIT), Karlsruhe, Germany

Karl-Heinz Kuck MD, PhD
Electrophysiology Laboratory, II. Medizinische Abteilung, Asklepios Klinik St. Georg, Hamburg, Germany

Di Lang MS
Department of Biomedical Engineering, Washington University in St. Louis, MO, USA

Pier D. Lambiase MD, PhD
Institute of Cardiovascular Science, University College London, London, UK

Albert C. Lardo PhD
Division of Cardiology, The Johns Hopkins Hospital, Baltimore, MD, USA

Byron K. Lee MD
Cardiac Electrophysiology, Division of Cardiology, Department of Medicine, University of California San Francisco, CA, USA
List of Contributors

Peter Leong-Sit MD, MSc
Cardiac Electrophysiology, Division of Cardiology, Western University, London, ON, Canada

Shien-Fong Lin MD
KranMeck Institute of Cardiology, Division of Cardiology, Department of Medicine, Indiana University School of Medicine, Indianapolis, IN, USA

Yenn-Jiang Lin MD, PhD
School of Medicine, National Yang-Ming University, Taipei, Taiwan; Division of Cardiology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan

Yu Liu MD
Department of Cardiology, Renmin Hospital of Wuhan University, Wuhan, Hubei, China

Li-Wei Lo MD
School of Medicine, National Yang-Ming University, Taipei, Taiwan; Division of Cardiology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan

Yash Lokhandwala MD
Arrhythmia Associates, Mumbai, India

Jakob Lüker MD
University Heart Center, Hamburg, Germany

Srijoy Mahapatra MD
Atrial Fibrillation Division, St. Jude Medical, St. Paul, MN, USA

Leonid Maizels BSc
The Sohnis Family Research Laboratory for Cardiac Electrophysiology and Regenerative Medicine, Bruce Rappaport Institute in the Medical Sciences, Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel

Shailesh Male MD
Heart Rhythm Institute at the University of Oklahoma, Health Sciences Center, Oklahoma City, OK, USA

Moussa Mansour MD
Cardiac Electrophysiology Laboratory, Massachusetts General Hospital; Harvard Medical School, Boston, MA, USA

Francis E. Marchlinski MD
Cardiovascular Division, Department of Medicine; University of Pennsylvania Perelman School of Medicine; Philadelphia, PA, USA

Michael Markl PhD
Department of Radiology, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA; Department of Biomedical Engineering, McCormick School of Engineering, Northwestern University, Chicago, IL, USA

Nassir F. Marrouche MD
CARMA Center and Cardiac Electrophysiology Laboratories, University of Utah Health Sciences Center, Salt Lake City, UT, USA

Stéphane Massé MASc
The Hull Family Cardiac Fibrillation Management Laboratory, University Health Network, Toronto, ON, Canada

Nilesh S. Mathur MD
UCLA Cardiac Arrhythmia Center, UCLA Health System, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA

William J. McKenna MD, DSc
Institute of Cardiovascular Science, University College London, London, UK

Andreas Metzner MD
Electrophysiology Laboratory, II. Medizinische Abteilung, Asklepios Klinik St. Georg, Hamburg, Germany

Thomas Meyer PhD
Multi Channel Systems, Reutlingen, Germany

Kristina D. Micheva PhD
Department of Molecular and Cellular Physiology, Stanford University School of Medicine, Stanford, CA, USA

John M. Miller MD
Indiana University School of Medicine, Indianapolis, IN, USA

Shinsuke Miyazaki MD
Service de Rhythmologie, Hôpital Cardiologique du Haut Lévêque, Université Bordeaux II, Pessac, France

Fred Morady MD
Division of Cardiovascular Medicine, University of Michigan, Ann Arbor, MI, USA

Gustavo Morales MD
University of Kentucky, Lexington, KY, USA

Gisela Mueller MD
Department of Radiology, University of Michigan, Ann Arbor, MI, USA

Rachel C. Myles MBBS, PhD
British Heart Foundation Cardiovascular Research Centre, University of Glasgow, Glasgow, UK

Koonlawee Nademane MD
Pacific Rim Electrophysiology Research Institute at White Memorial Hospital, Los Angeles, CA, USA; Bangkok Medical Center, Bangkok, Thailand

Kumaraswamy Nanthakumar MD
The Hull Family Cardiac Fibrillation Management Laboratory, University Health Network, Toronto, ON, Canada

Sanjiv Narayan MD
Veteran Affairs Medical Center and University of California San Diego, San Diego, CA, USA

Jagat Narula MD, DM, PhD
Zena and Michael A. Wiener Cardiovascular Institute, Mount Sinai School of Medicine, New York, NY, USA

Andrea Natale MD
Texas Cardiac Arrhythmia Institute at St. David’s Medical Center, Austin, TX, USA; Department of Biomedical Engineering University of Texas, Austin, TX, USA; California Pacific Medical Center, San Francisco, CA, USA

Stanley Nattel MD
Department of Medicine, University of Montreal, Montreal, QC, Canada; Electrophysiology Research Program, Montreal Heart Institute Research Center, Montreal, QC, Canada

Jan Němec MD
Department of Medicine, Cardiovascular Institute, University of Pittsburgh, Pittsburgh, PA, USA

Denis Noble PhD
Department of Physiology, Anatomy & Genetics, University of Oxford, Parks Road, Oxford, UK

Jeffrey E. Olgin MD
Cardiac Electrophysiology, Division of Cardiology, Department of Medicine, University of California San Francisco, San Francisco, CA, USA

Hakan Oral MD
Division of Cardiovascular Medicine, University of Michigan, Ann Arbor, MI, USA

Ali Oto MD
Hacettepe University Faculty of Medicine, Cardiology Department, Ankara, Turkey
List of Contributors
List of Contributors

Eduardo Back Sternick MD, PhD
Instituto de Pos Graduação, Faculdade de Ciências Medicas de Minas Gerais, Biocor Instituto, Belo Horizonte, Brazil

Daniel Steven MD
University Heart Center, Hamburg, Germany

William G. Stevenson MD
Cardiovascular Division, Brigham and Women’s Hospital, Boston, MA, USA

Arian Sultan MD
University Heart Center, Hamburg, Germany

Matthew J. Swale MBBS
Division of Cardiovascular Diseases, Mayo Clinic, Rochester, MN, USA

Paul B. Tabereaux MD, MPH
Heart Center, Inc. Huntsville, AL, USA

Harikrishna Tandri MD
The Johns Hopkins Hospital, Baltimore, MD, USA

Roland Richard Tilz MD
Electrophysiology Laboratory, II. Medizinische Abteilung, Asklepios Klinik St. Georg, Hamburg, Germany

Jenks Thompson MD
University of Kentucky, Lexington, KY, USA

Amit J. Thosani MD
Division of Cardiac Electrophysiology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA

Michifumi Tokuda MD
Cardiovascular Division, Brigham and Women’s Hospital, Boston, MA, USA; The Jikei University School of Medicine, Tokyo, Japan

Natalia A. Trayanova PhD
Department of Biomedical Engineering and Institute for Computational Medicine, The Johns Hopkins University, Baltimore, MD, USA

Nicola Trevisi MD
Arrhythmia Unit and Electrophysiology Laboratories, San Raffaele Hospital, Milan, Italy

Roderick Tung MD
UCLA Cardiac Arrhythmia Center, UCLA Health System, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA

Karthikeyan Umapathy PhD
Ryerson University and The Hull Family Cardiac Fibrillation Management Laboratory, University Health Network, Toronto, ON, Canada

Smit Vasaiwala MD
Cardiovascular Institute, Loyola University Medical Center, Maywood, IL, USA

Alexander I. Veress PhD
Department of Mechanical Engineering, University of Washington, Seattle, WA, USA

Pasquale Vergara MD, PhD
Arrhythmia Unit and Electrophysiology Laboratories, San Raffaele Hospital, Milan, Italy

Ramya Vijayakumar MS
Department of Biomedical Engineering, Washington University in St. Louis, St. Louis, MO, USA

Nathalie Virag PhD
Medtronic Europe, Tolochenaz, Switzerland

Laura Vitali Serdoz MD
Cardiology Department, Ospedali Riuniti and University of Trieste, Trieste, Italy

Marc A. Vos PhD
Department of Medical Physiology and the Division of Heart and Lungs, University Medical Center, University of Utrecht, Utrecht, the Netherlands

Edward P. Walsh MD
Cardiac Electrophysiology Division, Department of Cardiology, Children's Hospital Boston, Harvard Medical School, Cambridge, MA, USA

Tomos Walters MBBS
Department of Cardiology, Princess Alexandra Hospital, Brisbane, Australia

Kristina Wasmier MD
Division of Experimental and Clinical Electrophysiology, Department of Cardiology and Angiology, Hospital of the Westfaelische Wilhelms-University of Muenster, Muenster, Germany

Hein J. J. Wellens MD, PhD
CARIM, Cardiovascular Research Institute, Maastricht, The Netherlands

Wayne Whitwam MD
Division of Cardiology, Cardiac Electrophysiology Program, University of California San Diego, Sulpizio Cardiovascular Center, La Jolla, CA, USA

David J. Wilber MD
Cardiovascular Institute, Loyola University Medical Center, Maywood, IL, USA

Stephan Willems MD
University Heart Center, Hamburg, Germany

Stephen B. Wilton MD, MSc
Service de Rhytmologie, Hopital Cardiologique du Haut Léveque, Université Bordeaux II, Pessac, France

Jeffrey R. Winterfield MD
Cardiovascular Institute, Loyola University Medical Center, Maywood, IL, USA

Erik Wissner MD
Electrophysiology Laboratory, II. Medizinische Abteilung, Asklepios Klinik St. Georg, Hamburg, Germany

Andrew L. Wit PhD
College of Physicians and Surgeons, Columbia University, New York, NY, USA; Division of Cardiology, Beth Israel Hospital, Harvard University, Boston, MA, USA

Anita Wokhu MD
HealthEast HeartCare, St. Joseph’s Hospital, St. Paul, MN, USA

Raymond Yee MD
Cardiac Electrophysiology, Division of Cardiology, Western University, London, ON, Canada

Lilei Yu MD
Department of Cardiology, Renmin Hospital of Wuhan University, Wuhan, Hubei, China

Stephan Zellerhoff MD
Division of Experimental and Clinical Electrophysiology, Department of Cardiology and Angiology, Hospital of the Westfaelische Wilhelms-University of Muenster, Muenster, Germany

Douglas P. Zipes MD
Indiana University School of Medicine, Krannert Institute of Cardiology, Indianapolis, IN, USA
Preface to the Fourth Edition

The first edition of Cardiac Mapping was published in 1993, followed by the second and third editions in 2003 and 2009. This fourth edition is unique in many ways. First, we are very fortunate to have the godfather of ventricular tachycardia mapping, Dr. Mark E. Josephson, join us as a senior editor. Secondly, the significant advances in the field, both clinical and basic electrophysiology on one hand and the unimaginable progress in mapping, imaging and technology on the other, obliged us to include many leading world authorities in the field. As a result, the number of chapters increased from 41 chapters in the third edition to 80 chapters in the present edition. Imaging has become an integral part of mapping in cardiac and interventional electrophysiology; therefore, we have included imaging as relevant to mapping and arrhythmias. The fourth edition is not an update of the previous one; rather it is entirely new and remains the only text in the field. This book covers the entire range of mapping from basic to the most advanced; this is useful to readers of all disciplines dealing with basic and clinical rhythmology.

Choosing the table of contents and the leading authorities to contribute was no easy assignment. We have been fortunate to have all contributors accept our invitation and produce their best state-of-the-art work.

The book is divided into five parts: Part one includes seven chapters on methodology and technological considerations. Part two deals with 12 chapters on mapping and imaging in experimental models of cardiac arrhythmias including computer modeling. Part three contains 18 chapters describing mapping and imaging in supraventricular arrhythmias with a major portion dedicated to atrial fibrillation. Part four encompasses 13 chapters covering all aspects of mapping and imaging of ventricular tachyarrhythmias, including techniques of epicardial mapping. Finally, Part 5 consists of 30 chapters dealing with future directions in mapping and imaging of arrhythmias, including non-invasive electrocardiographic imaging, imaging in channelopathies, light imaging and array tomography. The final chapter of this section gives the reader not only a perspective of the entire text but also what the future holds for cardiac mapping and imaging.

This edition is accompanied by an online access code, which includes video clips. We are confident that the reader will enjoy and find this text very useful.

We greatly appreciate the Foreword, the European Perspective and the Epilogue by the three giants in the field; namely Douglas P. Zipes, A. John Camm and Denis Noble.

The Editors
Preface to the First Edition

Cardiac mapping has always been an integral part of both experimental and clinical electrophysiology. Indeed, Sir Thomas Lewis systematically investigated the activation sequence 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 had paved the road to this point would think it necessary to join us in this effort, especially in this 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 that would subsequently be published in this, the only comprehensive book to present 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 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 impetus to stimulate new ideas for cardiac mapping in the future.

The Editors
For the foreword to the last edition of this textbook, I wrote in part,

“The Merriam-Webster online dictionary defines a map as ‘representation . . . of the whole or 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 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. Molecu-
W. H. Gaskell, a physiologist from Cambridge, England was a very early pioneer in cardiac mapping, although he measured cardiac contraction in order to work out the sequence of cardiac activation. He developed the basis for investigation of cardiac arrhythmias, not only by mapping the heart beat but by establishing the dual autonomic nervous supply to the heart and the myogenic origin of the heartbeat. But Gaskell was a neurophysiologist and could take it no further. He left it to other colleagues, such as Thomas Lewis, working at University College in London, to directly map the heart and begin to establish the mechanism of common arrhythmias such as atrial flutter. Much has happened since then.

On PubMed “cardiac mapping” describes multiple measures of cardiac structure and function ranging from gene mapping to the effects of the effect of mapped smoke inhalation on sudden cardiac death. Altogether there are 12,360 references, and of these over 5,000 refer to mapping the electrical activity of the heart with electrocardiograms, electrograms, action potential and ion channel currents of various sorts. The number of reports has risen from less than 20 per year in the 1970s to about 200 per year nowadays. It is therefore no surprise that it is necessary to re-write and republish this now classic compendium on all manner of cardiac mapping which deals with current research and clinical/basic science applications of maps of electrical cardiac activity. Doctor Shenasa and his fellow editors are to be congratulated on this comprehensive volume of contemporary electrophysiology.

Mapping of single and multiple beats of the heart at a cellular, integrated electrophysiological preparation or whole heart level, from within or outside the heart (and body) are now fundamental to our therapeutic approach to the management of cardiac arrhythmias. Our knowledge of mechanisms has been enormously enriched by detailed mapping of cardiac activation. From this knowledge clinical and basic scientists have developed most of the therapeutic approaches that we use today. Drug-based management relies on a sophisticated appreciation of the mechanism of arrhythmia, device treatment of cardiac arrhythmias requires knowledge of the origin and expression of the rhythm disturbance, and ablation techniques rely absolutely on detailed information regarding the mechanism and origin of the arrhythmia, together with an understanding of the substrate which maintains the arrhythmia. Thus critical, vulnerable and aberrant conduction must be identified in order to allow the selective destruction of the tissue responsible for supporting the arrhythmia. The therapeutic insights and developments that stem from cardiac mapping are the decisive test of the value and deductions derived from cardiac mapping. As an example, it was ultimately the surgical division of an accessory pathway that demonstrated conclusively the pathophysiological reality and relevance of “Kent” pathway conduction.

We now move forward with techniques that improve the resolution and the accuracy of data collected directly or remotely from the heart. Electrical activity is progressively correlated with histopathology, biochemistry, microRNA and the like, moving us closer to better solutions for the management of the majority of cardiac arrhythmias. Cardiac mapping techniques provide extraordinary tools to advance this science. But there is still far to go, for unlike the assertion of Sir Thomas Lewis on giving up his research on atrial fibrillation that the “cream was off the milk,” we can anticipate accelerated and exciting progress in this arena – “the cat has still to get to the cream.”

A. John Camm
Professor of Cardiology
British Heart Foundation
St. George's, University of London
London, UK
A project of this magnitude would be impossible without the support and excellent contributions of our expert contributors to this edition. Despite their many commitments they have all provided work that was beyond our expectations. We wish to thank the staff at Wiley-Blackwell, especially Thomas Hartman, Ian Collins, Kate Newell, Alice Nelson, Rebecca Huxley and Ben Honour. A special thank you to Alice Nelson for the final production, which is greatly appreciated. Thank you also to Fatemah Shenasa for her artistic talents for the cover.

Finally the secretarial support of Ms. Mona Soleimanieh, who spent infinite hours from the beginning to the end of this work, is warmly recognized.
PART

Methodological and Technical Considerations
CHAPTER 1

Evolution of Cardiac Mapping: From Direct Analog to Digital Multi-dimensional Recording

Jacques M. T. de Bakker¹–³ & Marc A. Vos¹

¹Department of Medical Physiology and the Division of Heart and Lungs, University Medical Center Utrecht, the Netherlands
²The Center of Heart Failure Research, Department of Experimental Cardiology, Academic Medical Center, Amsterdam, the Netherlands
³Interuniversity Cardiology Institute of the Netherlands, Utrecht, the Netherlands

Summary

Mapping of the electrical activity of the heart started in the late 1870s and has evolved from indirect recordings with a rheotome by Engelmann to highly sophisticated direct recordings of cardiac potentials with multi-terminal electrodes. This chapter mainly focuses on direct recordings from the heart. Developments of cardiac mapping from the rheotome via the string galvanometer and cathode ray tube to computerized digital mapping systems will be followed, and focus will be directed to various aspects that are important for mapping procedures. The advantages and disadvantages of different recording modes will be addressed and the different types of information that are derived from electrograms will be discussed. Ways to obtain three-dimensional information from catheters or multi-electrode arrays will be reviewed, and various other techniques to obtain information about propagation and repolarization of the action potential from the heart are explained.

Introduction

Cardiac mapping involves the recording of electrical activity of the heart at various sites to estimate the electrical status of the heart. The information concerning cardiac conduction and repolarization has both scientific and clinical interest. Earliest systems were only able to record one signal at a time and to obtain information from multiple sites: the recording probe had to be repositioned several times in sequence. This implies that during its earliest time mapping was only possible in case of a stable rhythm. In the clinical setting, a large number of arrhythmias are indeed monomorphic and sustained and can be mapped in a sequential way using catheter-based systems like the CARTO system ( Biosense-Webster, Baldwin Park, CA, USA). However, also for clinical purposes, multi-terminal electrode systems have been developed, allowing mapping of irregular rhythms.

In exceptional cases the display of multiple electrograms, one below the other, can be useful to follow changes in the electrical activity in time. This might be of importance when one is interested in changes induced by rate, drugs or the autonomic nervous system. However, most often data reduction is needed for quick understanding and parameters like activation times or fractionation are derived from the signals. An important hallmark of mapping is the recording mode. Although technically data gathering is not a problem, for analysis the choice of a unipolar or bipolar signal is of importance because certain electrophysiological parameters can only be derived from one or the other (Table 1.1). The type of recording electrode used highly depends on the question to be solved and the spatial resolution needed. A spatial resolution that is too low may result in incorrect information and possibly the wrong decisions for treatment in the clinical setting.

In the following text, developments of mapping are reviewed, characteristics of the different recording modes are discussed, as well as the information that can be derived from electrograms and various recording electrodes, and alternative mapping methods are considered.
Table 1.1 Characteristics of three different recording modes.

<table>
<thead>
<tr>
<th>Recording mode</th>
<th>Characteristics of electrograms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unipolar</td>
<td>1. Reveal local + distant activation</td>
</tr>
<tr>
<td></td>
<td>2. Sensitive for 60 Hz interference and remote activation</td>
</tr>
<tr>
<td></td>
<td>3. Accurate activation time estimation</td>
</tr>
<tr>
<td></td>
<td>4. Repolarization time estimation possible</td>
</tr>
<tr>
<td></td>
<td>5. Morphology is direction independent</td>
</tr>
<tr>
<td></td>
<td>6. Interpretation of the morphology is easy</td>
</tr>
<tr>
<td>Bipolar</td>
<td>1. Reveal local activation only</td>
</tr>
<tr>
<td></td>
<td>2. Suppresses 60 Hz interference and remote activation</td>
</tr>
<tr>
<td></td>
<td>3. Inaccurate activation time estimation (because of point 5 above)</td>
</tr>
<tr>
<td></td>
<td>4. No information about repolarization</td>
</tr>
<tr>
<td></td>
<td>5. Morphology is direction dependent</td>
</tr>
<tr>
<td></td>
<td>6. Interpretation of the morphology is difficult</td>
</tr>
<tr>
<td>Laplacian</td>
<td>1. Reveal local activation only</td>
</tr>
<tr>
<td></td>
<td>2. Suppresses 60 Hz interference and remote activation</td>
</tr>
<tr>
<td></td>
<td>3. Accurate activation time estimation</td>
</tr>
<tr>
<td></td>
<td>4. No information about repolarization</td>
</tr>
<tr>
<td></td>
<td>5. Morphology is direction independent</td>
</tr>
<tr>
<td></td>
<td>6. Interpretation of the morphology is easy</td>
</tr>
</tbody>
</table>

Indirect recordings of the electrical activity from the heart

The first primitive electrocardiogram (ECG) was plotted in 1878 by Theodor Wilhelm Engelmann at the Department of Medical Physiology in Utrecht in the Netherlands with the help of a differential rheotome, an instrument that alternately delivered a stimulus to tissue and measured the resulting current through it (Figure 1.1a) [1–3]. Differential rheotome data obtained by Frederick James Montague Page in the same year were good enough to provide for the first time indirect, global information about the time course of depolarization and repolarization of the myocardium. However, a better instrument was needed, especially a recording one that could provide a direct plot of voltage versus time. Such an instrument, the capillary electrometer, had already been developed a few years earlier by Gabriel Lippman. The function of the capillary electrometer is based on the principle of polarization and surface tension at a mercury–sulfuric acid interface. The mercury column of the electrometer was connected to the patient’s chest, whereas the sulfuric acid column was connected to the back. If the potential difference changed, the mercury meniscus moved and its position was observed by a microscope. With this instrument Augustus Desiré Walter recorded the first wave form of heart activity from the body surface (Figure 1.1b). Recordings from the exposed hearts of animals had already been made with the capillary electrometer by Engelmann and Page. Electrical sensitivity was sufficient, but mechanics (the inertia of the heavy mercury column) distorted the signal.

Willem Einthoven, who started his research in ophthalmology and respiratory physiology was unsatisfied with the capillary electrometer to study action potentials [4,5]. In contrast to Walter, Einthoven was convinced that the electrogram would be an important aid in the diagnosis of heart disease. He observed how similar the patterns of normal subjects were and how distinctively different the pattern of diseased patients. He therefore felt the need to replace the capillary electrometer by a simpler and more accurate instrument. This led to the use of the string galvanometer, in which a light coil of wire was positioned between the poles of a permanent magnet (Figure 1.1c). Current flow through the coil caused it to be deflected with the flight proportional to the current. The deflections were observed optically. His first design was a huge machine with five people needed to run it. It weighed 250 kg and the electromagnet provided a field strength of 22.000 Gauss and got so hot that it had to be cooled with water. The ECGs he recorded were however of high quality. Apart from devising the instrument, Einthoven...
demonstrated the clinical power of the ECG and introduced the equilateral-triangle method (the Einthoven triangle).

The first commercial version of the instrument was made by Sir Horace Darwin, founder of the Cambridge Scientific Instrument Company in England. The first model went to Sir Thomas Lewis at University College Hospital London and was used primarily for research purposes. The principle of string galvanometry and optical amplification to enhance the signal remained in general use for many years until inexpensive cathode-ray oscilloscopes became available in the late 1930s. Until 1932 studies mainly focused on non-arrhythmic abnormalities (bundle branch block, myocardial infarction [MI], the effect of digitalis).

From the instrumentation point of view, the next great advance came in 1920 when vacuum tube amplifiers and oscilloscopes came in more general use. The advantages of electronic amplification and visualization of ECG signals were obvious. Instruments became smaller and transportable. The first commercial instrument in which vacuum tubes and oscilloscopes were used was developed by Siemens and Halske in 1921, but the string galvanometer remained in use in the UK until the 1940s.

**Direct recordings of the electrical activity from the heart**

Up until the 1950s very few experiments were carried out to obtain an accurate analysis of the activation in the different layers of the ventricular wall, mainly because of the fact that the string galvanometer and direct-writing pen equipment were too slow to allow exact studies of time relationships. To circumvent these problems, Durrer and van der Tweel developed a recording system that was equipped with two pairs of cathode-ray tubes, one pair for photographic registration and the second pair used for continuous visual observation. The system had a bandwidth of about 3 kHz and a noise level of 10 mV rms [6]. Direct recordings were made in canine hearts with needle electrodes consisting of eight terminals and impaled into the left ventricular wall. Recordings were made sequentially with a switch box that allowed every required combination of electrodes onto each of the two recording channels. A similar system with a high fidelity recording system and a fast running film was used by Jouve et al. [7] to determine epicardial activation in man. In their classic study about total excitation of the human heart, Durrer et al. [8] recorded electrograms on a 14-channel Ampex physiological tape recorder and used an 8-channel oscilloscope for monitoring. For analysis the signals were played back from the tapes at a lower speed and the electrograms were printed out on an Elema ink writer. Final time resolution was better than 1 ms.

The introduction of semiconductor technology has dramatically accelerated the miniaturization of recording systems, and the rising use of computers made analysis of electrograms easier and more accurate. The development of computer technology made it possible to simultaneously register electrograms from multiple sites with sufficient temporal and spatial resolution to visualize individual activation fronts during propagation and their repolarization patterns.

The first intraoperative cardiac activation mapping was applied by Lewis and Rothschild in 1915 using a rotating probe (a single hand-held probe) positioned at several sites in sequence [9]. The drawback of this technique is that it is a time-consuming procedure it is impossible to map non-periodic rhythms such as polymorphic ventricular tachycardias (VTs) and ventricular fibrillation (VF) and that positioning of the electrode at predefined distances is often difficult to perform.

**Multi-channel mapping systems**

A variety of mapping systems for clinical purposes are available today. The number of channels they can handle is usually less than 100. Although these systems can record multiple channels simultaneously, they usually use one catheter for mapping, meaning that it is a sequential recording technique like, for instance, the CARTO system (Biosense-Webster, Baldwin Park, CA, USA). The newest CARTO systems can however record multiple electrograms simultaneously. Multi-channel systems like the EnSite system (St. Jude Medical, Inc., St. Paul, MN, USA) record 64 signals simultaneously, but use a non-contact mapping catheter. Electrograms at the endocardium are calculated using an inverse procedure.

Several sophisticated electrophysiological mappings systems with more than 200 channels for experimental and clinical use are commercially available nowadays. The UniEmap system (Uni. Services, Ltd, Auckland, New Zealand) has been developed by the Auckland Bioengineering Institute of the University of Auckland in New Zealand. This is a versatile mapping system that allows both electrical mapping and pacing. Although the base unit comprises 448 channels, the number of channels is virtually unlimited. The system has unipolar or true bipolar inputs and a sampling rate of 1–5 kHz. Analog signal conditioning, like gain setting, filter setting and stimulation facility can be set separately for individual channels. The system further includes specialized electrodes and software designed for processing, analysis and display of a large number of data channels.

Another system that is frequently used for cardiac mapping, both from the body surface and directly from the heart is the ActiveTwo system from BioSemi (Amsterdam, the Netherlands). This mapping system has a basic configuration of 256 channels (+ 8 auxiliary channels) all housed in a single ultra-compact box (size 120 × 150 × 190 mm, weight 1.1 kg) and is expandable to 512 channels. The system uses
a 24 bit A/D converter for each channel, which provides a high dynamic range, allowing true DC measurements. The sample rate ranges from 2 to 16 kHz per channel, depending on the number of channels to be acquired. Acquisition is done with a personal computer via an USB 2.0 interface connected to the mapping system. Special software allows display and acquisition of the signals as well as signal conditioning (unconditioned DC data are however stored). Data analysis might be done by MapLab, an experimental software package for multi-channel ECG-recordings and developed by Mark Potse [10]. The ActiveTwo system is battery operated and can record 256 channels continuously for 5 hours on fully loaded batteries.

A similar system is provided by TMS International. The REFA system from TMSI (Oldenzaal, the Netherlands) can handle up to 272 channels and uses a 22- or 24-bit A/D converter for true DC recordings. The sample frequency ranges from 2 to 20 kHz and the box size is 210 x 360 x 92 mm for 136 channels.

Multi-terminal electrodes

To study the activation pattern of polymorphic tachycardias and fibrillation, a simultaneous recording technique is a pre-requisite and multi-terminal electrode systems are needed. Electrode arrays like epicardial sock and plaque electrodes, endocardial balloon electrodes and intramural needles were the first multi-terminal electrodes used for cardiac mapping [11]. These electrodes were custom-made and used to perform epicardial, endocardial or intramural mapping.

A great variety of multi-terminal electrodes have been developed over time by various research groups with form, size and number of electrode terminals depending on the research question to be answered or treatment strategy to be followed (Figure 1.2). Flexible or ridged grid electrodes have been designed for epicardial and endocardial mapping. Flexible electrodes are required if large areas of the heart have to be covered; for small areas ridged electrodes might be sufficient. Flexible electrodes usually consist of a silicon rubber sheet or cast, in which the electrode terminals are embedded.

The construction of large electrode arrays with more than 100 electrode terminals is tedious by using classic techniques and often yields irregular electrode spacing. Modern construction techniques are less time consuming and use, for instance, fine pitch, isolated, copper ribbon cables or flexible printed circuit flat cables that are assembled together, such that the active surface is the cut end of the cable. In this way multi-electrodes with spacings < 200 μm have been made with up to 400 electrode terminals [12]. Photolithographic manufacturing processes have been applied as well. Electrodes are present on flexible polyimide foil or printed circuit board foil [13]. For endocardial mapping of the entire endocardial surface, silicon balloon electrodes and basket electrodes have been developed and applied. The balloon electrode requires an empty cavity and therefore is used only in isolated, Langendorf-perfused hearts or during extracorporeal circulation. The balloon electrode has been used frequently in the past during antiarrhythmic surgery in patients with VT due to remote MI [14]. For experimental endocardial mapping of the atria, ridged electrodes can be used, consisting of a cast of the atrial cavity with embedded electrodes. Such electrodes are usually custom-made (Figure 1.3).

Catheter-based multi-electrodes

Several catheter-based multi-electrodes have been developed in the past and are still being developed, usually by industry. The basket is a catheter device harboring eight splines with eight electrode terminals on each spline. The basket is inserted into the cavity in a non-deployed condition using a sheath. If the basket is positioned at the right position in the cavity, the sheath is withdrawn and the basket deployed. This device allows the recording of 64 endocardial electrograms simultaneously and has been used to guide ablation of atrial flutter and to determine the arrhythmogenic area of VTs [15,16]. For the atrium, several special multi-terminal catheters have been developed for the rapid assessment of focal and reentrant arrhythmias and areas with complex fractionated electrical activity. Jones et al. [17] describe the use of a high density catheter with 20 poles with a distal spiral configuration (7-F shaft, 4-F spiral ring). The electrode is deployed in the appropriate chamber through a long sheath. An alternative electrode system, especially
Evolution of Cardiac Mapping

Figure 1.3 (a) Cast of the cavity of the left atrium of a dog heart. In the cast, 120 electrode terminals are installed (black dots). (b) A three-dimensional (3D) activation map during stimulation at a site in between the pulmonary veins (indicated by the stimulation marker in part (a)).

for the atrium is the 20-polar PentaRay catheter ( Biosense-Webster, Baldwin Park, CA, USA). This mapping catheter has five soft radiating splines, with four 1 mm electrode terminals per spline and a 4 mm inter-electrode spacing. The electrodes cover an area of approximately 9.6 cm² [18,19].

Unipolar versus bipolar recordings

One common problem in all mapping systems is the choice of the recording mode, which, in its simplest form is unipolar or bipolar [20]. In the unipolar mode, the recording (different) electrode is located at the site of interest on the heart and connected to the positive input of a differential amplifier, whereas the indifferent electrode is located far away from the heart (theoretically at infinity). This electrode is connected to the negative input of the differential amplifier. In bipolar mode, the different and indifferent poles of the electrode are positioned close together (usually the distance between the poles is in the millimeter range). If the poles are close together, the bipolar signal approximates the first derivative of the unipolar signal, which takes into consideration that there are important differences between the unipolar and bipolar mode. The derivative of a signal results in a reduction of the low frequency components in the signal. A wave front distant from the recording site will generate low frequency components in the unipolar signal, because the signal will change only marginally if the front moves. If the distance between an activation front and the recording site is small, the recorded signal will change rapidly, resulting in high frequency components in the signal. Thus, for unipolar recordings, low frequency components refer to remote wave fronts, whereas high frequency components refer to local wave fronts. The bipolar mode will filter out the low (remote) frequency components and retain the high frequency (local) components. Thus, a major difference between the two recording modes is that unipolar electrograms contain information of both local and distant activation, whereas bipolar electrograms mainly reflect local activation. Because we are frequently interested in the (local) activation time at the recording site, the bipolar recording seems to be preferable. However, bipolar recordings have several disadvantages: (i) the signal is dependent on the direction of the wave front and activation fronts running parallel to the line between the poles do not generate a signal; (ii) deriving activation times from bipolar signals is problematic because of the direction dependence and the differentiating nature of the electrode; (iii) interpretation of the configuration of the bipolar electrogram is difficult, in contrast to the unipolar electrogram, where a biphasic deflection refers to a passing wave front, a negative deflection to a site where activation is initiated and a negative deflection to a site where activation comes to an end [21].

The dilemma of the choice between unipolar and bipolar mode can best be solved by recording them both simultaneously, which is not a problem with current technology. Unipolar and bipolar recordings provide independent information (Table 1.1): unipolar recordings provide local and remote activation as well as accurate activation times, whereas bipolar recordings provide accurate local activation. Thus, the bipolar signal shows you which part of the unipolar signal is local and that allows an accurate determination of the activation time (Figure 1.4a). If grid electrodes are used with fixed distances between the poles, bipolar signals can easily be constructed mathematically from the recorded unipolar electrograms. Combined unipolar and bipolar electrogram criteria have also been used to evaluate the transmurality of atrial ablation lesions [22]. In addition, unipolar electrograms allow determination of (local) repolarization times.

The Laplacian recording mode

A modification/extension of the bipolar recording mode is the Laplacian mode [23]. The Laplacian signal is calculated as the difference between the signal at the target electrode and the weighted sum of surrounding electrodes at equidistant. In a regular grid, this can easily be done mathematically for all terminals (except at the rim of the electrode) if
PART I Methodological and Technical Considerations

1.5 Unipolar and Bipolar Endocardial Electrograms

Unipolar signals are recorded. It can be shown that the Laplacian is the second derivative of the unipolar signal and reflects the local (at the center electrode) transmembrane current. The morphology resembles that of the unipolar electrogram, but the deflection is sharper because of the second derivative (Figure 1.4b). The signal is independent of the direction of the wave front in the plane of the electrode; only wave fronts that proceed perpendicular to that plane do not generate a signal. To be independent of the wave front in all directions, a configuration with needle electrodes is required. A comparable recording mode is obtained by the coaxial electrode, which consists of a central electrode surrounded by a circular one [24]. The ring serves as the reference electrode and is connected to the negative pole of the amplifier. As with the Laplacian, the ring gives the mean of the signals around the central electrode and therefore cancels the dependence of the direction effect of the electrode.

Information extracted from extracellular electrograms

Although the display of a large number of electrograms, one below the other, can provide some insight into the activation process (Figure 1.5), crucial information, like spatial information, will be lost. Therefore, special features are usually derived from the electrograms.

Signal morphology: mono- and biphasic, double potentials, fractionation

Interpretation of the morphology of unipolar electrograms is usually straightforward in contrast to bipolar electrograms. An activation front that approaches the recording site will generate a positive deflection if unipolar signals are recorded. It can be shown that the Laplacian is the second derivative of the unipolar signal and reflects the local (at the center electrode) transmembrane current. The morphology resembles that of the unipolar electrogram, but the deflection is sharper because of the second derivative (Figure 1.4b). The signal is independent of the direction of the wave front in the plane of the electrode; only wave fronts that proceed perpendicular to that plane do not generate a signal. To be independent of the wave front in all directions, a configuration with needle electrodes is required. A comparable recording mode is obtained by the coaxial electrode, which consists of a central electrode surrounded by a circular one [24]. The ring serves as the reference electrode and is connected to the negative pole of the amplifier. As with the Laplacian, the ring gives the mean of the signals around the central electrode and therefore cancels the dependence of the direction effect of the electrode.

![Figure 1.4](image1.png)

(a) Simultaneous recording of a unipolar (upper tracing) and bipolar (lower tracing) endocardial electrogram from the human right ventricle. The black square in the upper panel is the activation time in the unipolar electrogram and corresponds with a sharp (local) deflection in the bipolar electrogram (black square). Black dots in the unipolar recording are local deflections as verified by the bipolar deflections. The deflection marked by the open arrow in the unipolar recording is remote (not present in the bipolar recording). The deflection marked by the black triangle is the T-wave which consists of low frequency components and therefore is not visible in the bipolar recording. (b) Morphology of a unipolar, bipolar and Laplacian recording at the same location.

![Figure 1.5](image2.png)

(a) Electrocardiogram during baseline (blue tracing) and peak ajmaline (purple tracing). (b) Electrocardiogram map of a Brugada syndrome patient before and after application of ajmaline, a sodium channel blocker. After application of the drug, ST-segment elevation occurs (marked by red circle). Electrocardiogram sections of 800 ms are plotted one behind the other and clearly illustrate the increase and decrease of the ST segment following ajmaline application.