Clinical Handbook of Cardiac Electrophysiology

Benedict M. Glover
Pedro Brugada
Editors

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BMG: Pro auxilio sempiterno eorum, toti familiae meae, maxime, uxori, Nualae et filiae, Luciae et filio, Hugo, maximas gratias ago. Cum amore, Benedictus

Foreword

Clinical Handbook of Cardiac Electrophysiology, written and edited by Benedict M. Glover and Pedro Brugada, is a unique book. As the authors acknowledge in the preface, many excellent textbooks have been published on this topic. However, Glover and Brugada make the point that few provide a practical synopsis to bridge the chasm separating basic physiology, anatomy, and pharmacology from its practical application. That is the admirable goal of this book: to serve as the conduit between the basic scientist and beginner, for cardiology fellows, residents, and support personnel. The first three chapters lay a foundation for the rest of the book, including cardiac anatomy and basic electrophysiology (Chap. 1); the electrophysiology study, maneuvers, and ablation (Chap. 2); and electroanatomic mapping (Chap. 3). This book then embarks on a journey discussing the major cardiac arrhythmias including AV nodal reentrant tachycardia (Chap. 4), accessory pathway conduction (Chap. 5), atrial tachycardia (Chap. 6), atrial flutter (Chap. 7), atrial fibrillation (Chap. 8), ventricular tachycardia (Chap. 9), and antiarrhythmic drugs (Chap. 10).

I found this book to be authoritative and to the point with its main strength being the presentation at a level easily comprehended by the early learner. The many figures are very well done in that regard, very helpful and easily comprehended. This book will serve as an excellent stepping-stone for those who wish to delve further into electrophysiology mysteries, or as a final resting place for those contents with a basic understanding. Either way, *Clinical Handbook of Cardiac Electrophysiology* is an important contribution for learners.

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Preface

Cardiac arrhythmia management has evolved as one of the most rapidly expanding fields within medicine. The development of catheter ablation has transformed the treatment of many arrhythmias, providing highly effective treatment options for the majority of tachyarrhythmias. There is also considerable research and development of more effective antiarrhythmic and anticoagulant drugs. Despite these huge technical advances, it is important to understand the basic principles of arrhythmia mechanisms in order to help make a diagnosis and chose an effective treatment strategy.

Although there are many excellent and detailed reference texts in this field, there are few handbooks which provide a practical overview bridging the gap between basic physiology, anatomy, pharmacology and interventional catheter ablations with precise details which should help in the intricate management of the patient.

This book covers all the important aspects of cardiac electrophysiology, presented in an easy-to-use format. For each arrhythmia, the aetiology, classification, clinical presentation, mechanism, electrophysiology set up (including precise set up and ablation parameters) and trouble-shooting are presented and demonstrated using illustrations, fluoroscopy images, ECGs and endocavity electrograms.

The overall aim of this book is to provide a logical and practical approach to cardiac arrhythmia management. We hope that this provides a useful resource and, importantly, helps to promote this wonderful sub-specialty.

This book is aimed at cardiac electrophysiologists, fellows, cardiologists, physicians, family practitioners, cardiology trainees, students, allied professionals and nurses. Given its succinct summary of electrophysiology, this should be available as a reference guide in the electrophysiology laboratory. We hope that this reaches a truly international audience and provides an important guide for those studying for heart rhythm exams.

Kingston, ON, Canada — Benedict M. Glover
Brussels, Belgium — Pedro Brugada

Contents

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Chapter 1
Cardiac Anatomy and Electrophysiology

Benedict M. Glover, Orla Buckley, Siew Yen Ho, Damian Sanchez-Quintana, and Pedro Brugada

Abstract Cardiac electrophysiology has rapidly moved from the mapping and ablation of accessory atrioventricular connections and ectopic foci to more extensive mapping and substrate modification. Training in cardiac electrophysiology requires a detailed knowledge of the anatomy and physiology of the heart. In order to understand the basis of cardiac electrophysiology it is important to discuss the different phases of the cardiac action potential, variability in morphology and duration throughout the heart and the most important ion channels and electrolyte shifts responsible for depolarization and repolarization of the cardiac cells. Electrophysiology continues to rely heavily on an understanding of these basic principles as well as the relevant anatomy of all cardiac chambers and surrounding structures. It is therefore fundamental to have a thorough understanding of cardiac anatomy as visualized on fluoroscopy, echocardiography, CT, MRI and 3 dimensional cardiac mapping systems.

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The Cardiac Action Potential

Spontaneous depolarization of cells within the sinus node (SN) results in propagation of excitation throughout adjacent cells within the right atrium (RA) and left atrium (LA). The electrical impulse spreads through the atrioventricular (AV) junction into the His bundle, through the Purkinje network and then into the ventricular muscle where activation occurs from the septum spreading through the endocardium, mid-myocardium and finally the epicardium.

Each cardiac cell undergoes a process of depolarization and repolarization, which is recorded across the cell membrane as an action potential and occurs as a result of the relative concentration of ions (predominantly potassium, sodium and calcium) and electrostatic forces across the membrane. As shown in Fig. 1.1 this is composed of 5 components in atrial and ventricular myocytes and 3 components in the SN and AV node. The QTc on the surface ECG is an approximation of the mean duration of the ventricular action potential.

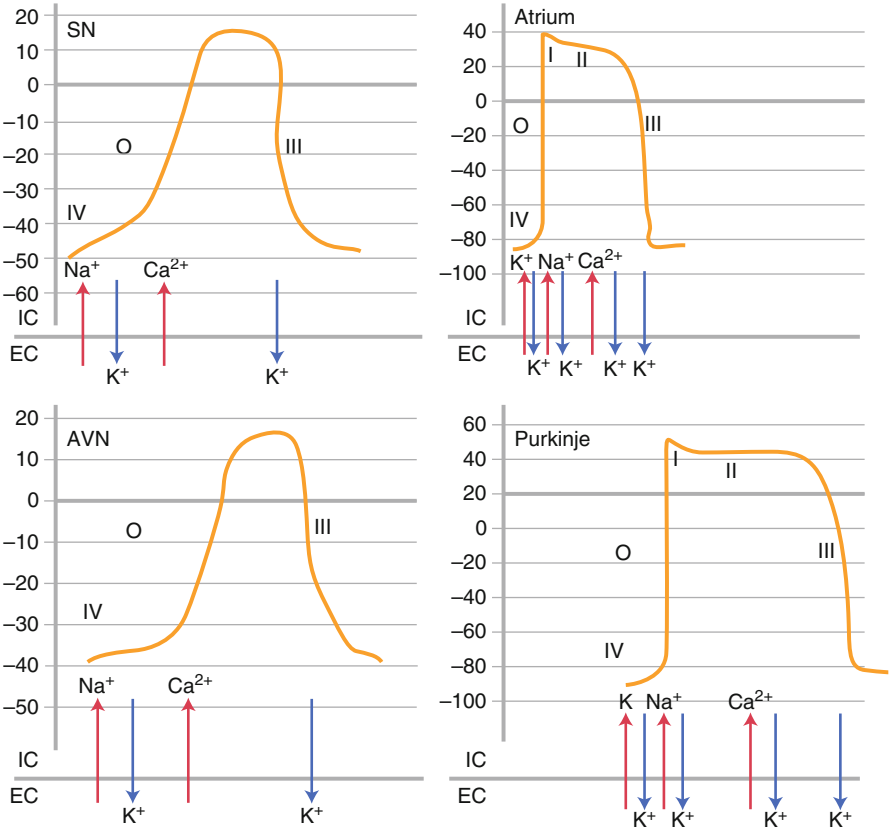


Fig. 1.1 Cardiac action potentials recorded from the SN (*top left*), atrium (*top right*), AV node (AVN) (*bottom left*) and Purkinje network (*bottom right*) and the predominant ionic currents responsible for theses changes in membrane potential (*IC* intracellular, *EC* extracellular, Na^+ sodium, Ca^{2+} calcium, K^+ potassium)

Phase IV is known as the **resting membrane potential**. This is recorded as −80 to −95 mV in atrial, Purkinje and ventricular cells. It is slightly less negative in the atrium than the ventricle. In the SN it is −50 to −60 mV and the AV node −60 to −70 mV. In both the SN and AV nodes there is a slow spontaneous diastolic depolarization which merges with Phase 0 resulting in spontaneous automaticity while Phase IV in other cells is generally more flat.

This is followed by **Phase 0** where the membrane potential becomes positive and is therefore known as **rapid depolarization**.

Phase I, **rapid repolarization** occurs in the atrium and ventricle but not in the SN and AV node. It is much more prominent in the Purkinje and epicardial cells.

Phase II is the **plateau phase** where the action potential becomes relatively flat and does not occur in the SN or AV node. It is followed by **Phase III**, which is known as **rapid repolarization** resulting in restoration of the membrane potential to the resting phase.

Phase IV (Resting Phase)

In the atrium and the ventricle this occurs largely as a result of the balance of potassium (K^+) across the cell membrane and is relatively flat with only a very slight slope.

K^+ is found in much higher concentrations in the intracellular space compared with the extracellular space. As a result of this there is an outward motion of K^+ leaving predominantly negative anions inside the cells at baseline.

This is counteracted during the resting phase by the inward rectifying current, (IK1). In general rectifier currents allow current to pass in a preferential direction. In the case of IK1 the transmembrane channel responsible allows the inward movement of K^+ at more negative potentials than the reversal outward K+ potential with less current movement at more positive membrane potentials [1]. This results in a very slight upward curve as the cell becomes less negative.

The resting phases in the SN and AV node are different from those recorded in the atrium and ventricle. As well as being less negative there is a continual slow spontaneous diastolic depolarization. This occurs as a result of the funny current (If) which plays the predominant role in this phase as opposed to the Ik1 current. This current is activated at voltages in the diastolic range resulting in a slow and steady inward Na^+ current (INa) which would normally occur in the depolarization phase in atrial and ventricular cells. There is also a slow outward movement of K^+ with the overall combined effect of a less negative cell membrane potential.

Phase 0 (Depolarization)

In the atrium and ventricle as a result of electrical stimulation from adjacent myocytes, a rapid inward sodium current (INa^+) results in the abrupt initial upstroke in the action potential known as Phase 0.

There are principally two Na^+ gates responsible for depolarization called the **activation** and **deactivation gates**. At the start of depolarization the activation gates are closed while the deactivation gates are open. As the action potential becomes less negative the activation gates tend to open rapidly allowing the inward movement of Na^+ while the deactivation gates tend to close slowly. This continues beyond zero voltage at which point the rate of Na^+ entry into the cell slows. As the deactivation gates close the fast Na^+ channels become inactive. These remain closed until Phase III of the action potential.

Depolarization in the SN and AV node does not occur as a result of INa^+ but rather as a result of calcium entry through the L-type calcium channels (ICaL) and T-type calcium channels (ICaT).

Phase I (Early Repolarization)

As the vast majority of the inward current deactivates, a rapid transient outward potassium current (Ito) results in early rapid repolarization. Phase I is much more prominent in Purkinje fibers and in epicardial myocytes and does not occur in the SN or the AV node.

Phase II (Plateau Phase)

The plateau phase occurs in the atrium and ventricles as a result of an inward movement of calcium ions (ICaL) combined with an outward movement of potassium (IKs, IKr and IKUr). As the voltage becomes less negative during depolarization the ICaL and ICaT channels become active.

ICaL channels are the predominant type found in cardiac myocytes and are activated when the voltage reaches −30 mV. ICaT channels which are less common in cardiac myocytes are activated at more negative voltages.

Overall ICaL activation begins in late depolarization. Ca^{2+} crosses from outside the cell where the concentration is higher relative to the inside.

K^+ shift is also partially responsible for the plateau phase. The balance of K^+ across the cell membrane is similar to that during the resting phase but the voltage is positive rather than negative which results in an outward movement of K^+ from the cell. The overall balance between the inward movement of calcium and the outward movement of K^+ results in the plateau phase. The transient outward current (Ito) is expressed in the atrium more than the ventricle. As a result of this there is a greater outward movement of K^+ versus the inward movement of calcium resulting in a shorter plateau phase.

Phase II does not occur in the SN or the AV node.

Phase III (Repolarization)

As the outward movement of K^+ exceeds the inward movement of Ca^{2+} the voltage becomes more negative resulting in repolarization. Although the delayed rectifier currents Ikr and Iks are activated during depolarization their action tends to be delayed and gradually increases during the plateau phase. Next to Ito the inwardly rectified K^+ current (Ik1) is also responsible for repolarization although this is more active as the voltage across the cell membrane becomes less negative and is responsible for the small bump seen in the action potential during repolarization.

All these K^+ currents are responsible for restoration of the K^+ balance. The Na^+ which entered the cell during depolarization is removed by the Na^+/K^+ ATPase enzyme while calcium which entered the cell during the plateau phase is removed by the Na^+/Ca^{2+} exchanger.

Repolarization in the SN occurs as a result of the rapid outward movement of K^+ as well as inactivation of the inward Ca^{2+} current making the cell more negative.

Refractoriness

Refractoriness describes the period after phase 0 of the cardiac action potential during which a stimulus does not result in a new depolarization.

There are three different types of refractory periods (RP): relative, absolute and effective.

The **relative RP** is the longest coupling interval resulting in local capture therefore marking the end of refractoriness.

The **absolute RP** is the longest coupling interval which does not result in local capture. The absolute and relative RP's are depicted in Fig. 1.2.

The **effective RP** is the longest coupling interval delivered which fails to propagate through the distal tissue.

In the clinical electrophysiology laboratory the RP is calculated by performing an **extrastimulus test**. In order to perform this the threshold for stimulation is measured in diastole by pacing at a fixed rate and decreasing the intensity of the pacing stimulus until capture fails.

Following a drive of eight beats at a fixed rate (to establish a steady state) a single extrastimulus is introduced at twice the diastolic threshold at shorter intervals until capture no longer occurs. This can be seen in Fig. 1.3 where pacing from the high RA is performed at a cycle length of 600 msec for 8 beats (drivetrain) in order to achieve a steady state followed by a decremental extrastimulus. In this example the first beat on the left is the final beat of the drive train. The extrastimulus occurs at a cycle length of 280 msec and captures the atria but fails to conduct over the AV node. This is considered to be the AV node ERP.

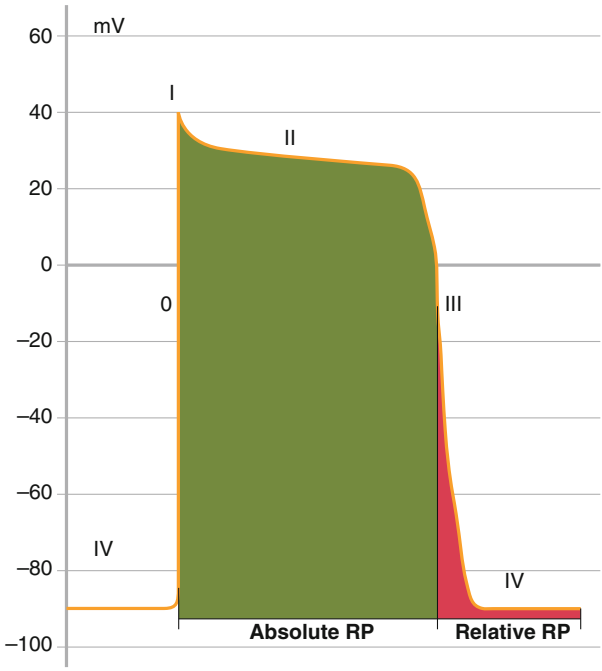


Fig. 1.2 Diagram showing the absolute RP and relative RP during the cardiac action potential. The absolute RP occurs from phase 0 until the transmembrane potential reaches -60 mV during phase III. During this time a stimulus will not result in depolarization. The relative refractory period follows this in which a high voltage stimulus may result in further depolarization

Arrhythmia Mechanisms

Arrhythmias may be classified as either **macro re-entry** or **focal**. Focal arrhythmias may be caused by **micro re-entry**, **enhanced automaticity**, **or triggered activity**.

Re-entry

A very common mechanism of clinical cardiac arrhythmia is re-entry. During re-entry a wave of excitation moves around a circuit which is determined anatomically, functionally or a combination of the two. A macro re-entry circuit which makes understanding of re-entry easy is the circuit during circus movement tachycardia in patients with the Wolf-Parkinson-White (WPW) syndrome (Fig. 1.4).

For re-entry to occur the following conditions have to be fulfilled:

1. There must be two or more pathways for conduction (for example the AV node and accessory pathway in WPW)
2. Unidirectional block in one pathway
3. Alternative conduction over the other pathway with sufficient delay as to retrogradely invade the formerly blocked pathway.

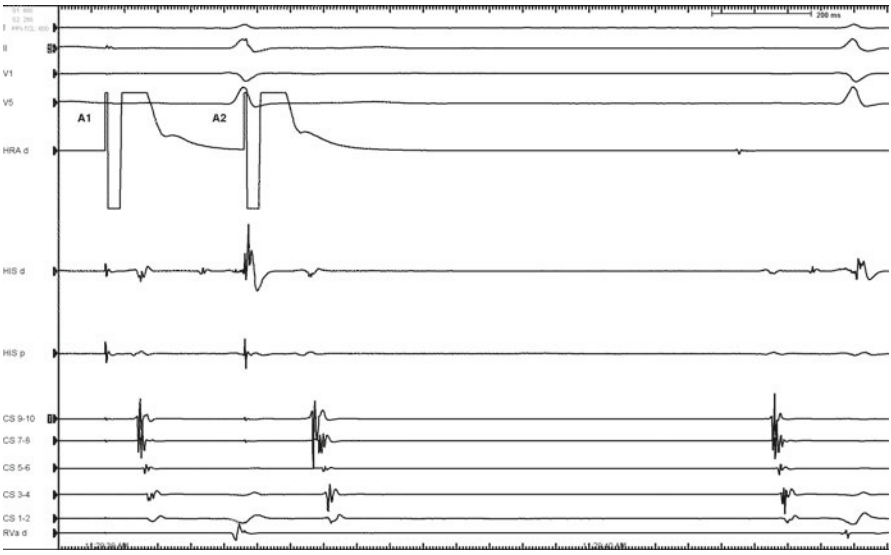


Fig. 1.3 Example of extrastimuli testing by pacing from the high RA (HRA d). The first paced beat on the *left of the image* is the final beat of the drive train where pacing is performed at 600 msec (*A1*). This beat conducts through the His to the ventricle via the AVN. This is followed by an extrastimuli which is performed at a progressively shorter cycle length. In this example this occurs at 280 msec (*A2*). Capture is seen on the high RA (HRA d) and the coronary sinus (*CS*) with lack of conduction through the AV node. This is considered to represent the AV node refractory period. (CS 9–10 is positioned in the proximal CS while CS 1–2 is in the distal CS, His d is positioned along the distal His, His p along the proximal His and RV a d is positioned in the RV apex)

For a re-entry circuit to sustain, the length of the circuit must be greater than or equal to the product of the conduction velocity and the refractory period termed the wavelength of the circuit. The pathways involved in these circuits must therefore have different conduction properties and refractoriness. A slow conduction pathway ensures that the wave of depolarization does not reach tissue which is refractory and thus terminate the arrhythmia.

Another requirement is the existence of a region of conduction block. This may be either anatomical or functional. Anatomical block may be structural such the tissue which exists between the slow and fast pathways in AV nodal re-entry tachycardia (AVNRT) or scar tissue in ischemic VT or functional such as occurs in typical atrial flutter. Functional block occurs as wavelets collide with each other and thus prevents the leading edge of the circuit stimulating refractory tissue resulting in termination of the arrhythmia. Most re-entry circuits involve a combination of structural and functional regions of block. A diagrammatic representation of a re-entry circuit is shown in Fig. 1.5.

The **wavelength of the circuit** is a product of the conduction velocity and the refractory period.

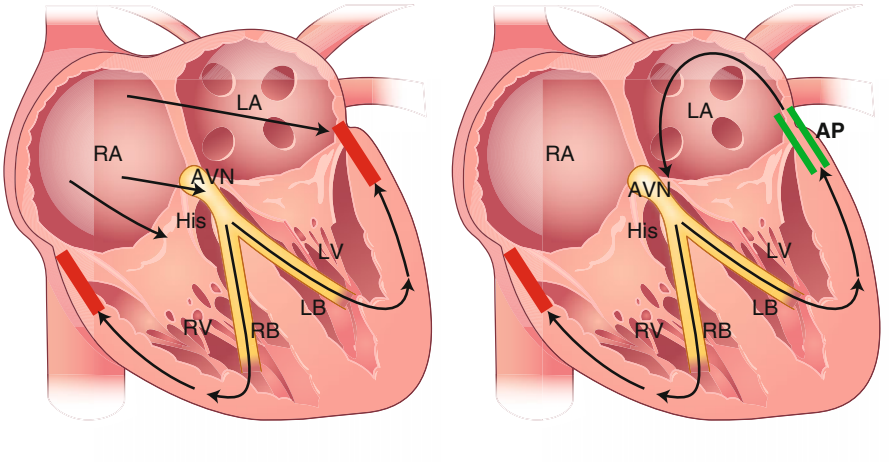


Fig. 1.4 Diagram showing the initiation of circus movement tachycardia (CMT) in a patient with WPW. In the *left image* conduction occurs antegradely through the AV node and is blocked retrogradely as there is no accessory pathway present. In the *right image* a re-entry tachycardia is demonstrated utilizing the AV node as the antegrade limb and the AP as the retrograde limb. *Arrows* indicate the predominant direction of conduction. The *red lines* indicate blocked conduction which prevents a re-entry circuit while the green lines indicate retrograde conduction over an accessory pathway. A denotes atrium, AVN is the AV node, V is ventricle and AP is the accessory pathway

Automaticity

Automaticity results from spontaneous depolarization during phase IV of the AP. Although this is a feature of automatic cells such as the SN, AV node, His bundle and Purkinje cells, if it occurs in other cells then it is considered to be abnormal (ectopic focus).

Spontaneous depolarization does not normally occur in atrial and ventricular myocytes but may occur as a result of various physiological or pathological changes which on a cellular level may result in a reduction in the expression or function of the IK1 channel [2].

Latent automatic cells are normally suppressed by SN activity and only become functional if the sinus rate becomes slower than the rate of spontaneous discharge of these cells. Some regions of increased automaticity are protected from SN discharge and therefore discharge independently of this. These cells which demonstrate evidence of entrance block with exit conduction are called **parasystolic foci** and tend to result in ectopic beats with intervals which are multiples of each other [2]. Incomplete entrance block may also occur resulting in entrainment of the focus at a defined rate resulting in ectopic beats with a fixed coupling interval.

One of the typical features of increased automaticity is the ability to overdrive pace at a rate faster than the tachycardia cycle length. This occurs as a result of an

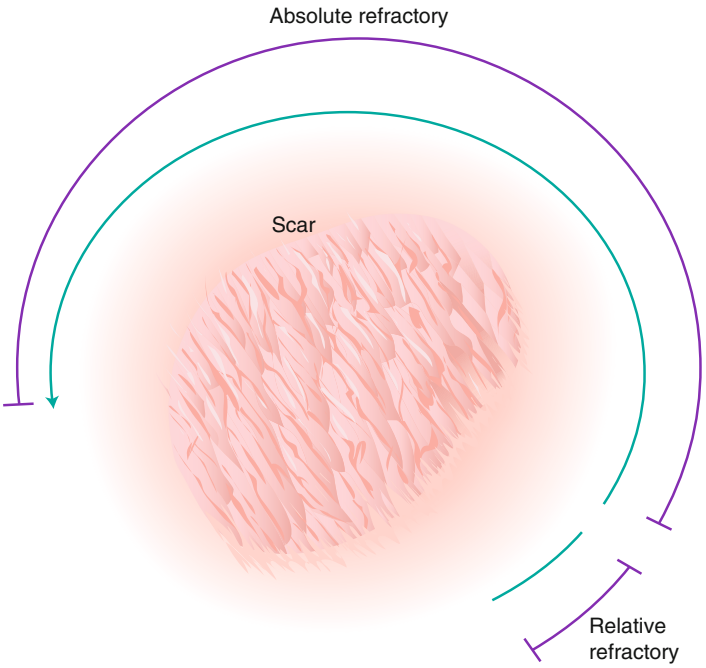


Fig. 1.5 Diagrammatic representation of a re-entry circuit circulating around a conduction barrier in this case scar. The region of tissue where the wavefront is propagating corresponds with tissue during the absolute RP. The tail of the wavefront corresponds with tissue during the relative RP

increase in the activity of the Na^+/K^+ ATPase pump resulting in the generation of a hyperpolarizing current which inhibits phase IV of the action potential [3].

Afterdepolarizations and Triggered Activity

Afterdepolarizations are defined as depolarizations which occur after Phase 0 of the cardiac action potential and may result in a spontaneous action potential known as a triggered response. These are divided into early afterdepolarization (EAD) or delayed afterdepolarization (DAD). These are depicted in Fig. 1.6.

EAD occurs during phase II and phase III while DAD occur after the cardiac action potential is complete. EADs tend to occur when there is an increase in the inward movement of positive ions during the plateau phase of the action potential.

DAD occur as a result of an increase in the inward movement of calcium. This can occur in the setting of digoxin toxicity or in conditions such as catecholamine induced polymorphic ventricular tachycardia (CPVT).

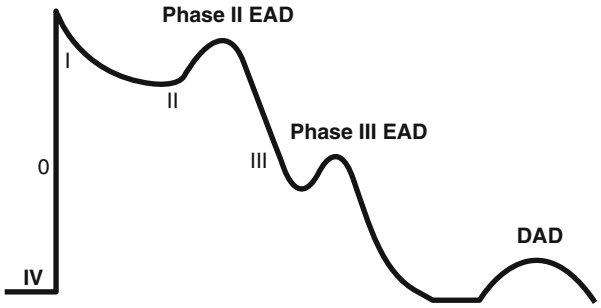


Fig. 1.6 Diagrammatic representation of phase II and phase III early atrial depolarizations (*EADs*) and delayed atrial depolarizations (*DADs*) at the end of the cardiac AP

Anatomy of the Cardiac Chambers

The cardiac chambers may be visualized prior to a complex ablation using computed tomography (CT) or magnetic resonance imaging (MRI) or during the procedure using fluoroscopy, echocardiography and electroanatomic mapping (EAM). The majority of procedures rely on a certain amount of fluoroscopic imaging and often our anatomical understanding is based on the locations of the catheters in various views. The most common views in the electrophysiology laboratory are the right anterior oblique (RAO), left anterior oblique (LAO), posterior – anterior (PA) and left lateral (LL). These views are shown in Fig. 1.7.

The RAO projection helps to demonstrate the postero-anterior (PA) location of a catheter within the cardiac chambers and shows the AV groove more clearly than the PA view. In this view the spine is on the left. Moving the catheter to the right results in a more anterior orientation while moving to the left is more posterior. The left cardiac border is formed by the RV outflow tract (RVOT) superiorly with the RV superior wall inferior to this and the LV apex at the apex. More steep RAO images result in a greater proportion of the RV being visualized with less LV present. The inferior wall of the RV forms the base of the image while the right cardiac border is formed by the posterior wall of the RA and posterior wall of the LA. The AV annular fat strip is best seen in the RAO projection. This 1 cm thick white line is formed as a result of the overlap of the ring of fat in the right anterior, septal and left posterior annulus and either marks the course of, or is slightly ventricular to the coronary sinus (CS). Any catheter posterior to the fat strip is in the atrium and anterior to this is in the ventricle.

In the LAO view the AV rings are viewed parallel to the image. The left cardiac border is formed by the LA superiorly and the lateral wall of the LV inferiorly. Steeper LAO views image more LA and less LV. The right cardiac border is formed by the right atrial appendage superiorly and the RV free wall inferiorly. In this view the spine is on the right side of the image. In the LAO projection anterior is to the left and posterior to the right.

In the PA view the left cardiac border is formed superiorly by the tip of the left atrial appendage (LAA) and the anterior wall of the left ventricle (LV) more inferiorly and the LV apex at the apex. The right heart border is formed by the superior

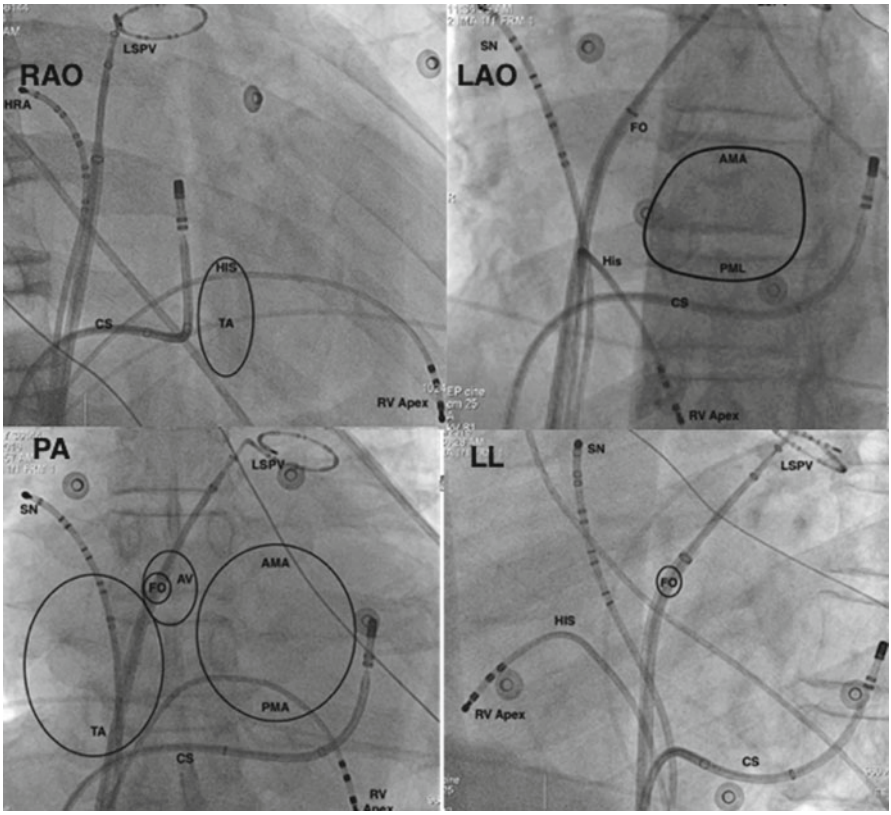


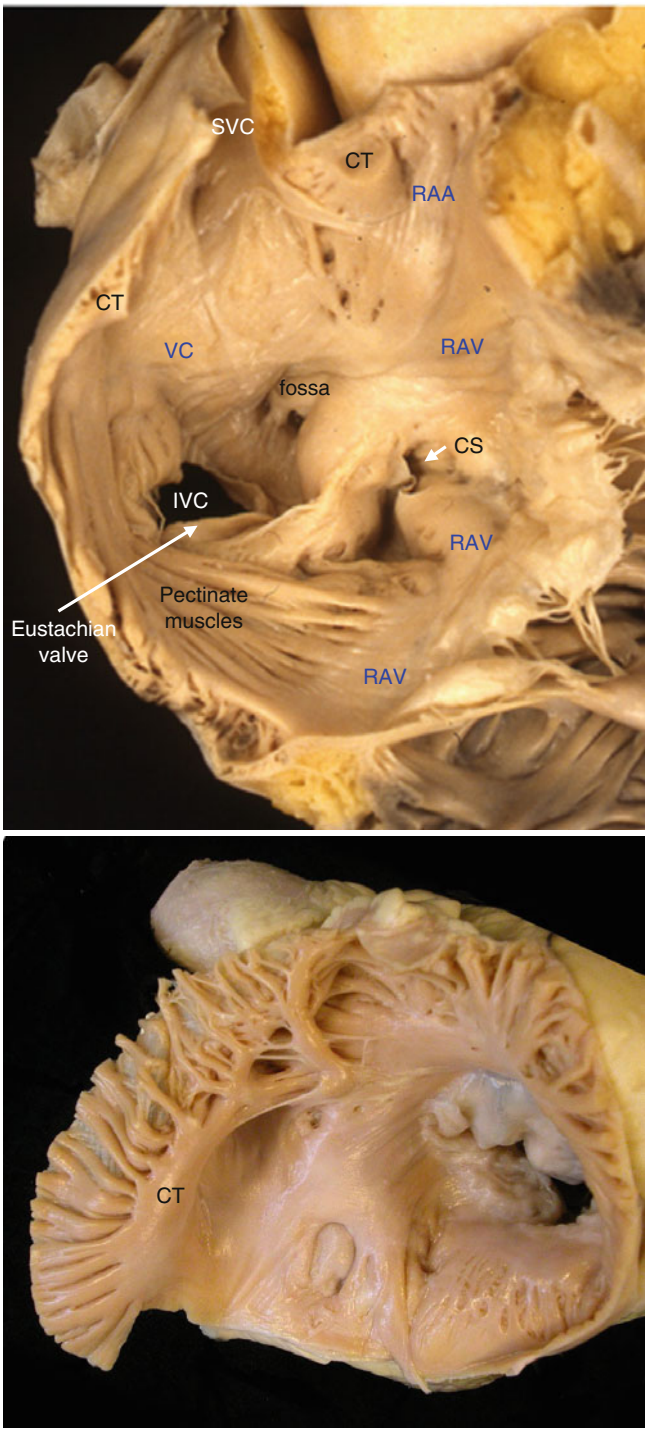
Fig. 1.7 The main fluoroscopic views used in the electrophysiology laboratory. All images have a catheter positioned in the coronary sinus (*CS*), RV apex, high right atrium (*HRA*) close to the sinus node (*SN*) and a catheter positioned across the fossa ovalis (*FO*) into the left superior pulmonary vein (*LSPV*). The location of the His is superimposed on the image. The tricuspid annulus (*TA*), mitral annulus (*MA*, anterior mitral annulus (*AMA*) and posterior mitral annulus (*PMA*)) and aortic valve (*AV*) are superimposed on the four views. The *top left view* shows the RAO projection, *top right* shows an LAO projection, *bottom left* a PA view and the *bottom right* shows a *left lateral view*

vena cava (SVC) to right atrial (RA) junction superiorly and the lateral wall of the RA inferior to this. The base is comprised of the inferolateral wall of the RV.

The LL view is very helpful in determining the anterior – posterior location of the catheter. This is useful for trans-septal access as well as for epicardial access in VT ablation.

The RA

The RA lies anterior, inferior and rightward from the LA and is composed of the venous component, appendage and vestibule. The anatomy of the RA is shown in Fig. 1.8.


SVC
CT
RAA
CT
VC
RAV
fossa
CS
IVC
RAV
Pectinate muscles
Eustachian valve
RAV
CT

The superior and inferior vena cava drain systemic blood into the smooth-walled posterior venous component of the RA. Coronary blood flows through the CS into the RA through the CS os which is located between the inferior vena cava (IVC) and the tricuspid annulus (TA). The CS os is to a variable degree covered by the Thebesian valve which is a thin crescent shaped structure attached at the posterior and inferior boundary of the coronary sinus os. The degree of coverage varies but may practically occlude the CS os in up to 25 % of individuals [4].

The RA appendage is a triangular broad based structure composed of pectinate muscles originating from the **crista terminalis** and is generally where atrial pacemaker leads are positioned for stability. The crista terminalis is one of the most common regions responsible for focal atrial tachycardia's as well as acting as a functional electrical barrier essential for typical atrial flutter. It separates the pectinated appendage from the venous component (or intercaval area) of the atrial body. The latter is posterior whereas the vestibule which surrounds the atrial outlet leading to the tricuspid valve is anterior.

The SN

The SN is a collection of nodal cells within a tough matrix of connective tissue lying just below the epicardium and separated from the endocardium by a layer of atrial myocardium. It is located at the junction between the superior vena cava and the RA, at the antero-lateral quadrant marked by the crista terminalis (CT) (Fig. 1.8) and statistically measures 10–20 mm in length, 3 mm in width and 1 mm in depth but there is an enormous anatomical variation between individuals [5]. Cells in the SN tend to be much smaller than those in the RA measuring approximately 5–10 μm. Typical nodal cells known as P cells are located in the centre of the SN and are generally poorly organized myofilaments. There are fibroblasts and collagen fibers interspersed throughout the SN. There is a gradual transition between the SN and the RA with a disparity in conduction velocity between the cells thus preventing SN depolarization as a result of atrial depolarization [6].

Spontaneous phase IV diastolic depolarization starts at −65 mV until the activation threshold is reached at −40 mV resulting in rapid depolarization. The action potential of the SN differs from that of a Purkinje myocyte with a more gradual upslope and the absence of a plateau phase. Diastolic depolorization occurs as a

Fig. 1.8 Anatomy of the RA (*top image*) and the crista terminalis (*bottom*). The RA is antero-inferior to the LA and is composed of the venous component (*VC*), RA appendage (*RAA*) and RA vestibule (*RAV*). The superior (*SVC*) and inferior vena cava (*IVC*) are seen connected posteriorly into the RAV. The RA appendage is an anterior structure composed of pectinate muscles originating from the crista terminalis (*CT*). The coronary sinus (*CS*) is inferior and posterior. Superior and slightly posterior on the interatrial septum is the fossa ovalis. In the image below the crista terminalis is seen with pectinate muscles radiating out

result of activation of the If current. This operates in a voltage range more negative than normally occurs in the central pacemaker cells (less than −45 mV). It therefore has maximum activity during hyperpolarization and progressively increases opposing repolarization and then initiating diastolic depolarization [7].

The rate of diastolic depolarization in the SN is affected by both sympathetic adrenergic and parasympathetic muscarinic stimulation. This is predominantly affected by the If channel.

Sympathetic adrenergic stimulation results in an increase in the gradient and duration of diastolic depolarization with minimal effects on the overall action potential duration [8]. This occurs as a result of a shift in the activation curve to more positive voltages without a change in the conductance of the If channel as a result of an increase in intracellular cAMP [9].

The reverse occurs with parasympathetic muscarinic stimulation [10]. Slow inward Ca^{2+} channels are involved in the later phase of diastolic depolarization [8] as well as the upslope in the action potential. The transient T type Ca^{2+} channel is activated at more negative voltages and therefore opens first followed by the long lasting L component which opens during the upslope of the action potential [8].

The delayed rectifier Ik channel is the predominant potassium channel in the SN and contributes to repolarization allowing the following depolarization to be initiated.

Respiratory sinus arrhythmia occurs as a result of a reduction in the PP interval with inspiration and a prolongation of the PP interval with expiration. The maximum difference between the longest PP and shortest PP interval should be less than 160 ms. This phenomenon reduces with age.

Ventriculophasic sinus arrhythmia is seen in association with third degree AV block in which the PP interval surrounding a QRS complex is shorter than the PP interval not surrounding a QRS complex.

SN dysfunction encompasses sinus bradycardia, sinus pause, sinoatrial exit block, chronotropic incompetence and inappropriate sinus tachycardia.

Sinus bradycardia is a relatively common finding and in the absence of symptoms is generally of no clinical significance. A sinus pause is defined as the absence of a P wave for greater than or equal to 2 s (although generally not considered clinically significant unless greater than or equal to 3 s while awake or 5 s while asleep). If the duration of the sinus pause is a multiple of the PP interval, then sinoatrial node exit block should be considered. **Chronotropic incompetence** is defined as failure to achieve 70–80 % of maximal predicted heart rate (maximal predicted heart rate = 220-age) during peak exercise.

Inappropriate sinus tachycardia is a persistent elevation in heart rate greater than 100 bpm at rest with no obvious precipitating cause. There is an exaggerated increase in sinus rate with minimal activity and a reduction or normalization of sinus rate during sleep. The p wave morphology and axis are unchanged.

It is important to rule out all potential causes as well as other arrhythmias such as right atrial tachycardia close to the SN or SN re-entry tachycardia. Inappropriate sinus tachycardia is most likely multifactorial with a change in the overall autonomic supply to the SN which may include a reduction in the sensitivity to