

From Electrophysiology to Modern Device Therapy



A close-up photograph of a DDD MRI Compatible pacemaker. The device is a small, oval-shaped, metallic component with a clear plastic protective cap. The text "DDD MRI COMPATIBLE" is printed on the metallic surface. A thin, clear tube is attached to the top of the device.



A photograph of a CRT-D (Cardiac Resynchronization Therapy Defibrillator) device. It is a small, rectangular, metallic-looking device with several wires extending from it. The text "CRT-D" is printed on the top and bottom of the device.



Basic Principles and Advanced Concepts



Cardiac Function and Pressure Analysis



CARDIAC CATHETERIZATION



PACING

Conventional,
Physiologic and
Resynchronization



DEVICE THERAPY

Pacemakers, ICDs,
CRT and Future
Perspectives

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ANATOMY AND PHYSIOLOGY OF THE CARDIAC CONDUCTION SYSTEM

METİN KARAYAKALI¹

Introduction

For the heart to perform its pump function fully and effectively, the four chambers must contract in a specific sequence and timing. The cardiac conduction system, which ensures this coordination, is a specialized tissue network that is histologically and functionally distinct from contractile myocardium. A key characteristic of this system is its ability to generate spontaneous electrical impulses without requiring any external stimulus. In clinical medicine, this feature is referred to as "automaticity" and forms the basis for the heart's ability to continue beating in its denervated state even after transplantation (Anderson, et al., 2009: 99–113; Epstein, et al., 2008: e1–62).

The first comprehensive descriptions of conduction system anatomy date back to the early 20th century. In 1839, Jan Evangelista Purkinje described a gray, gelatinous network of fibers on the subendocardial surface of sheep ventricles (Cavero, Guillon, &

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Holzgrefe, 2017: 528–538; Purkinje, 1845: 281–295). In 1893, Wilhelm His Jr. discovered the muscle bundle connecting the atria to the ventricles; subsequently in 1906, Sunao Tawara provided a detailed description of the distal branching pattern of the His bundle and the atrioventricular node (Anderson & Mori, 2016: 637–643; Tawara, 1906). Finally, in 1907, the identification of the sinoatrial node by Arthur Keith and Martin Flack completed the fundamental components of the cardiac conduction system (Keith, 1907: 172–189.). Keith and Flack described this structure as "a small area of condensed tissue at the junction where the superior vena cava enters the right atrium."

Today, the cardiac conduction system is considered to comprise four main components: the sinoatrial (SA) node, internodal and interatrial pathways, the atrioventricular (AV) node, and the His-Purkinje network (Epstein, et al., 2008: e1–62; Klabunde, 2026). Each of these components is characterized by a unique ion channel expression profile, cell morphology, and autonomic nervous system response. Structural or functional disturbances in the conduction system can lead to various clinical presentations, such as bradycardia, conduction blocks, and reentrant arrhythmias; thus, a detailed understanding of this system is essential as a foundation for the treatment of tachyarrhythmias and bradyarrhythmias, comprehension of pacemaker indications, and device-based therapies.

Structure and Automaticity of the Sinoatrial Node

Anatomical Location and Histology

The sinoatrial node is a spindle-shaped structure located subepicardially on the superior-lateral wall of the right atrium, at the junction of the superior vena cava and right atrium, at the level of the sulcus terminalis (crista terminalis) (Epstein, et al., 2008: e1–62; Keith, 1907: 172–189.; Monfredi, et al., 2010: 1392–1406). In

adults, the SA node measures approximately 13–20 mm in length, 2–5 mm in width, and 1–2 mm in thickness (Csepe, et al., 2016: 164–178; Monfredi, et al., 2010: 1392–1406). The structure consists of specialized myocytes embedded within a dense connective tissue matrix in which the sinoatrial nodal artery is centrally located. The SA nodal artery originates from the right coronary artery in about 55–65% of cases, and from the circumflex artery in the remainder (Sanchez-Quintana, et al., 2005: 189–194).

The cellular organization of the SA node is explained by two principal models. According to the "gradient model," cell size, gap junction density, and ion channel expression change progressively from the center to the periphery of the node (Boyett, Honjo, & Kodama, 2000: 658–687). The central region contains small, pale-staining "P cells" (pale cells / pacemaker cells), which have few myofibrils, abundant glycogen, and a limited number of organelles. Toward the periphery, "transitional cells" are encountered; these possess both nodal and atrial myocyte properties (Boyett, Honjo, & Kodama, 2000: 658–687; Chandler, et al., 2009: 1562–1575; Monfredi, et al., 2010: 1392–1406). Alternatively, the "mosaic model" proposes that nodal and atrial cells intermix in variable proportions throughout the center-to-periphery axis (Boyett, Honjo, & Kodama, 2000: 658–687).

Electrical insulation of the SA node from the surrounding atrial myocardium is vital for structural integrity. Around the node, anatomical barriers comprised of connective tissue, adipose tissue, and vessels are present. These barriers protect pacemaker cells from the hyperpolarizing influence of the surrounding atrial myocardium and ensure that impulse exit occurs via specific conduction pathways (Fedorov, Glukhov, & Chang, 2012: H1773–1783; N. Li, et al., 2017). One such pathway, the Bachmann bundle, transmits excitation from the SA node to the left atrium, enabling synchronized

contraction of both atria (Epstein, et al., 2008: e1–62; Klabunde, 2026).

Automaticity Mechanism: The Coupled Clock Model

The most distinctive feature of SA node cells is the absence of a stable resting membrane potential. In contractile myocytes, membrane potential is maintained at approximately -90 mV during phase 4, whereas in pacemaker cells, following the termination of the action potential, the membrane potential spontaneously depolarizes in a positive direction from around -60 mV. When this spontaneous diastolic depolarization reaches threshold (-40 mV), it triggers a new action potential (DiFrancesco, 2010: 434–446; Klabunde, 2026).

For many years, the mechanism of this automatic activity was attributed solely to membrane ion channels. According to this, the "membrane clock" or "voltage clock" model proposes that the pacemaker current (I_f) is the primary source of diastolic depolarization (Accili, et al., 2002: 32–37; DiFrancesco, 2010: 434–446). The I_f current, described by DiFrancesco and Ojeda in 1979 in rabbit SA node cells, is carried by the HCN (hyperpolarization-activated cyclic nucleotide-gated) channel family; it is activated by hyperpolarization and is permeable to both Na^+ and K^+ ions (Accili, et al., 2002: 32–37; DiFrancesco, 2010: 434–446). Four isoforms of HCN channels (HCN1–4) have been identified, with HCN4 being the predominant isoform in human SA node (Baruscotti, et al., 2011: 1705–1710). A key feature of the I_f current is its direct modulation by cyclic AMP (cAMP); this property is fundamental for the regulation of heart rate by the autonomic nervous system (Accili, et al., 2002: 32–37; DiFrancesco, 2010: 434–446).

Since the early 2000s, Lakatta and colleagues have proposed that SA node automaticity cannot be explained solely by membrane ion channels, introducing the concept of the "calcium clock"

(Lakatta & DiFrancesco, 2009: 157–170; Maltsev & Lakatta, 2009: H594–615). In this model, calcium (Ca^{2+} sparks / local calcium releases) is rhythmically released from the sarcoplasmic reticulum (SR) via ryanodine receptors (RyR2), generating a net inward current through the sodium-calcium exchanger (NCX1) and contributing to diastolic depolarization. Calcium reuptake into the SR by the SERCA2a pump maintains the cycle.

The currently accepted "coupled clock" model predicts that the membrane clock and the calcium clock are not independent, but function as two interdependent subsystems that mutually reinforce each other (Lakatta & DiFrancesco, 2009: 157–170; Maltsev & Lakatta, 2009: H594–615). The synchronized function of membrane ion channels and SR calcium cycling ensures robust and flexible pacemaker activity. Dysfunction in one of these systems may result in a loss of function exceeding the compensatory capacity of the other.

At the molecular level, calcium/calmodulin-dependent protein kinase II (CaMKII) is a critical enzyme acting as a bridge between these two clocks. CaMKII phosphorylates L-type calcium channels (CaV1.2 and CaV1.3), phospholamban, and RyR2, thereby increasing both calcium entry and SR calcium release (Wu & Anderson, 2014: 48). Notably, CaMKII inhibition does not alter basal heart rate but reduces the chronotropic response to sympathetic stimulation (isoproterenol) by approximately 50% (Wu & Anderson, 2014: 48). This finding suggests that CaMKII is required for the heart rate increase during the "fight-or-flight" response, but is not essential for basal pacemaker activity.

Table 1. *Comparison of SA Node and Ventricular Myocyte Action Potentials*

Feature	SA Node (Slow Response)	Ventricular Myocyte (Fast Response)
Phase 0	L-type Ca^{2+} channels (ICa,L)	Fast Na^{+} channels (INa / NaV1.5)
Phase 4	Spontaneous diastolic depolarization (unstable)	Stable resting potential (≈ -90 mV)
Resting / Maximum Diastolic Potential	≈ -60 mV (unstable)	≈ -90 mV (stable)
Threshold Potential	≈ -40 mV	≈ -70 mV
Main Ionic Currents	If, ICa,L, ICa,T, INCX	INa, Ito, ICa,L, IKr, IKs, IK1
Conduction Velocity	0.01 – 0.05 m/s	0.3 – 1.0 m/s (myocardium)

Atrioventricular Node and His-Purkinje System

Anatomy and Function of the AV Node

The atrioventricular node is a small but critical structure positioned subendocardially within the septal wall of the right atrium, in an anatomical area known as the triangle of Koch. The boundaries of the triangle of Koch are defined by the septal leaflet of the tricuspid valve, the ostium of the coronary sinus, and the tendon of Todaro (Epstein, et al., 2008: e1–62; Hucker, et al., 2008: 204–215; Klabunde, 2026). In 80-90% of cases, arterial supply to the AV node is provided by the posterior descending branch of the right coronary artery (Sanchez-Quintana, et al., 2005: 189–194).

The most prominent physiological characteristic of the AV node is its ability to delay electrical conduction by approximately 120–200 milliseconds and the dynamic modulation of conduction velocity according to the rate of incoming impulses. This conduction delay is the main determinant of the PR interval on surface ECG and provides crucial hemodynamic timing: allowing the atria to complete contraction and fill the ventricles with blood (Epstein, et al., 2008: e1–62; Klabunde, 2026). The conduction property of the AV node is "decremental conduction," meaning that as the frequency of incoming impulses increases, conduction velocity slows even further—functioning as a natural filter that protects the ventricles from uncontrolled activation during rapid atrial arrhythmias (Epstein, et al., 2008: e1–62; Meijler & Janse, 1988: 608–647).

Histologically, the AV node is comprised of specialized myocytes that resemble those in the SA node, being small and containing few myofibrils. However, unlike the SA node, the cells of the AV node are organized within a loose connective tissue matrix, and Purkinje-like cells as well as contractile myocardial fibers can also be observed in this structure (Hucker, et al., 2008: 204–215). The AV node is functionally divided into three regions: the transitional zone, the compact node, and the lower nodal/His bundle region. The transitional zone consists of fibers extending from atrial myocardium to the compact node; a significant portion of conduction delay occurs here (Meijler & Janse, 1988: 608–647).

The latent pacemaker capacity of the AV node is clinically significant. When SA node pacemaker function is lost, the AV node can generate an "escape rhythm" at 40–60 beats per minute, thus serving as a backup pacemaker (Epstein, et al., 2008: e1–62; Klabunde, 2026). This backup mechanism can provide partial hemodynamic support even in patients who develop complete AV block; however, this rate is often insufficient for adequate cardiac output and requires permanent pacemaker implantation.

His Bundle and Bundle Branches

The His bundle (fasciculus atrioventricularis), which emerges from the distal end of the AV node, is the sole physiological connection allowing electrical conduction between atrial and ventricular myocardium (Anderson & Mori, 2016: 637–643; Caverio, Guillon, & Holzgrefe, 2017: 528–538; Epstein, et al., 2008: e1–62). This structure was first described in 1893 by Wilhelm His Jr. The His bundle traverses the central fibrous body and proceeds along the superior border of the membranous interventricular septum (Anderson & Mori, 2016: 637–643; Bressi, et al., 2023: C234–C241; Caverio, Guillon, & Holzgrefe, 2017: 528–538).

Anatomically, the His bundle is divided into three segments: the "penetrating" portion that passes through the atrioventricular septum (0.25–0.75 mm in humans), the "non-branching" portion that advances unbranched along the membranous septum (2–3 mm in humans), and the "branching" (bifurcation) region where it divides into the right and left bundle branches (Anderson & Mori, 2016: 637–643; Bressi, et al., 2023: C234–C241; Caverio, Guillon, & Holzgrefe, 2017: 528–538). This short course of the His bundle is an anatomical detail that increases its susceptibility to injury during surgical and interventional procedures. Preservation of this structure is especially important during procedures such as aortic valve replacement and repair of membranous ventricular septal defects.

The His bundle divides into right and left bundle branches at the crest of the muscular septum. The right bundle branch is a relatively thin, cord-like structure that proceeds subendocardially along the right surface of the interventricular septum and reaches the free wall of the right ventricle via the moderator band. The left bundle branch, in contrast, is broader and fan-shaped and typically divides into two or three subdivisions: the anterior fascicle, posterior fascicle, and in some cases, a septal fascicle (Bressi, et al., 2023:

C234–C241; Demoulin & Kulbertus, 1972: 807–814; Epstein, et al., 2008: e1–62). The left posterior fascicle, owing to dual arterial supply, is relatively resistant to ischemic injury, whereas the left anterior fascicle and the right bundle branch, each supplied by a single vessel, are more vulnerable to ischemia.

Purkinje Fiber Network

Purkinje fibers, the terminal extensions of the bundle branches, form an extensive subendocardial network throughout the ventricular myocardium. Purkinje cells are the largest-diameter cells in the heart, and because of this characteristic, achieve conduction velocities of 1–4 m/s (Bressi, et al., 2023: C234–C241; Miquerol, et al., 2004: 77–86). For comparison, conduction velocity in atrial myocardium is 0.3–1.0 m/s and only 0.01–0.05 m/s in the AV node (Klabunde, 2026).

This high conduction velocity of the Purkinje fibers allows for nearly simultaneous activation of the ventricles from apex to base. Consequently, the ventricular myocardium produces the most hemodynamically efficient contraction pattern: blood is ejected toward the outflow tracts at the ventricular base. Disruption of this conduction pattern—for example, with the development of a bundle branch block—causes ventricular contraction to become asynchronous and leads to reduced cardiac output. Cardiac resynchronization therapy (CRT) and His-Purkinje conduction system pacing (His-bundle pacing, left bundle branch area pacing) are modern therapeutic strategies aimed at restoring this physiological conduction pattern (Bressi, et al., 2023: C234–C241).

Table 2. Regional Conduction Velocities and Main Features of the Cardiac Conduction System

Structure	Conduction Velocity (m/s)	ECG Correspondence	Main Function
SA Node	< 0.05	P wave (onset)	Impulse generation (primary pacemaker)
Atrial Myocardium	0.3 – 1.0	P wave	Atrial depolarization and contraction
AV Node	0.01 – 0.05	PR interval (PR segment)	Physiological delay, frequency filter
His Bundle	1.0 – 1.5	PR interval (final part)	AV connection, electrical bridge
Bundle Branches	1.0 – 2.0	QRS onset	Rapid conduction to ventricles
Purkinje Fibers	1.0 – 4.0	QRS complex	Synchronous activation of ventricular myocardium

Action Potential and Ion Channels

Resting Membrane Potential

The basis of electrical activity in cardiac myocytes is formed by ion concentration gradients across the cell membrane and by ion channels that regulate the passage of these ions through the membrane. At rest, the intracellular K^+ concentration (≈ 140 mM) is much higher than the extracellular concentration (≈ 4 mM), while Na^+ and Ca^{2+} concentrations are the opposite (Klabunde, 2026; Nerbonne & Kass, 2005: 1205–1253). These concentration gradients are actively maintained by the Na^+/K^+ -ATPase (sodium-potassium

pump). In each cycle, this pump extrudes 3 Na⁺ ions from the cell while importing 2 K⁺ ions; thus, it maintains the concentration gradients and directly contributes about -3 mV to the resting potential via net outward movement of positive charge (Klabunde, 2026; Nerbonne & Kass, 2005: 1205–1253).

In ventricular myocytes, the resting membrane potential is approximately -90 mV. The most critical factor in determining this value is the high resting membrane permeability to potassium. The inward rectifier potassium current (IK1), through channels that remain open during phase 4, keeps the membrane potential close to the potassium Nernst equilibrium potential ($E_K \approx -94$ mV) (Klabunde, 2026; Nerbonne & Kass, 2005: 1205–1253). The reason why the membrane potential is not exactly equal to E_K is that the membrane also has a slight permeability to other ions such as sodium and calcium.

Fast Response Action Potential (Contractile Myocytes and Purkinje Fibers)

Atrial myocytes, ventricular myocytes, and Purkinje fibers generate a "fast response" action potential. This action potential consists of five phases, each of which is the result of different activation and inactivation kinetics of various ion channels (Klabunde, 2026; Nerbonne & Kass, 2005: 1205–1253).

Phase 0 (Rapid Depolarization): When the membrane potential reaches the threshold value (between -70 and -60 mV), voltage-gated fast Na⁺ channels (NaV1.5, INa) open. A large Na⁺ influx into the cell occurs, raising the membrane potential in milliseconds from -90 mV to about +20-30 mV. This rapid depolarization corresponds to the QRS complex on the ECG. The "m" gate (activation) of the Na⁺ channels opens rapidly at the voltage threshold, while the "h" gate (inactivation) closes with a slight delay

of a few milliseconds; this double-gate mechanism self-limits the current (Klabunde, 2026; Nerbonne & Kass, 2005: 1205–1253).

Phase 1 (Early Repolarization): With Na^+ channel inactivation and activation of the transient outward K^+ current (Ito), the membrane potential briefly drops, producing a characteristic notch on the action potential curve. The Ito current is especially prominent in epicardial myocytes and less so in endocardial cells; this difference is the main source of heterogeneity in action potential morphology across the ventricular wall (Klabunde, 2026; Nerbonne & Kass, 2005: 1205–1253; Sanguinetti & Tristani-Firouzi, 2006: 463–469).

Phase 2 (Plateau Phase): This is the phase where the cardiac action potential most distinctly differs from that of skeletal muscle and lasts about 200–300 milliseconds. The balance between inward calcium current through L-type Ca^{2+} channels (ICa_L) and outward potassium current via delayed rectifier K^+ channels (IKr and IKs) keeps the membrane potential stable around 0 mV (Klabunde, 2026; Nerbonne & Kass, 2005: 1205–1253). This long plateau serves two critical functions. First, calcium influx triggers excitation-contraction coupling: Ca^{2+} entering via L-type channels induces calcium-induced calcium release (CICR) from the SR, activating the contractile apparatus. Second, because of the long plateau duration, the cell remains in the absolute refractory period for an extended time; this prevents the heart from tetanic contraction and ensures a period of relaxation between each beat (Klabunde, 2026; Nerbonne & Kass, 2005: 1205–1253). On the ECG, the plateau phase corresponds to the ST segment.

Phase 3 (Repolarization): As the L-type Ca^{2+} channels inactivate and the delayed rectifier K^+ channels (especially IKr and IKs) are fully activated, the outward K^+ current predominates. The membrane potential rapidly progresses in the negative direction,

returning to the resting level (Klabunde, 2026; Nerbonne & Kass, 2005: 1205–1253). This phase corresponds to the T wave on the ECG. Mutations in the hERG (KCNH2) gene, which encodes the IKr current, cause prolongation of repolarization and hence QT prolongation, increasing the risk of torsades de pointes ventricular tachycardia (Sanguinetti & Tristani-Firouzi, 2006: 463–469).

Phase 4 (Resting Potential): In contractile myocytes, during this phase, the membrane potential is kept stable at around -90 mV by the IK1 current and the Na⁺/K⁺-ATPase pump (Klabunde, 2026; Nerbonne & Kass, 2005: 1205–1253). In Purkinje fibers, however, phase 4 is not fully stable; due to the If current, there is slow spontaneous depolarization, endowing these cells with latent pacemaker capacity (20–40 beats per minute) (Klabunde, 2026).

Slow Response Action Potential (Pacemaker Cells)

The action potential generated in SA node and AV node cells fundamentally differs from the contractile myocyte action potential. In these cells, the fast Na⁺ channels (NaV1.5) are either not expressed at all or are inactivated due to chronic depolarization (DiFrancesco, 2010: 434–446; Klabunde, 2026; Nerbonne & Kass, 2005: 1205–1253). Therefore, phase 0 depolarization is carried by L-type Ca²⁺ channels (ICa,L) rather than fast Na⁺ current. Because Ca²⁺ current has slower kinetics than Na⁺ current, depolarization occurs more slowly; this results in a less steep upstroke of the action potential (lower dV/dt) and reduced conduction velocity. The plateau phase is not pronounced, and phase 1 is practically absent (DiFrancesco, 2010: 434–446; Klabunde, 2026).

The most distinctive feature of these cells is spontaneous diastolic depolarization during phase 4. The components of the coupled-clock mechanism described above (If, ICa,T, ICa,L, NCX, SR calcium release) gradually bring the membrane potential to the threshold (DiFrancesco, 2010: 434–446; Klabunde, 2026; Lakatta &

DiFrancesco, 2009: 157–170; Maltsev & Lakatta, 2009: H594–615). Very low expression of the IK1 current in these cells is another factor facilitating spontaneous depolarization; a strong IK1 current would keep the membrane hyperpolarized and suppress automaticity (DiFrancesco, 2010: 434–446; Klabunde, 2026).

Refractory Periods

The concept of refractory period is a fundamental protective mechanism for the electrical safety of the heart. During the absolute refractory period (ARP), the h-gates of Na⁺ channels are inactivated, and no matter how strong a stimulus is applied, a new action potential cannot be generated (Klabunde, 2026; Nerbonne & Kass, 2005: 1205–1253). The ARP covers the period from phase 0 to the middle of phase 3 of the action potential. The relative refractory period (RRP) occurs in the latter part of phase 3, when some of the Na⁺ channels have recovered from inactivation; during this time, a stimulus stronger than normal can trigger a weak and slowly conducting action potential (Klabunde, 2026; Nerbonne & Kass, 2005: 1205–1253). Clinically, premature stimuli during the RRP may provide a substrate for reentrant arrhythmias; this is the physiological basis for the dangerous nature of ventricular premature complexes that fall on the T wave, known as the "R-on-T phenomenon".

Autonomic Nervous System Effects

Although the heart has the capacity to beat with its own intrinsic rhythm without external innervation, under physiological conditions, heart rate and conduction parameters are continually modulated by the autonomic nervous system. The parasympathetic and sympathetic divisions act in opposition on the SA node, AV node, and contractile myocardium, forming a dynamic balance (Epstein, et al., 2008: e1–62; Klabunde, 2026; Shivkumar, et al., 2016: 3911–3954).

Table 3. *Phases of the Fast Response Action Potential, Ion Channels, and ECG Correlations*

Phase	Name	Main Ion Currents	Change in Membrane Potential	ECG Equivalent
0	Rapid Depolarization	INa (NaV1.5) → Na ⁺ into the cell	−90 → +20 mV	QRS complex
1	Early Repolarization	Ito → K ⁺ out of the cell	+20 → +5 mV	J point
2	Plateau	ICa,L (inward) ↔ IKr, IKs (outward)	≈ 0 mV (steady)	ST segment
3	Repolarization	IKr, IKs → K ⁺ out of the cell	0 → −90 mV	T wave
4	Resting	IK1, Na ⁺ /K ⁺ -ATPase	≈ −90mV (stable)	TP segment

Parasympathetic (Vagal) Effects

Parasympathetic innervation of the heart is provided by the vagus nerve (n. vagus, cranial nerve X). Vagal preganglionic fibers originate from the nucleus ambiguus and dorsal motor nucleus and synapse in intrinsic ganglia surrounding the heart; postganglionic fibers directly innervate the SA node, AV node, and atrial myocardium. The direct effect of vagal innervation on ventricular myocardium is quite limited compared to that on the atria (Epstein, et al., 2008: e1–62; Shen & Zipes, 2014: 1004–1021; Shivkumar, et al., 2016: 3911–3954).

Acetylcholine released from vagal postganglionic fibers binds to muscarinic M_2 receptors on SA and AV node cells. Activation of the M_2 receptor decreases intracellular cAMP levels by suppressing adenylyl cyclase activity via inhibitory G proteins (G_i). Reduced cAMP shifts the activation curve of I_f channels (HCN) to more negative potentials, thereby slowing the rate of diastolic depolarization (DiFrancesco, 2010: 434–446; Klabunde, 2026; Shivkumar, et al., 2016: 3911–3954). In addition, acetylcholine-dependent potassium channels (IKACh / Kir3.1-Kir3.4), directly activated via G proteins, increase K^+ efflux, hyperpolarizing the membrane and shifting the maximum diastolic potential to more negative values (Klabunde, 2026; Shivkumar, et al., 2016: 3911–3954). The combined effect of these two mechanisms is to decrease heart rate (negative chronotropy), slow AV node conduction velocity (negative dromotropy), and prolong the refractory period of the AV node.

At rest, vagal tone predominates over sympathetic tone. This is responsible for reducing the intrinsic rate of the SA node (approximately 100 beats per minute) to the physiological resting heart rate (60–75 beats per minute). The clinical confirmation of this parasympathetic dominance comes from the elevation of resting heart rate to around 90–110 bpm following heart transplantation, where vagal innervation is lost (Epstein, et al., 2008: e1–62; Klabunde, 2026).

Sympathetic Effects

The preganglionic neurons of cardiac sympathetic innervation arise from the intermediolateral cell column of the thoracic spinal cord (T1–T5) and synapse in the stellate (cervicothoracic) ganglion. Postganglionic adrenergic fibers innervate the SA node, AV node, and the entire ventricular myocardium; in contrast to the parasympathetic system, the effects

of sympathetic innervation on the ventricle are pronounced (Epstein, et al., 2008: e1–62; Shen & Zipes, 2014: 1004–1021; Shivkumar, et al., 2016: 3911–3954).

Noradrenaline (norepinephrine) released from postganglionic fibers and adrenaline (epinephrine) released into the circulation from the adrenal medulla bind to myocardial β_1 -adrenergic receptors. Activation of β_1 receptors increases intracellular cAMP by activating adenylyl cyclase via stimulatory G proteins (G_s). Increased cAMP acts through activation of protein kinase A (PKA) on multiple targets (Klabunde, 2026; Shivkumar, et al., 2016: 3911–3954): it shifts the activation curve of If channels positively, accelerating diastolic depolarization (positive chronotropy); increases Ca^{2+} influx via L-type Ca^{2+} channel phosphorylation (positive inotropy); facilitates diastolic relaxation by relieving SERCA2a inhibition through phospholamban phosphorylation (positive lusitropy); and increases conduction velocity through the AV node (positive dromotropy).

A portion of sympathetic activation proceeds through the CaMKII pathway described above. The β -adrenergic stimulation-induced increase in intracellular Ca^{2+} activates CaMKII via the Ca^{2+} /calmodulin complex. Phosphorylation by CaMKII of L-type Ca^{2+} channels, RyR2, and phospholamban complements the effects of PKA, accounting for about half the sympathetic chronotropic response (Wu & Anderson, 2014: 48).

Baroreceptor Reflex and Autonomic Balance

Mechanoreceptors (baroreceptors) located in the carotid sinus and aortic arch detect changes in arterial blood pressure and relay this information to cardiovascular centers in the medulla oblongata. When blood pressure rises, baroreceptor afferent activation increases; in response, the cardiac inhibitory center (nucleus ambiguus) in the medulla is activated, strengthening vagal

tone and suppressing sympathetic output. As a result, heart rate decreases and blood pressure is balanced, accompanied by peripheral vasodilation. Conversely, when blood pressure falls, sympathetic tone is increased, elevating heart rate and peripheral resistance (Klabunde, 2026; Shivkumar, et al., 2016: 3911–3954). This negative feedback loop is the key mechanism for maintaining short-term hemodynamic stability.

Normal and Pathological Conduction Patterns

Normal Conduction Sequence and ECG Correlation

Under physiological conditions, the electrical impulse, once generated in the SA node, spreads through the entire heart in a specific hierarchy and timing. The impulse formed in the SA node first propagates along the right atrial myocardium, then reaches the left atrium via the Bachmann bundle. Depolarization of both atria is seen as the P wave on the ECG and takes approximately 80–100 milliseconds (Epstein, et al., 2008: e1–62; Klabunde, 2026). On reaching the AV node, the impulse is delayed by about 120–200 ms due to decremental conduction; this delay constitutes the majority of the PR interval. After passing through the AV node, the impulse is transferred to the His bundle, then to the right and left bundle branches, and rapidly activates the ventricular myocardium from apex to base via the Purkinje fibers. Ventricular depolarization appears on the ECG as the QRS complex (normally < 120 ms) (Epstein, et al., 2008: e1–62; Klabunde, 2026).

Conduction Disorders

Sick sinus syndrome (SSS): This includes impaired impulse generation by the SA node or impaired conduction of the impulse produced into the surrounding atrial tissue. The clinical picture may include sinus bradycardia, sinus arrest, sinoatrial exit block, and tachycardia-bradycardia syndrome (SSS) (1). Underlying

mechanisms include SA node fibrosis, loss of P cells, changes in ion channel expression, and imbalances in autonomic tone. Symptomatic SSS is one of the most common indications for permanent pacemaker implantation (Epstein, et al., 2008: e1–62).

Atrioventricular blocks: This refers to partial or complete blockage of AV conduction. In first-degree AV block, the PR interval exceeds 200 ms but all P waves are conducted. In second-degree block Mobitz type I (Wenckebach), the PR interval progressively lengthens, resulting in a dropped QRS; this pattern generally reflects block at the compact AV node and is often benign. In Mobitz type II, the PR interval remains constant but sudden QRS drops occur; this indicates block at the His bundle or infranodal level, with a high risk of progression to complete block. In third-degree (complete) AV block, the atria and ventricles function independently; ventricular rhythm depends on AV node or His-Purkinje escape foci and ranges from 20–50 beats per minute (Epstein, et al., 2008: e1–62; Klabunde, 2026; Meijler & Janse, 1988: 608–647).

Bundle branch blocks: Conduction delay or block in the right or left bundle branch causes the QRS duration to exceed 120 ms and produces characteristic morphological changes. In left bundle branch block (LBBB), the normal apex-to-base pattern of ventricular activation is lost; this can lead to ventricular dyssynchrony and contribute to progressive heart failure. In the presence of LBBB, cardiac resynchronization therapy (CRT) is a treatment option proven to reduce mortality and morbidity in these patients (Bressi, et al., 2023: C234–C241; Epstein, et al., 2008: e1–62).

Preexcitation syndromes: The presence of an accessory conduction pathway (such as a Kent bundle) outside the AV node results in early activation of the ventricles without the normal AV node delay. In the Wolff-Parkinson-White (WPW) pattern, the ECG shows a short PR interval (< 120 ms), a delta wave at the start of the

QRS, and broadening of the QRS complex (Brugada, et al., 2020: 655–720). This may be asymptomatic but can predispose to orthodromic or antidromic atrioventricular reentrant tachycardias. The most dangerous scenario in WPW is rapid conduction of atrial fibrillation to the ventricles via the accessory pathway; in this situation, drugs that block the AV node (verapamil, diltiazem, digoxin, adenosine) are contraindicated, as these agents abolish the filtering effect of the AV node and may further increase the ventricular response, leading to ventricular fibrillation (Brugada, et al., 2020: 655–720). This risk is especially seen when the accessory pathway has rapid conduction and a short refractory period.

Age-Related Changes

The cardiac conduction system undergoes progressive structural and functional remodeling during the aging process. These changes increase the frequency of bradyarrhythmia and conduction disorders in elderly individuals and constitute the basis for the parallel rise with age of pathologies most commonly leading to pacemaker implantation (X. Li, et al., 2025: 107954; Steenman & Lande, 2017: 131–137).

Structural Changes: Fibrosis and Cell Loss

With aging, interstitial and replacement fibrosis increases in all components of the conduction system. Classic histopathological studies specifically examining the SA node have shown that, in individuals over 50 years of age, the number of SA node cells decreases by approximately 39% compared to adolescents and young adults (Shiraishi, et al., 1992: 2176–2184; Steenman & Lande, 2017: 131–137). This cell loss predominantly occurs in the periphery of the node and is replaced by fibrous tissue and fat infiltration. In elderly individuals, the volume of fibrous connective tissue in the SA node has been reported to increase by around 49% (Shiraishi, et al., 1992: 2176–2184; Steenman & Lande, 2017: 131–

137). Similar fibrotic changes are observed in the AV node, His bundle, and left bundle branch as well (X. Li, et al., 2025: 107954; Steenman & Lande, 2017: 131–137).

Fibrosis exerts multiple adverse effects on the conduction system. The accumulation of connective tissue disrupts the electrical conduction pathways between specialized myocytes, resulting in nonuniform anisotropic conduction; this increases conduction delays and creates a substrate for reentrant arrhythmia (Jansen, et al., 2020: 147–159; Steenman & Lande, 2017: 131–137). On the ECG, these changes manifest with age as prolongation of P wave duration, PR and QT intervals, reduction in QRS voltage, and a leftward shift of the QRS axis (Steenman & Lande, 2017: 131–137).

Ion Channel and Gap Junction Changes

During the aging process, changes also occur in the ion channel expression profile of SA node cells. Animal models have demonstrated that HCN4 expression declines with age, and this contributes to a reduction in I_f current density, thereby slowing intrinsic heart rate (Csepe, et al., 2016: 164–178; X. Li, et al., 2025: 107954). Additionally, changes in L-type Ca^{2+} channel expression and decreased SERCA2a activity negatively affect both the membrane clock and calcium clock mechanisms, weakening pacemaker function.

Age-dependent changes in gap junction proteins (connexins) have also been reported. The reduction in Cx43 expression and the lateralization of connexin distribution slow intercellular electrical conduction and predispose to conduction disturbances (Jansen, et al., 2020: 147–159; Steenman & Lande, 2017: 131–137). When these molecular-level changes are considered together with the aforementioned structural fibrotic remodeling, the reasons for the high prevalence of sinus node dysfunction, AV block, and bundle

branch blocks in elderly individuals become more readily understood.

Oxidative Stress and the Role of CaMKII

In advanced age, increased oxidative stress is a critical molecular trigger in the degeneration of the conduction system. Reactive oxygen species (ROS) oxidize methionine residues (Met-281/282) in the autoregulatory domain of CaMKII, rendering the enzyme constitutively active (oxidized CaMKII, ox-CaMKII) independent of Ca^{2+} and calmodulin (Swaminathan, et al., 2011: 3277–3288; Wu & Anderson, 2014: 48). Chronic accumulation of ox-CaMKII induces apoptosis in SA node cells, accelerates fibrosis, and reduces pacemaker cell volume. The reduction of functional pacemaker cell mass results in the inability to provide the electrical charge (“source”) necessary to depolarize the surrounding atrial tissue (“sink”). This “source-sink mismatch” leads to impaired impulse generation and exit (N. Li, et al., 2017; Swaminathan, et al., 2011: 3277–3288; Wu & Anderson, 2014: 48).

Comorbid conditions such as diabetes and heart failure accelerate this process. In diabetic hyperglycemia, increased mitochondrial ROS production contributes to ox-CaMKII accumulation. Angiotensin II, through NADPH oxidase activation, raises atrial oxidative stress and triggers the apoptotic process in SA node cells (Swaminathan, et al., 2011: 3277–3288; Wu & Anderson, 2014: 48). These findings reveal that conduction system diseases associated with aging are not merely a passive degeneration process, but are also driven by active molecular mechanisms.

Clinically, these age-related changes collectively justify the need for pacemaker therapy. Symptomatic bradyarrhythmias resulting from degeneration of the SA node or AV conduction system currently constitute the most frequent indications for permanent pacemaker implantation. In this context, a detailed understanding of

conduction system anatomy and physiology provides clinicians with the necessary foundation to correctly plan pacemaker indications, mode selection, and lead positioning.

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FROM GALVANI TO LEADLESS DEVICES: A HISTORICAL PERSPECTIVE ON CARDIAC PACING-I

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Introduction

Studies on the electrical stimulation of the heart represent one of the most striking examples of how modern medicine has tilted the balance in favor of human life. Conditions such as bradyarrhythmias, advanced atrioventricular blocks, and sinus node dysfunction were, prior to the development of permanent pacemaker technology, associated with high mortality rates and constituted clinical domains in which physicians were often left helpless. Today, more than one million patients worldwide receive a permanent pacemaker each year; these devices not only save lives but also substantially improve quality of life.

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The attainment of this current state in cardiac pacing is the product of more than two centuries of cumulative scientific advancement. The phenomenon of "animal electricity," demonstrated by Luigi Galvani on frog muscle in 1791, established the electrical excitability of living tissue and thereby laid the cornerstone not only of physiology but also of the discipline of cardiac pacing that was to emerge in subsequent eras. The journey constructed upon this foundation reached a new milestone with each passing decade: the characterization of Adams-Stokes syndrome in the 19th century, Hyman's introduction of the concept of the "artificial pacemaker" in the early 20th century, Zoll's translation of transcutaneous pacing into clinical practice, and finally, in 1958, the implantation of the world's first implantable device in Arne Larsson by Senning and Elmqvist.

In the ensuing period, Furman's transvenous approach radically reduced surgical morbidity, while Greatbatch's lithium-iodine battery technology extended device longevity beyond ten years, thereby transforming the pacemaker from a temporary expedient into a long-term therapeutic instrument. The transition from single-chamber asynchronous models to the dual-chamber, physiological DDD mode, followed by the emergence of Cardiac Resynchronization Therapy (CRT) for patients with heart failure, and the introduction of ICDs into clinical use under the pioneering leadership of Mirowski, transformed cardiac pacing from a technology that merely "accelerated the slow heart" into a multilayered therapeutic platform capable of preventing sudden cardiac death, correcting mechanical dyssynchrony, and emulating the natural conduction system.

The aim of this chapter is to present, within a coherent chronological framework, the two-century-long progression extending from Galvani to the leadless devices and conduction system pacing (CSP) of the present day, through the lens of landmark

scientific discoveries, pioneering physicians, and pivotal technological innovations. A thorough grasp of this historical background will enable us to understand why and how each of the technologies we apply in routine practice today was developed; at the same time, it will provide a solid perspective from which to evaluate the next-generation device designs and physiological pacing strategies that await us in the near future.

From Galvani to the 20th Century: The Discovery of the Relationship Between Electricity and the Heart

The foundations of cardiac electrophysiology and clinical pacing technologies date back to the late 18th century, when the electrical nature of living tissue was first elucidated. The initial spark of this long-standing scientific endeavor was ignited in 1791, when the Italian scientist Luigi Galvani introduced his theory of "animal electricity." Through his observations on frog muscles, Galvani demonstrated that electricity was an intrinsic component of organic tissues and that external electrical stimuli could elicit mechanical contractions. During this period, the effects of electricity on the heart also began to be investigated; indeed, as early as 1775, the Danish physician Peter Christian Abildgaard succeeded in arresting the heart of a chicken with an electrical shock delivered across the chest and subsequently restoring its rhythm with a second shock—representing a primitive form of defibrillation (Aquilina, 2006: 17–81).

The 19th Century: Characterization of Physiological Mechanisms and Clinical Syndromes

In the early 19th century (circa 1800–1804), Giovanni Aldini, the nephew of Galvani, extended his uncle's work by attempting to alleviate cardiac syncope using "galvanic energy" and conducted experiments inducing muscular contractions on the bodies of executed criminals. During the same period, Marie François Xavier

Bichat and Nysten reported their ability to restore cardiac contractions in individuals executed by guillotine through the application of electrical current (Aquilina, 2006: 17–81).

In the clinical domain, the relationship between heart rate and bodily functions began to be defined with greater precision. The association between bradycardia and syncope, first proposed by Geronimo Mercuriale in the 1580s, was subsequently incorporated into the medical literature in the 19th century by Robert Adams and William Stokes as the "Adams-Stokes Syndrome" (Aquilina, 2006: 17–81; Ballantyne, Chew, & Vandenberg, 2023). The characterization of this syndrome prompted clinicians to seek methods of artificially augmenting the diminished heart rate.

By the late 19th century, the concept of directly accessing and modulating the heart had become an experimental reality. In 1882, Hugo von Ziemssen conducted his investigations on a patient named Catharina Serafin, whose heart lay beneath only a thin layer of skin due to a tumor in the chest wall; he demonstrated that the patient's heart rate could be modulated at will through the application of electrical current (Aquilina, 2006: 17–81; Suarez & Banchs, 2019: 3652–3661). During this same period, the British physician John MacWilliam analyzed the data accumulated up to that point and articulated the fundamental concepts of modern cardiac pacemakers and the theory of rhythmic stimulation.

The Diagnostic Revolution: The Birth of Electrocardiography (ECG)

The capacity to measure the heart's intrinsic electrical signals was of critical importance for the advancement of electrical stimulation technologies. In 1887, Augustus Desiré Waller succeeded in obtaining the first electrical recordings from the surface of the human body. However, the figure who truly transformed this field was Willem Einthoven, who produced the first ECG recordings

in 1892 and subsequently developed the "string galvanometer." Einthoven established the modern terminology still in use today by designating the electrical activities of the heart with the letters P, Q, R, S, and T, and was awarded the Nobel Prize in Physiology or Medicine in 1924 for these contributions (Aquilina, 2006: 17–81).

The First External Cardiac Pacemakers: Lidwell, Hyman, and Zoll

The first half of the 20th century represented a transitional period in which theoretical knowledge was translated into functional devices. In 1928, the Australian physician Mark Lidwell resuscitated an infant in cardiac arrest by employing a needle inserted into the ventricle in conjunction with alternating current (Aquilina, 2006: 17–81). The transition of cardiac pacing technology from the laboratory to clinical practice was subsequently achieved through the pioneering work of Albert Hyman and Paul Zoll in the mid-20th century (Furman, 2002: 2–3).

Albert S. Hyman and the "Artificial Pacemaker" (1930s)

The first clinically applicable artificial pacemaker design was developed in 1932 by the American physiologist Albert S. Hyman. Hyman designed a device that converted mechanical energy into electrical energy, specifically intended to restart hearts in standstill (Furman, 2002: 2–3).

Mechanism of Operation: The device was a generator producing direct current (DC) by means of a hand-cranked mechanism and a spring-driven motor assembly (Ballantyne, Chew, & Vandenberk, 2023).

Electrode Configuration: Electrical stimuli were delivered to the heart via a bipolar needle electrode inserted directly into the right atrium through the chest wall (Furman, 2002: 2–3).

Clinical Reception: Hyman coined the term "artificial pacemaker" for this device, a designation that remains in use to this day. However, the device was deemed unethical by the medical community of the era, who viewed it as an "intervention against natural death," and consequently it was subjected to intense criticism (Furman, 2002: 2–3).

Paul Zoll and Transcutaneous Pacing (1950s)

In the early 1950s, the Boston cardiologist Paul Zoll is recognized as the figure who inaugurated the modern era of clinical cardiac pacing (Aquilina, 2006: 17–81). In contrast to Hyman's transthoracic needle approach, Zoll developed a system capable of delivering stimulation through the closed chest without penetrating the chest wall.

Technological Configuration: The device developed by Zoll was a benchtop generator powered by mains electricity and capable of producing voltages of up to 150 volts (van Hemel & van der Wall, 2008: S3–4).

Method of Application: The system employed metal disc electrodes approximately one inch in diameter, placed on the right and left sides of the chest and coupled to the skin via conductive gel (van Hemel & van der Wall, 2008: S3–4).

Limitations: The high voltages required to stimulate an adult heart through the thoracic cage produced severe, painful contractions of the skeletal muscles and significant cutaneous burns. Consequently, patients had to be maintained under continuous sedation (Furman, 2002: 2–3).

Portability: The device was considerably heavy and cumbersome; it was transported on a wheeled cart and could be moved only as far as the reach of its power cable would permit (Aquilina, 2006: 17–81).

The First Implantable Pacemakers: The Contributions of Senning, Elmqvist, and Furman

The late 1950s are regarded as the "Golden Years" of cardiac pacing technology, marking the transition from external, cumbersome devices to modern systems that could be implanted within the body. Among the most prominent figures of this revolution were the Swedish investigators Ake Senning and Rune Elmqvist, together with the American Seymour Furman.

Ake Senning and Rune Elmqvist: The World's First Implantable Pacemaker

The world's first fully implantable pacemaker procedure was performed on October 8, 1958, at the Karolinska Hospital in Sweden. Developed through the collaboration of the surgeon Ake Senning and the engineer Rune Elmqvist, this system was implanted in Arne Larsson, a 43-year-old engineer whose condition was deemed hopeless and who was experiencing 20 to 30 Adams-Stokes attacks per day (Aquilina, 2006: 17–81; Larsson, et al., 2003: 114–124; Lemke, 2024: 18–54).

The development and implementation of this historic device incorporated the following notable features:

Design and Fabrication: In shaping the initial prototypes of the device, Rune Elmqvist employed shoe polish tins of the then-popular "Kiwi" brand as casting molds. The circuit components were encapsulated in epoxy resin to enhance biocompatibility (Larsson, et al., 2003: 114–124).

Power Supply: The device incorporated a blocking oscillator constructed from silicon transistors (newly imported at the time) and was powered by rechargeable nickel-cadmium batteries. The batteries could be recharged transcutaneously through inductive

coupling by means of an external coil applied to the patient's abdomen (Larsson, et al., 2003: 114–124).

Clinical Outcomes: Although the first device implanted functioned for only a few hours, a second device implanted the following morning provided pacing for approximately six weeks. Arne Larsson underwent more than 20 pacemaker replacements over the course of his lifetime and ultimately died in 2001 at the age of 86, thereby providing the most compelling testimony to the success of this technology (Jeffrey & Parsonnet, 1998: 1978–1991).

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FROM GALVANI TO LEADLESS DEVICES: A HISTORICAL PERSPECTIVE ON CARDIAC PACING-II

ATAÇ ÇELİK¹

Introduction

The history of cardiac pacing constitutes one of the most compelling narratives in modern medicine, representing a field in which fundamental discoveries in electrophysiology, advances in materials science and engineering, and the imperatives of clinical practice have converged to transform a once-fatal disturbance of cardiac rhythm into a manageable chronic condition. From Luigi Galvani's eighteenth-century observations of "animal electricity" to the implantable devices that today sustain the lives of millions of patients worldwide, this trajectory has been defined by a succession of conceptual and technological breakthroughs (Aquilina, 2006: 17–81; Furman, 2002: 2–3).

The first part of this account traced the conceptual and experimental origins of cardiac electrotherapy, from the earliest investigations of bioelectricity through the emergence of the first

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external and implantable pulse generators of the late 1950s. The present chapter takes up the narrative at the threshold of the modern era, examining the series of innovations that progressively rendered cardiac pacing safer, more durable, and increasingly physiological. Taken together, these developments are unified by a single guiding principle: the continual pursuit of devices that are smaller, more reliable, and more faithful to the heart's own electrical physiology.

Accordingly, this chapter follows several intertwined lines of development. It begins with Seymour Furman's introduction of the transvenous approach, which spared patients the trauma of thoracotomy and established the foundation of contemporary implantation technique (Lopez, 2008: 54–57; Toon & Roberts, 2023: 735–746). It then considers the advent of lithium-iodine battery technology, which transformed the pacemaker from a short-lived expedient into an instrument of long-term therapy (van Hemel & van der Wall, 2008: S3–4). The discussion proceeds to the evolution of pacing modes—from asynchronous (VOO) stimulation, through demand (VVI) pacing, to the fully physiological dual-chamber (DDD) systems (Jeffrey & Parsonnet, 1998: 1978–1991; Casavant & Belk, 2021: 4625–4632)—and to the development of the implantable cardioverter-defibrillator, realized through the perseverance of Michel Mirowski against considerable institutional resistance (Ammannaya, 2020: e163–e170). It concludes with cardiac resynchronization therapy and the more recent advent of conduction system pacing, which together represent the contemporary effort to restore not merely the rate but the natural sequence of cardiac activation (Sahu, Acharya, & Totade, 2023: e46389; Cohen & Thurber, 2022: 476–483).

Seymour Furman: The Transvenous (Endocardial) Pacing Revolution

In the early years of cardiac pacing, the principal challenge was the necessity of suturing electrodes onto the external surface of the heart (the epicardial approach) through surgical opening of the thoracic cage (thoracotomy). In 1958, the American physician Seymour Furman initiated a major transformation in the surgical paradigm by introducing the transvenous approach (Lopez, 2008: 54–57; Toon & Roberts, 2023: 735–746; Trohman, 2025).

Furman's contributions were of critical importance in the following respects:

Methodology: Furman succeeded in pacing the heart from within by advancing a catheter electrode through the internal jugular vein in the neck into the right ventricle (the endocardium) (Suarez & Banchs, 2019: 3652–3661; Trohman, 2025).

Advantages: This approach obviated the need for patients to undergo the trauma of open surgery and dramatically reduced operative morbidity (Lopez, 2008: 54–57; Toon & Roberts, 2023: 735–746).

Furman's temporary application in 1958 and his publication in 1959 inaugurated the era of transvenous electrodes. From the mid-1960s onward, this approach supplanted epicardial pacing and became the standard for contemporary pacing practice (Aquilina, 2006: 17–81).

The Revolution Brought About by Lithium-Iodine Battery Technology

Lithium-iodine battery technology is regarded as a true revolution in the history of implantable cardiac pacemakers, transforming these devices from short-term temporary solutions into

instruments of long-term chronic therapy (van Hemel & van der Wall, 2008: S3–4).

In the pre-lithium era, the zinc-mercuric oxide (Ruben-Mallory) batteries employed during the first decade of implantable pacemakers had a relatively short service life, averaging 1.5 to 2 years. The principal technical limitation of these batteries was the liberation of hydrogen gas during the chemical reaction. To allow for the venting of this gas, the device casings had to be coated with semi-permeable materials; this configuration left the devices vulnerable to exposure to bodily fluids, resulting in corrosion and short circuits (Jeffrey & Parsonnet, 1998: 1978–1991; Larsson, et al., 2003: 114–124; Lemke, 2024: 18–54).

Wilson Greatbatch and the Lithium Revolution

In the early 1970s (1970 according to some sources, 1973 according to others), Wilson Greatbatch optimized the lithium-iodine battery design for medical implants and brought it into serial production (DeForge, 2019: 40–50).

The fundamental innovations introduced by this technology are as follows:

High Energy Density and Extended Longevity: This advancement extended the operational lifespan of pacemakers beyond 10 years on a single cell, thereby significantly reducing the risk that patients would require repeated surgical procedures due to battery depletion (van Hemel & van der Wall, 2008: S3–4).

Hermetic (Airtight) Design: As no gas was liberated during the reaction, the batteries and the entire generator circuitry could be fully sealed within titanium casings by means of welding. This achievement completely isolated the device from bodily fluids and thereby prevented corrosion (van Hemel & van der Wall, 2008: S3–4).

Miniaturization: The higher energy density permitted a substantial reduction in device dimensions.

Predictable Discharge Curve: The linear increase in the internal resistance of the battery over time prevents an abrupt drop in voltage. This characteristic enables clinicians to predict the time of battery depletion (ERI-Elective Replacement Indicator) with accuracy, months in advance.

Lithium-iodine battery technology continues to serve as the principal power source for modern pacemakers and certain advanced ICD systems, and remains in use in millions of patients worldwide.

From Single Chamber to Dual Chamber: The Evolution of Pacing Technology from VVI to DDD

Pacing modes are designated by means of the international NASPE/BPEG generic code, employing three to five letters: the first letter denotes the chamber paced (A: atrium, V: ventricle, D: dual), the second letter the chamber sensed, and the third letter the response to sensing (I: Inhibited, T: Triggered, D: Dual). Within this framework, VOO refers to asynchronous ventricular pacing at a fixed rate; VVI denotes a mode that senses the ventricle and paces only when required; and DDD defines a fully physiological mode capable of both sensing and pacing the atrium and ventricle.

The early years of pacemaker technology began with asynchronous (VOO) devices that focused solely on life preservation rather than emulating the heart's natural rhythm. These devices were unable to detect the intrinsic electrical activity of the heart and delivered impulses at a continuous fixed rate; consequently, an artificial stimulus could coincide with the vulnerable T wave of the cardiac cycle, thereby triggering lethal arrhythmias (the R-on-T phenomenon) (Jeffrey & Parsonnet, 1998: 1978–1991).

In the mid-1960s, the concept of "demand" pacing (developed through the contributions of Barouh Berkovits) gave rise to the VVI mode. In the VVI mode, the device not only paces the ventricle but also senses the intrinsic ventricular signals; if the heart contracts on its own within the predetermined interval, the device withholds stimulation. Although this advancement enhanced safety, it disregarded the mechanical synchronization between the atria and the ventricles altogether. This shortcoming gave rise to the clinical entity known as "Pacemaker Syndrome," characterized by the loss of the atrial contribution to ventricular filling and manifesting in symptoms such as fatigue and dizziness (Casavant & Belk, 2021: 4625–4632; Lak & Goyal, 2026).

Physiological Pacing and the Transition to DDD

From the 1950s onward, animal studies had demonstrated that dual-chamber pacing offered superior hemodynamic advantages by preserving the atrial contribution. The clinical evolution in this field proceeded through the following stages:

VAT Mode (1963): Introduced by Cordis, this mode sensed the right atrium and triggered ventricular pacing accordingly.

DVI Mode: The first bifocal systems emerged, capable of pacing both the atrium and the ventricle but unable to track the atrial rate.

DDD Mode (1980s): Following Funke's introduction of the "Universal DDD" concept in 1977, Cordis launched the first true DDD pacemaker in the United States in 1982 (Greenspon, et al., 2012: 1540–1545).

By virtue of its capacity to both sense and pace the atrium and the ventricle, the DDD mode emulates the natural sequence of electrical activation of the heart. Large-scale clinical trials (such as MOST and DAVID) have demonstrated that DDD pacing improves

quality of life and significantly reduces the risk of atrial fibrillation and stroke (Ballantyne, Chew, & Vandenberg, 2023; Casavant & Belk, 2021: 4625–4632).

The principal technological elements that enabled this evolution were the extended longevity afforded by lithium-iodine battery technology, advances in circuit logic, and the development of "J curve" tipped leads that facilitated electrode placement in the atrium. At present, more than 80% of implants performed in the United States are in DDD mode. Furthermore, advanced algorithms such as MVP (Managed Ventricular Pacing) which promote intrinsic conduction by minimizing unnecessary ventricular pacing have become standard features in contemporary devices (Casavant & Belk, 2021: 4625–4632).

The Development of the Implantable Cardioverter-Defibrillator (ICD) and Michel Mirowski

The ICD technology, which revolutionized the management of ventricular fibrillation (the most common mechanism underlying sudden cardiac death) was shaped largely by the vision and persistent efforts of Dr. Michel Mirowski, a Polish-born Holocaust survivor.

Mirowski's motivation to develop this device originated in 1966, when his mentor in Israel, Professor Harry Heller, died suddenly following an episode of ventricular tachycardia. Mirowski envisioned a "sentinel" device capable of continuously monitoring the patient and terminating lethal arrhythmias within seconds. However, in the late 1960s, external defibrillators were colossal machines weighing approximately 120 kg, and the medical community did not believe that such a system could be implanted within the body. Leading cardiologists of the era, such as Bernard Lown, characterized the idea as "impossible" and "unethical," and Mirowski's project proposals were rejected by the NIH (National Institutes of Health) (Ammannaya, 2020: e163–e170).

Notwithstanding all this opposition, Mirowski continued his work alongside Morton Mower at Sinai Hospital in Baltimore. In 1975, the first prototype small enough to be implanted in a dog was successfully tested, and the film recordings demonstrating the device's ability to terminate fibrillation generated considerable resonance within the scientific community (Coats, Politte, & Flaker, 2010: 48–52).

The first successful implantation in a human being was performed on February 4, 1980, at Johns Hopkins Hospital. Implanted by the surgeon Levi Watkins, these initial devices were approximately the size of a deck of playing cards and weighed between 250 and 280 grams; their placement required a thoracotomy (open-chest surgery) to suture large epicardial patch electrodes onto the external surface of the heart, while the generator was positioned in the abdominal region (Ammannaya, 2020: e163–e170).

Technological Evolution and the Modern Era

ICD technology has undergone substantial transformations from the 1980s to the present day:

The Transvenous Revolution: With the development of transvenous leads in the late 1980s, which eliminated the requirement for thoracotomy, the procedure was transformed into a straightforward intervention performed under local anesthesia.

Biphasic Waveform: The adoption of biphasic waveforms in the 1990s (which achieved higher success rates at lower energy levels than their monophasic predecessors) enabled a marked reduction in the size of devices and batteries (currently approximately 30 mL).

Tiered Therapy: With the advent of third-generation devices, Antitachycardia Pacing (ATP) features were incorporated,

enabling the painless termination of ventricular tachycardia rather than the direct delivery of a shock to the patient.

S-ICD and Future Directions: At present, ongoing efforts are directed toward the integration of subcutaneous ICDs (S-ICDs)—which entirely obviate the corrosion and infection risks associated with intravascular leads—and leadless systems implanted directly within the heart (Ammannaya, 2020: e163–e170).

Biventricular Pacing and the Emergence of Cardiac Resynchronization Therapy (CRT)

For decades, permanent cardiac pacing technology employed the right ventricular apex (RVA) as the principal pacing site, owing to the technical ease of electrode placement and its mechanical stability (Casavant & Belk, 2021: 4625–4632). However, accumulating clinical evidence over time has demonstrated that single-site pacing of the right ventricle induces an artificial electrical delay and dyssynchrony on the left ventricle, analogous to left bundle branch block (LBBB). This condition disrupts the coordinated contraction between the septum and the left ventricular free wall, reduces the left ventricular ejection fraction (LVEF), and gives rise to the clinical entity known as "pacing-induced cardiomyopathy" (Ballantyne, Chew, & Vandenberg, 2023).

Technological Foundations of CRT and the First Clinical Applications

To address this mechanical insufficiency, systems were developed capable of simultaneously pacing the lateral or posterolateral wall of the left ventricle—the latest activated region of the heart. In 1994, Serge Cazeau and colleagues laid the clinical foundations of Cardiac Resynchronization Therapy (CRT) by performing, for the first time, four-chamber pacing (biatrial and

biventricular) in a patient with advanced heart failure and a prolonged QRS duration (Sahu, Acharya, & Totade, 2023: e46389).

The operating principles of the CRT system are as follows:

Electrode Configuration: In addition to the conventional right atrial and right ventricular electrodes, a third specialized electrode is employed, advanced through the coronary sinus (CS) and positioned along the left ventricular free wall.

Mechanical Synchronization: By means of this third electrode, both ventricles are paced almost simultaneously (BiVP-Biventricular Pacing), thereby restoring the coordinated contraction of the myocardium and mechanical synchrony (Sahu, Acharya, & Totade, 2023: e46389).

Clinical Evidence and Evolution

Large-scale clinical trials such as MIRACLE, COMPANION, CARE-HF, MADIT-CRT, and RAFT have demonstrated that CRT is highly effective in alleviating heart failure symptoms, reducing left ventricular dimensions (reverse remodeling), and significantly lowering mortality rates. At present, biventricular pacing has become a standard therapeutic modality, particularly for patients with an LVEF below 35% and evidence of electrical dyssynchrony (prolonged QRS) (Abraham, et al., 2002: 1845–1853; Bristow, et al., 2004: 2140–2150; Cleland, et al., 2005: 1539–1549).

Future Perspective: Physiological Pacing

Although CRT has offered hope to millions of patients, it is well established that approximately one-third of patients fail to respond to therapy (non-responders) due to unfavorable coronary sinus anatomy or myocardial scarring. To overcome these limitations, the concept of Conduction System Pacing (CSP) which directly stimulates the heart's intrinsic conduction system has

emerged in recent years. Techniques such as His bundle pacing (HBP) and left bundle branch area pacing (LBBAP) are increasingly establishing themselves in clinical practice as compelling alternatives to conventional CRT, offering the potential to entirely eliminate mechanical dyssynchrony and to achieve a more physiological pattern of contraction (Cohen & Thurber, 2022: 476–483).

Conclusion

This two-century journey, extending from Galvani's observations on frog muscle in 1791 to the leadless and subcutaneous devices of the present day, represents one of the rare fields in which basic science, engineering, and clinical medicine have become inextricably intertwined. The progression from single-chamber asynchronous pacing to the fully physiological DDD mode, from epicardial placement to transvenous and ultimately to leadless systems, and from zinc-mercuric to lithium-iodine battery technology, has at every stage rendered devices smaller, safer, and more physiological. Today, conduction system pacing modalities such as His bundle and left bundle branch area pacing, together with leadless pacemaker and subcutaneous ICD technologies, are heralding a new era in the electrical management of the heart.

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PACEMAKER, ICD, CRT AND HIS-BUNDLE PACING INDICATIONS

MUSTAFA YILMAZ¹

Introduction

Sinus node dysfunction (SND) describes impairment in impulse formation by the sinoatrial node or in the conduction of generated impulses to the atria. Clinically, it may present as persistent or intermittent sinus bradycardia, sinus pause, sinus arrest, sinoatrial exit block, chronotropic incompetence, and tachycardia-bradycardia syndrome. It is primarily associated with degenerative fibrosis of the sinus node with advancing age; however, it may also develop due to drugs, metabolic disorders, autonomic dysfunction, myocardial ischemia, inflammatory diseases, and previous cardiac surgery. In patients with sinus node dysfunction, secondary causes of bradycardia should first be evaluated, and if a correctable secondary cause is present, the underlying cause should be treated (Kusumoto, et al., 2019: 932–987).

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Sinus Node Dysfunction

Permanent pacemaker implantation should be considered in patients in whom no secondary cause can be identified and whose symptoms are considered to be definitely related to bradycardia. The ACC/AHA/HRS guideline states that there is no established minimum heart rate or pause duration for permanent pacing in sinus node dysfunction; therefore, establishing a temporal correlation between symptoms and bradycardia is important when deciding whether permanent pacing is required (Kusumoto, et al., 2019: 932–987). The ESC guideline states that, in selected patients evaluated for syncope, permanent pacing may be considered in the presence of asymptomatic pauses of >6 seconds documented by an implantable loop recorder and associated with sinus arrest (Glikson, et al., 2021: 3427–3520). However, this approach should not be interpreted as a general indication threshold for incidentally detected isolated sinus pauses in completely asymptomatic individuals. The decision for permanent pacemaker implantation should only be made in cases where the relationship between symptoms and bradycardia has been clearly demonstrated (Glikson, et al., 2021: 3427–3520; Kusumoto, et al., 2019: 932–987).

Indication for Permanent Pacemaker Implantation in Sinus Node Dysfunction

In sinus node dysfunction, the main purpose of permanent pacemaker therapy is not to improve survival, but to reduce symptoms related to bradycardia and improve quality of life. Therefore, the presence of symptoms is central to the indication for permanent pacemaker implantation. Symptoms such as syncope, presyncope, dizziness, reduced exercise capacity, fatigue, confusion, worsening signs of heart failure, or exercise intolerance due to chronotropic incompetence are strong indications for permanent pacemaker implantation. In contrast, asymptomatic sinus

bradycardia, particularly physiological or sleep-related bradycardia, is not an indication for permanent pacemaker implantation (Fleischmann, et al., 2006: 653–659; Semelka, Gera, & Usman, 2013: 691–696).

Drug-induced suppression of the sinus node is a common condition. Beta-blockers, nondihydropyridine calcium channel blockers, digoxin, and other treatments that may cause bradycardia can unmask or worsen sinus node dysfunction. If drug-induced SND is suspected, the treatment should be discontinued or replaced with an alternative therapy. However, if drug therapy is essential and causes symptomatic bradycardia, permanent pacemaker implantation may be an appropriate option. In patients with tachycardia-bradycardia syndrome, permanent pacemaker implantation may be considered to prevent symptoms occurring during the bradycardic phase and to allow antiarrhythmic therapy to be administered safely (Lamas, et al., 2002: 1854–1862; Semelka, Gera, & Usman, 2013: 691–696).

Device Selection and Pacing Strategy

In sinus node dysfunction, an atrial-based pacing strategy is physiologically important. In patients with preserved atrioventricular conduction, atrial pacing provides more physiological activation than ventricular pacing. Depending on patient characteristics, AAI/AAIR or DDD/DDDR systems may be preferred; however, in patients with a risk of developing AV conduction disturbance or with concomitant conduction system disease, DDD/DDDR systems should be preferred. In patients with chronotropic incompetence, rate-responsive pacing modes may improve exercise capacity (Kuroda, et al., 2025: 133022; Nielsen, et al., 2011: 686–696). However, unnecessary right ventricular pacing should be avoided. Long-term and high-burden right ventricular pacing may increase the risk of ventricular dyssynchrony and

pacing-induced cardiomyopathy. Therefore, in patients who receive a DDD pacemaker for sinus node dysfunction, appropriate pacemaker programming should be performed to minimize unnecessary ventricular pacing (Sweeney, et al., 2007: 1000–1008).

Device Selection: Conventional Pacing, His-Bundle Pacing, and Left Bundle Branch Pacing

His-bundle pacing and left bundle branch pacing are physiological pacing approaches that aim to achieve more synchronous ventricular contraction through the native conduction system. Sinus node dysfunction alone is not a direct indication for His-bundle pacing or left bundle branch pacing. However, if the patient has significant AV conduction disease or is expected to require a high ventricular pacing burden, the pacing strategy may be modified. The 2023 HRS/APHRS/LAHR guideline states that in patients who require permanent pacing and are expected to have a substantial ventricular pacing burden, cardiac physiological pacing approaches may be preferred to reduce the risk of pacing-induced cardiomyopathy (Chung, et al., 2023: e17–e91).

In isolated sinus node dysfunction, the main device therapy is permanent pacemaker implantation; SND alone does not constitute an indication for ICD or CRT. ICD should be considered only in the presence of additional indications such as a history of cardiac arrest, sustained ventricular tachycardia, significant left ventricular systolic dysfunction, or an increased risk of sudden cardiac death related to cardiomyopathy (Zeppenfeld, et al., 2022: 3997–4126). CRT should be considered in additional clinical conditions requiring resynchronization therapy, such as left ventricular systolic dysfunction, prolonged QRS duration, particularly left bundle branch block morphology, symptomatic heart failure, or a high expected need for ventricular pacing (Chung, et al., 2023: e17–e91; Heidenreich, et al., 2022: e895–e1032). In summary,

device selection in SND should be individualized not only according to the presence of bradycardia, but also according to its relationship with symptoms, the presence of AV conduction disturbance, the expected ventricular pacing burden, and left ventricular function.

Atrioventricular Blocks

Atrioventricular blocks are characterized by delay, partial interruption, or complete loss of conduction of the atrial impulse to the ventricles. In clinical evaluation, the degree of block, anatomical level, presence of symptoms, reliability of the escape rhythm, and concomitant structural heart disease should be considered together. Syncope, presyncope, dizziness, reduced exercise capacity, and signs of heart failure may be associated with AV block. Demonstrating the relationship between symptoms and AV block is important when deciding on permanent pacing.

In first-degree AV block, all atrial impulses are conducted to the ventricles, but the PR interval is prolonged. This reflects AV conduction delay rather than a true interruption of conduction. In second-degree AV block, some P waves fail to conduct to the ventricles. In Mobitz type I block, the PR interval progressively prolongs and is then followed by a non-conducted P wave. This pattern is usually at the AV nodal level and is considered more benign in asymptomatic patients with a narrow QRS complex. In Mobitz type II block, the PR interval is usually constant, and intermittent conduction failure is observed. This condition often suggests infranodal conduction system disease and is considered more serious because of the risk of progression to complete AV block. In third-degree AV block, atrial and ventricular activity are independent of each other (Ahmed, Goyal, & Chhabra, 2026).

Before deciding on permanent pacemaker implantation, reversible causes must be investigated. Beta-blockers, nondihydropyridine calcium channel blockers, digoxin, and

antiarrhythmic drugs may suppress AV conduction. Electrolyte abnormalities, hypothyroidism, acute ischemia, myocarditis, and infectious causes should be included in the differential diagnosis. Lyme disease, sarcoidosis, amyloidosis, and other infiltrative diseases should be considered in selected cases. Transient or permanent AV block may also develop after cardiac surgery or transcatheter aortic valve implantation.

Indication for Permanent Pacemaker Implantation in AV Blocks

The indication for permanent pacemaker implantation in AV blocks is determined according to the type of block and the presence of reversible causes. First-degree AV block does not constitute an indication for permanent pacemaker implantation in most patients. In asymptomatic cases, follow-up is generally sufficient. However, if atrioventricular synchrony is impaired due to marked PR prolongation, symptoms such as exercise intolerance, hypotension, presyncope, or symptoms resembling pacemaker syndrome may develop. In this situation, permanent pacemaker implantation may be considered in selected patients.

In Mobitz type I AV block, the approach is generally conservative. In asymptomatic patients with a narrow QRS complex and findings suggesting nodal block, follow-up and review of possible drug effects are often sufficient. If symptoms are shown to be related to AV block, or if infranodal block is suspected, permanent pacemaker implantation becomes a consideration. In contrast, Mobitz type II AV block is considered more serious because it suggests His-Purkinje system disease and carries a risk of progression to complete AV block. In acquired Mobitz type II AV block without an identifiable reversible or physiological cause, permanent pacemaker implantation is recommended regardless of symptoms (Kusumoto, et al., 2019: 932–987).

In high-grade AV block and third-degree AV block, ventricular activity may become dependent on an escape rhythm. When the escape rhythm is slow, irregular, or unreliable, the risk of syncope, sudden asystole, and hemodynamic deterioration increases. Therefore, if there is no reversible or physiological cause, acquired high-grade AV block and third-degree AV block are indications for permanent pacemaker implantation (Kusumoto, et al., 2019: 932–987). If transient causes such as acute myocardial infarction, drug toxicity, or metabolic abnormalities are present, these conditions should be treated first. If the block becomes permanent or recovery is not expected, permanent pacing should be planned.

Device Selection: Conventional Pacing, His-Bundle Pacing, and Left Bundle Branch Pacing

Device selection should be based on the patient's rhythm, the need for AV synchrony, and the expected ventricular pacing burden. In patients with preserved sinus rhythm, DDD pacemaker systems that maintain atrioventricular synchrony may be preferred. In patients with atrial fibrillation, ventricular pacing strategies may be sufficient.

Since a high ventricular pacing burden may lead to ventricular dyssynchrony and pacing-induced cardiomyopathy, cardiac physiological pacing should be considered in patients who are expected to require a high ventricular pacing burden (Chung, et al., 2023: e17–e91). AV blocks alone do not constitute an indication for CRT or ICD. CRT should be evaluated according to left ventricular ejection fraction, symptomatic heart failure, QRS duration, left bundle branch block morphology, and the expected pacing burden (Chung, et al., 2023: e17–e91; Heidenreich, et al., 2022: e895–e1032). ICD should be considered in the presence of indications independent of AV block, such as a history of cardiac arrest, sustained ventricular tachycardia, significant left ventricular

systolic dysfunction, or an increased risk of sudden cardiac death related to cardiomyopathy (Zeppenfeld, et al., 2022: 3997–4126).

Bifascicular and Trifascicular Blocks

Bifascicular block is generally defined as right bundle branch block accompanied by left anterior or left posterior fascicular block. The most common form is the combination of right bundle branch block and left anterior fascicular block. Right bundle branch block with left posterior fascicular block is less common. The term trifascicular block is used for conditions in which bifascicular block is accompanied by PR prolongation. However, PR prolongation does not always indicate disease in the third fascicle. It may also be due to conduction delay at the AV nodal level. Therefore, the coexistence of bifascicular block and first-degree AV block alone should not be interpreted as true trifascicular conduction system disease.

These findings alone do not indicate a need for permanent pacemaker implantation. However, they suggest diffuse conduction system disease and become clinically important particularly in the presence of syncope or presyncope.

Evaluation in Terms of Permanent Pacemaker, CRT, and ICD

In asymptomatic bifascicular block, permanent pacemaker implantation is generally not indicated. In these patients, clinical follow-up, electrocardiographic monitoring, and evaluation of underlying structural heart disease are usually sufficient. However, in the presence of syncope or presyncope, the possibility of paroxysmal high-grade AV block should be investigated. For this purpose, ambulatory rhythm monitoring, an implantable loop recorder, or electrophysiological study may provide diagnostic value in selected patients. Demonstration of marked His–ventricular conduction delay or intra-/infra-Hisian block during electrophysiological study supports the indication for permanent

pacemaker implantation (Glikson, et al., 2021: 3427–3520; Kusumoto, et al., 2019: 932–987).

Alternating bundle branch block is a high-risk finding suggestive of diffuse His–Purkinje system disease and is considered a strong indication for permanent pacemaker implantation. Similarly, permanent pacing is indicated if documented high-grade AV block or third-degree AV block develops in the setting of bifascicular or trifascicular conduction disturbance (Kusumoto, et al., 2019: 932–987). Device selection should be based on the patient’s rhythm, the need for AV synchrony, left ventricular function, and the expected ventricular pacing burden. CRT should be considered not merely because of the presence of bundle branch block, but in the presence of additional criteria such as left ventricular systolic dysfunction, symptomatic heart failure, prolonged QRS duration, and a high need for ventricular pacing (Chung, et al., 2023: e17–e91; Heidenreich, et al., 2022: e895–e1032). ICD should be evaluated in the presence of clinical conditions independent of bundle branch block that create a risk of ventricular arrhythmia or sudden cardiac death (Zeppenfeld, et al., 2022: 3997–4126).

Atrial Fibrillation and Bradycardia

Bradycardia in atrial fibrillation may occur in different clinical settings. Slow ventricular response in persistent atrial fibrillation may present as long RR intervals or high-grade AV block. In paroxysmal atrial fibrillation, long pauses may be observed after termination of the tachyarrhythmia. These conditions are generally evaluated within the context of tachycardia-bradycardia syndrome. Clinical decision-making should be based not only on the presence of bradycardia, but also on the symptoms caused by bradycardia. When bradycardia is detected, the patient should first be assessed for symptoms. Syncope, presyncope, dizziness, fatigue, reduced

exercise capacity, and worsening signs of heart failure may be related to bradycardia. However, asymptomatic AF with slow ventricular response or incidentally detected long RR intervals alone should not be considered an indication for permanent pacemaker implantation. Therefore, the relationship between the rhythm disturbance and symptoms should be demonstrated using methods such as ECG, Holter monitoring, or an implantable loop recorder.

Medications must be carefully evaluated during assessment. Beta-blockers, nondihydropyridine calcium channel blockers, digoxin, and some antiarrhythmic drugs may excessively slow the ventricular rate. These drugs should be discontinued or their dose should be reduced. However, if treatment required for rate control or rhythm control causes symptomatic bradycardia and no alternative therapy is possible, permanent pacemaker implantation may be considered in selected patients.

Indication for Permanent Pacemaker Implantation

The indication for permanent pacemaker implantation in atrial fibrillation is mainly based on the presence of symptomatic bradycardia or clinically significant pauses. In a patient with persistent atrial fibrillation, pacemaker implantation should be evaluated if slow ventricular response is associated with syncope, presyncope, marked exercise limitation, or worsening signs of heart failure. Similarly, if long pauses occurring after termination of paroxysmal atrial fibrillation cause symptoms, permanent pacing may be an appropriate treatment option.

In asymptomatic patients, the decision should be made more cautiously. Low ventricular rate or a long RR interval alone, particularly if detected during sleep or under the influence of medications, does not directly constitute an indication for pacemaker implantation. In these patients, correction of reversible causes and clinical follow-up are often a more appropriate approach.

Device Selection and Pacing Strategy

Device selection should be based on the baseline rhythm. In patients with persistent atrial fibrillation, ventricular pacing systems are generally sufficient because atrial pacing is not required. Rate-responsive ventricular pacing may provide an appropriate increase in heart rate during exertion and reduce symptoms. In patients with paroxysmal atrial fibrillation or in those who may return to sinus rhythm, DDD systems may be preferred to preserve atrioventricular synchrony.

Long-term right ventricular pacing may lead to ventricular dyssynchrony, particularly in patients with a high pacing burden. Therefore, cardiac physiological pacing strategies should be evaluated in patients with impaired left ventricular function or in those expected to have a high ventricular pacing burden (Joza, et al., 2024: 4887–4901).

Evaluation in Terms of AV Node Ablation, CRT, and ICD

In atrial fibrillation, if ventricular rate cannot be controlled with medications, symptoms persist, and rhythm control is not appropriate or has not been successful, AV node ablation combined with permanent pacing may be considered (Van Gelder, et al., 2024: 3314–3414). This approach makes the ventricular rate regular and controllable. However, after the procedure, the patient becomes largely pacemaker-dependent. Therefore, the device type should be carefully selected before the procedure.

In patients planned for AV node ablation or expected to have a high ventricular pacing burden, left ventricular function is a key determinant. In patients with left ventricular systolic dysfunction, symptomatic heart failure, or a risk of pacing-induced cardiomyopathy, CRT or physiological pacing strategies should be considered (Brignole, et al., 2021: 4731–4739; Joza, et al., 2024:

4887–4901). Bradycardia accompanying atrial fibrillation alone does not constitute an indication for ICD.

Ventricular Tachycardias

Ventricular tachycardias are wide-QRS tachyarrhythmias originating distal to the His bundle or from the ventricular myocardium. Their clinical significance is determined by the duration of the arrhythmia, its hemodynamic impact, the presence of underlying structural heart disease, and the risk of sudden cardiac death. Ventricular tachycardia is defined as at least three consecutive ventricular complexes, usually occurring at a rate of >100 beats/min. Sustained ventricular tachycardia is defined as ventricular tachycardia lasting longer than 30 seconds or requiring termination because of hemodynamic compromise even if it lasts less than 30 seconds. Non-sustained ventricular tachycardia refers to ventricular tachycardia consisting of at least three consecutive ventricular beats, lasting less than 30 seconds, and terminating spontaneously. This distinction is important in terms of device therapy, because not every episode of ventricular tachycardia constitutes an indication for ICD implantation (Zeppenfeld, et al., 2022: 3997–4126).

ICD Indication

ICD therapy is the main device-based treatment for ventricular tachycardias. The purpose of ICD therapy is to prevent sudden cardiac death due to ventricular tachycardia or ventricular fibrillation. In patients with a history of cardiac arrest, ventricular fibrillation, or hemodynamically significant sustained ventricular tachycardia not caused by a reversible cause, ICD should be evaluated for secondary prevention (Antiarrhythmics versus Implantable Defibrillators, 1997: 1576–1583; Zeppenfeld, et al., 2022: 3997–4126). When making this decision, acute ischemia, electrolyte abnormalities, drug toxicity, and transient metabolic causes should be excluded. Ventricular arrhythmias occurring in the

early phase of acute myocardial infarction should be interpreted differently. In particular, ventricular tachycardia or ventricular fibrillation occurring within the first 48 hours is often related to the acute ischemic event and is not considered a permanent ICD indication by itself. In contrast, sustained ventricular arrhythmias developing in the late phase after myocardial infarction, when no reversible cause is identified, are associated with a higher risk of sudden cardiac death.

There is no ICD indication for non-sustained ventricular tachycardia alone. However, ICD may be considered after risk stratification in the presence of underlying cardiomyopathy, low left ventricular ejection fraction, myocardial scar, unexplained syncope, or a high-risk genetic disease. Therefore, in patients with non-sustained ventricular tachycardia, the decision should be based on the patient's overall risk profile rather than merely on the presence of the arrhythmia episode.

Structural Heart Disease and Idiopathic Ventricular Tachycardia

Ventricular tachycardias are generally considered higher-risk in patients with structural heart disease. The risk of sudden cardiac death is increased in ventricular tachycardias occurring in the setting of ischemic scar, dilated cardiomyopathy, arrhythmogenic cardiomyopathy, sarcoidosis, or previous myocarditis. In these patients, the ICD decision should be made by considering left ventricular function, arrhythmia type, history of syncope, cardiac magnetic resonance findings, and disease-specific risk markers (Zeppenfeld, et al., 2022: 3997–4126).

The approach is different in idiopathic ventricular tachycardias without structural heart disease. Tachycardias originating from the right ventricular outflow tract or fascicular system often have a more benign course. In these patients, treatment

is usually based on symptom control, medical therapy, or catheter ablation. ICD is not routinely recommended in idiopathic ventricular tachycardias. However, ICD may be considered if there is cardiac arrest, ventricular fibrillation, hemodynamically intolerable tachycardia, or additional findings suggesting structural or genetic heart disease.

Catheter Ablation

Catheter ablation is an important treatment option in the management of ventricular tachycardia. Catheter ablation should be considered in the presence of recurrent monomorphic ventricular tachycardia, frequent ICD shocks, electrical storm, or arrhythmia persisting despite antiarrhythmic therapy. Ablation may reduce arrhythmia recurrence and ICD shocks. However, in high-risk patients with structural heart disease, ablation should generally be considered not as a replacement for ICD therapy, but as a strategy that complements ICD treatment (Cronin, et al., 2019: 323–484). In selected patients with hemodynamically stable, well-tolerated ventricular tachycardia and limited scar burden, the treatment approach should be more individualized. ICD, ablation, and medical therapy should be evaluated together by considering left ventricular function, arrhythmia mechanism, comorbidities, and the risk of sudden death.

Evaluation in Terms of Pacemaker, CRT, and CRT-D

Ventricular tachycardia alone does not constitute an indication for permanent pacemaker implantation or CRT. Pacemaker implantation is considered only in the presence of concomitant symptomatic bradycardia, sinus node dysfunction, atrioventricular block, or clinically significant bradycardia related to antiarrhythmic therapy. CRT is considered not according to the presence of ventricular tachycardia, but according to standard criteria such as left ventricular systolic dysfunction, symptomatic

heart failure, QRS duration/morphology, or pacing-induced dyssynchrony. ICD is central to device therapy in ventricular tachycardias. ICD implantation should be considered for secondary prevention. after sustained ventricular tachycardia or ventricular fibrillation not caused by a reversible cause; in primary prevention, it is evaluated according to factors such as ventricular function, type of cardiomyopathy, scar burden, genetic risk, and history of syncope (Bardy, et al., 2005: 225–237; Zeppenfeld, et al., 2022: 3997–4126).

Carotid Sinus Syndrome and Neurocardiogenic Syncope

Carotid sinus syndrome and neurocardiogenic syncope are clinical conditions evaluated under the heading of reflex syncope. The main mechanism is transient cerebral hypoperfusion mediated by the autonomic nervous system. This response may be cardioinhibitory, vasodepressor, or mixed. In the cardioinhibitory response, marked bradycardia or asystole is prominent, whereas hypotension predominates in the vasodepressor response. This distinction is clinically important because it determines the expected benefit from pacemaker therapy.

In carotid sinus syndrome, syncope develops due to stimulation of the carotid sinus. For diagnosis, reproduction of symptoms during carotid sinus massage and demonstration of an accompanying cardioinhibitory or vasodepressor response are important. Carotid sinus hypersensitivity may be detected asymptotically, particularly in elderly patients. Therefore, diagnosis should not be based only on the presence of a physiological response; the response should be associated with reproduction of the patient's spontaneous symptoms. Neurocardiogenic syncope most commonly presents as vasovagal syncope. It may be triggered by prolonged standing, a hot environment, pain, emotional stress, or seeing blood. Nausea, sweating, flushing, blurred vision, and fatigue are typical. In some patients, syncope may be sudden, recurrent, and

traumatic. This group should be evaluated more carefully in terms of device therapy (Brignole, et al., 2018: 1883–1948).

Indication for Permanent Pacemaker Implantation

Permanent pacemaker implantation is not appropriate for every patient with reflex syncope. The group most likely to benefit from treatment consists of patients in whom the cardioinhibitory response is predominant and marked asystole associated with syncope has been documented. In cases where the vasodepressor component is predominant, the effect of pacemaker therapy is limited, because pacing has no effect on reflex hypotension. In carotid sinus syndrome, permanent pacemaker implantation should be considered particularly in patients with recurrent, unpredictable syncope or syncope carrying a risk of trauma. From a diagnostic perspective, reproduction of the patient's spontaneous symptoms during carotid sinus massage and demonstration of a cardioinhibitory response are important. Asymptomatic carotid sinus hypersensitivity is not considered an indication for pacemaker implantation (Brignole, et al., 2018: 1883–1948).

In neurocardiogenic syncope, the indication for pacemaker implantation is much more limited. In young patients and in typical vasovagal syncope with a clear prodrome, education, avoidance of triggers, regulation of fluid and salt intake, and physical counter-pressure maneuvers are the preferred initial approaches. Permanent pacemaker implantation should generally be considered in selected patients over 40 years of age who have frequent, recurrent, unpredictable, or traumatic syncope and a spontaneous or provoked asystolic cardioinhibitory response. Demonstration of a prolonged pause or asystole during symptoms, particularly with an implantable loop recorder, is a strong finding supporting pacemaker implantation (Brignole, et al., 2012: 2566–2571). In reflex syncope, the decision for device therapy is not based solely on the presence of syncope.

Age, attack frequency, risk of trauma, presence of prodrome, predominance of the vasodepressor component, and documentation of bradycardia are decisive factors in the indication for pacemaker implantation.

Evaluation in Terms of Device Selection, CRT, and ICD

If pacemaker therapy is planned in reflex syncope, dual-chamber systems are generally preferred. The aim is to preserve atrioventricular synchrony and provide appropriate rate support when sudden bradycardia develops. In selected patients, special algorithms or closed-loop stimulation features aimed at detecting the sudden cardioinhibitory response earlier may be evaluated (Brignole, et al., 2021: 508–516). However, patients should be informed that pacemaker therapy may not completely eliminate syncope recurrence. Symptoms related to hypotension may persist, particularly in the presence of a prominent vasodepressor component. There is no indication for CRT or ICD in carotid sinus syndrome or neurocardiogenic syncope alone.

Congenital Heart Diseases

Device therapy in congenital heart diseases is more complex than in acquired heart diseases. Anatomical variations, previous surgeries, residual lesions, systemic ventricular morphology, and venous access characteristics directly affect the decision-making process. Therefore, the decision for pacemaker, ICD, or CRT should not be based only on the rhythm disorder. The patient's congenital anatomy, surgical history, ventricular function, and long-term device-related risks should be evaluated together (Stout, et al., 2019: e698–e800; Writing Committee, et al., 2021: 1888–1924).

In congenital heart diseases, indications for permanent pacemaker implantation most commonly arise due to sinus node dysfunction, atrioventricular block, and postoperative conduction

disturbances. Sinus node dysfunction may be seen particularly in patients who have undergone atrial surgery, in Fontan circulation, or after atrial switch operations. Permanent pacing should be considered in the presence of symptomatic bradycardia, chronotropic incompetence, presyncope, syncope, or a marked reduction in exercise capacity. In congenital complete AV block or high-grade AV block, the decision should be made according to symptom status and risk assessment. The presence of syncope, heart failure, exercise intolerance, or marked bradycardia supports the indication for pacemaker implantation. In asymptomatic patients, findings such as a wide-QRS escape rhythm, long pauses, complex ventricular ectopy, QT prolongation, or a low mean heart rate are important in risk assessment. In postoperative high-grade AV block, the patient should be monitored because recovery may occur in the early period. However, if the block becomes persistent or recovery is not expected, permanent pacemaker implantation should be planned (Writing Committee, et al., 2021: 1888–1924).

Device Selection and Pacing Strategy

Device selection should be individualized according to congenital anatomy. In patients with preserved sinus rhythm, systems that maintain atrioventricular synchrony should be preferred. However, in complex anatomies, transvenous lead placement is not always possible or appropriate. The presence of Fontan circulation, venous anomalies, a mechanical tricuspid valve, or a residual intracardiac shunt may change the device approach. In these patients, epicardial systems or alternative pacing strategies may be considered.

Long-term ventricular pacing may create a risk of dyssynchrony and deterioration in ventricular function, particularly in patients with borderline systemic ventricular function. Therefore, cardiac physiological pacing options should be considered in cases

expected to have a high ventricular pacing burden. His-bundle pacing and left bundle branch area pacing may provide more physiological activation in some patients. However, because of anatomical differences in congenital heart diseases, feasibility is not always the same. Therefore, assessment should be performed in experienced centers and on an individualized basis (Writing Committee, et al., 2021: 1888–1924).

Evaluation in Terms of CRT and ICD

The diagnosis of congenital heart disease alone does not constitute an indication for CRT. CRT should be evaluated in the presence of additional conditions such as systemic ventricular systolic dysfunction, symptomatic heart failure, electrical or pacing-induced dyssynchrony, and a high need for ventricular pacing. Preservation of ventricular function is particularly important in patients with a systemic right ventricle or in those exposed to long-term right ventricular pacing.

The ICD decision should also be based not on the presence of congenital heart disease itself, but on the risk of sudden cardiac death. In patients with a history of cardiac arrest, sustained ventricular tachycardia, or ventricular fibrillation, ICD implantation should be considered for secondary prevention.. In primary prevention, the decision is more individualized. Ventricular dysfunction, unexplained syncope, complex ventricular arrhythmias, previous surgical scars, specific anatomical diagnoses, and disease-specific risk markers should be considered together. In conclusion, device therapy in congenital heart diseases should be planned with a multidisciplinary approach that considers not only standard indications but also the patient's anatomical and surgical characteristics (Baumgartner, et al., 2021: 563–645; Stout, et al., 2019: e698–e800; Writing Committee, et al., 2021: 1888–1924).

Cardiomyopathies

In cardiomyopathies, the decision for device therapy is based on ejection fraction and the presence of arrhythmia. The type of disease, genetic background, ventricular function, myocardial scar burden, history of syncope, and risk of ventricular arrhythmia should be evaluated together. Dilated, arrhythmogenic, hypertrophic, restrictive, and infiltrative cardiomyopathies have different clinical risk profiles. Therefore, decisions regarding pacemaker, ICD, and CRT should be individualized by considering disease-specific risk markers (Arbelo, et al., 2023: 3503–3626).

Indication for Permanent Pacemaker Implantation

In cardiomyopathies, permanent pacemaker implantation is mainly considered in the presence of standard pacing indications such as symptomatic bradycardia, sinus node dysfunction, or atrioventricular block. However, conduction system disease is more common in some types of cardiomyopathy. AV block or intraventricular conduction disturbances may develop particularly in lamin A/C-related cardiomyopathy, myotonic dystrophy, cardiac sarcoidosis, and infiltrative diseases. In these patients, not only the treatment of bradycardia but also the concomitant risk of sudden cardiac death should be evaluated (Arbelo, et al., 2023: 3503–3626).

The expected ventricular pacing burden is important when deciding on pacemaker implantation. Long-term high-burden right ventricular pacing may increase ventricular dyssynchrony and adversely affect systolic function. Therefore, in patients with impaired ventricular function or an expected high pacing burden, cardiac physiological pacing or CRT options should be evaluated instead of conventional right ventricular pacing (Chung, et al., 2023: e17–e91). If the patient also has an ICD indication, an appropriate system with defibrillator capability should be preferred rather than pacemaker implantation alone.

ICD Indication

The main purpose of ICD therapy in cardiomyopathies is to prevent sudden cardiac death. A history of cardiac arrest is a strong indication for ICD implantation. Ventricular fibrillation is evaluated in the same way. ICD should also be considered for secondary prevention in the presence of sustained ventricular tachycardia that is not due to a reversible cause and is not hemodynamically tolerated. This approach is independent of the type of cardiomyopathy (Zeppenfeld, et al., 2022: 3997–4126).

In dilated cardiomyopathy and hypokinetic nondilated cardiomyopathy, the decision for primary prevention is not based solely on left ventricular ejection fraction. ICD should be considered in symptomatic patients with persistent significant left ventricular systolic dysfunction despite optimal medical therapy. In addition, ICD should be strongly considered in the presence of unexplained syncope, late gadolinium enhancement on cardiac magnetic resonance imaging, inducible sustained monomorphic VT during electrophysiological study, and high-risk genetic variants such as LMNA, PLN, FLNC, or RBM20 (Arbelo, et al., 2023: 3503–3626).

In arrhythmogenic cardiomyopathy, the ICD decision should be made by evaluating the history of ventricular arrhythmia, presence of syncope, degree of right or left ventricular dysfunction, and genetic/phenotypic risk markers together. ICD is indicated in the presence of hemodynamically intolerable VT or VF. ICD may also be considered in hemodynamically tolerated sustained monomorphic VT. A similar approach applies to hypertrophic cardiomyopathy; intolerable VT/VF constitutes a secondary prevention indication, whereas tolerated sustained monomorphic VT and other sudden death risk markers should be evaluated on an individual basis. In hypertrophic cardiomyopathy, the primary prevention decision should be made according to sudden cardiac death risk stratification. A family history of sudden death, unexplained syncope, massive hypertrophy, non-sustained

ventricular tachycardia, apical aneurysm, extensive fibrosis, and left ventricular systolic dysfunction are important in risk assessment (Ommen, et al., 2024: e1239–e1311). In inflammatory and infiltrative cardiomyopathies, the decision is more individualized. In cardiac sarcoidosis, documented sustained VT or resuscitated cardiac arrest constitutes a strong indication for ICD; even when LVEF is preserved, findings such as extensive LGE, moderate systolic dysfunction, or inducible sustained monomorphic VT may support the ICD decision. In amyloidosis, ICD should be evaluated more selectively because the mechanism of sudden death is not always a shockable ventricular arrhythmia; in AL or ATTR amyloidosis, the presence of hemodynamically intolerable VT is an important finding in favor of ICD (Arbelo, et al., 2023: 3503–3626).

CRT and Cardiac Physiological Pacing

CRT is considered not because of the diagnosis of cardiomyopathy itself, but in the presence of left ventricular systolic dysfunction, symptomatic heart failure, and electrical or pacing-induced dyssynchrony. The strongest benefit is expected in patients with reduced left ventricular ejection fraction, sinus rhythm, left bundle branch block morphology, and markedly prolonged QRS duration. In non-LBBB morphology or with narrower QRS durations, the benefit is more limited, and patient selection should be performed more carefully (Heidenreich, et al., 2022: e895–e1032). In cardiomyopathy patients with a high need for ventricular pacing, CRT or cardiac physiological pacing may be evaluated to prevent pacing-induced cardiomyopathy or reduce existing dyssynchrony (Chung, et al., 2023: e17–e91). His-bundle pacing and left bundle branch area pacing aim to activate the ventricles in a manner closer to the native conduction system. These approaches become particularly important in patients with borderline ventricular function, an expected need for long-term pacing, or a need to avoid conventional right ventricular pacing.

In conclusion, device therapy in cardiomyopathies should not be reduced to a single algorithm. The pacemaker decision should be based on bradycardia and conduction disturbance, the ICD decision on the risk of sudden cardiac death, and the CRT decision on the presence of systolic dysfunction and dyssynchrony. Genetic findings, cardiac magnetic resonance results, arrhythmia burden, and the patient's clinical course are the main factors determining device selection.

Channelopathies

Channelopathies are primary electrical diseases caused by genetic or functional abnormalities in cardiac ion channels. Long QT syndrome, Brugada syndrome, catecholaminergic polymorphic ventricular tachycardia, and short QT syndrome are the main clinical entities in this group. In these patients, structural heart disease is often not evident. Nevertheless, there may be a risk of malignant ventricular arrhythmia and sudden cardiac death. Therefore, the decision for device therapy should be based not only on ECG findings, but also on symptom history, genotype, family history, and documented arrhythmic events (Priori, et al., 2013: 1932–1963).

Indication for Permanent Pacemaker Implantation

The role of permanent pacemaker implantation in channelopathies is limited. The main treatment generally consists of lifestyle modifications, avoidance of triggers, disease-specific pharmacological therapy, and ICD implantation in selected patients. Pacemaker implantation is considered only when standard pacing indications such as concomitant symptomatic bradycardia, sinus node dysfunction, or atrioventricular block are present. In long QT syndrome, bradycardia or long pauses may facilitate torsades de pointes episodes. Therefore, in selected patients with pause-dependent arrhythmias, pacing may be considered as a supportive strategy. However, a pacemaker does not replace beta-blocker

therapy or ICD therapy when it is required. In Brugada syndrome, short QT syndrome, and catecholaminergic polymorphic ventricular tachycardia, there is no routine indication for pacemaker implantation. In these patients, the pacing decision should be based on concomitant conduction system disease rather than the diagnosis of channelopathy itself.

ICD Indication

The main purpose of ICD therapy in channelopathies is to prevent sudden cardiac death. In patients with a history of cardiac arrest, ventricular fibrillation, or hemodynamically severe ventricular tachycardia, ICD implantation should be considered for secondary prevention.. In primary prevention, the decision is more selective, because long-term lead problems, inappropriate shocks, and psychosocial effects may cause important clinical problems in young patients (Priori, et al., 2013: 1932–1963).

In long QT syndrome, first-line therapy in most patients is beta-blocker treatment. Nonselective beta-blockers such as nadolol or propranolol are particularly preferred. ICD becomes a consideration in patients with a history of cardiac arrest or in high-risk patients who develop recurrent arrhythmic syncope or ventricular arrhythmia despite appropriate medical therapy. In some patients, left cardiac sympathetic denervation is also among the treatment options.

In Brugada syndrome, the ICD decision should be evaluated particularly in the presence of documented ventricular fibrillation, cardiac arrest, or arrhythmic syncope associated with a spontaneous type 1 ECG pattern. In contrast, ICD implantation is not routine in patients with only an asymptomatic Brugada ECG pattern. Avoidance of fever, early treatment of fever, and avoidance of drugs that may accentuate the Brugada pattern are the main preventive approaches.

In catecholaminergic polymorphic ventricular tachycardia, the basis of treatment is restriction of exercise and adrenergic triggers together with beta-blocker therapy. Flecainide may be added in patients with an inadequate response. ICD should be considered in selected patients who have survived cardiac arrest or continue to have life-threatening arrhythmic events despite optimal therapy. However, in these patients, ICD shocks may increase the adrenergic response and worsen the arrhythmia burden. Therefore, ICD should not be regarded as sufficient treatment alone and should always be planned together with effective pharmacological therapy.

Data are more limited in short QT syndrome. ICD is evaluated in patients with a history of cardiac arrest or documented malignant ventricular arrhythmia. In patients with arrhythmic syncope, a family history of sudden death at a young age, and marked QT shortening, the decision should be individualized. In some patients, quinidine therapy may be considered as an adjunct to ICD or as an alternative approach when ICD is not appropriate.

Evaluation in Terms of CRT

Channelopathies alone do not constitute an indication for CRT. In these diseases, the main problem is usually malignant electrical instability rather than ventricular dyssynchrony. CRT should be evaluated only if standard criteria independent of the channelopathy are present, such as left ventricular systolic dysfunction, symptomatic heart failure, prolonged QRS duration, or a high need for ventricular pacing.

In conclusion, device therapy in channelopathies is mainly shaped by ICD indications. Pacemaker implantation is considered only in the presence of concomitant bradycardia or conduction disturbance. CRT is planned not according to the diagnosis of channelopathy, but according to heart failure and dyssynchrony criteria.

Heart Failure

In heart failure, device therapy should be planned according to the disease phenotype, left ventricular ejection fraction, QRS duration and morphology, rhythm status, symptom burden, and expected survival. In this patient group, pacemaker, ICD, and CRT are used for different purposes. Pacemaker therapy treats bradycardia or conduction disturbance. ICD aims to prevent sudden cardiac death. CRT aims to improve ventricular synchronization by reducing electrical or pacing-induced dyssynchrony. Therefore, the diagnosis of heart failure alone is not sufficient for device implantation. The decision should be made by evaluating current guideline criteria together with the patient-specific clinical context (Heidenreich, et al., 2022: e895–e1032; McDonagh, et al., 2021: 3599–3726).

Indication for Permanent Pacemaker Implantation

In heart failure, the indication for permanent pacemaker implantation usually arises in the presence of concomitant symptomatic bradycardia, sinus node dysfunction, or atrioventricular block. Isolated heart failure alone does not constitute an indication for pacemaker implantation. However, in selected patients in whom guideline-directed medical therapy cannot be administered because of bradycardia, the pacing decision may be evaluated individually. In this setting, the aim is not only to increase heart rate, but also to reduce symptoms and allow the continuation of necessary therapies.

Dyssynchrony related to conventional right ventricular pacing is particularly important in patients with heart failure. Long-term high-burden right ventricular pacing may worsen left ventricular function. This may lead to pacing-induced cardiomyopathy or aggravate pre-existing heart failure. Therefore, in patients who require permanent pacemaker implantation and are

expected to have a high ventricular pacing burden, the device strategy should be carefully selected before implantation. In patients with reduced or borderline left ventricular function, CRT or cardiac physiological pacing options may be considered (Chung, et al., 2023: e17–e91).

ICD Indication

The main purpose of ICD therapy in heart failure is to prevent sudden cardiac death. The indication is clearer for secondary prevention. ICD should be considered in patients with a history of cardiac arrest, ventricular fibrillation, or symptomatic ventricular tachycardia. When making this decision, it should also be investigated whether the arrhythmia is related to a reversible cause.

For primary prevention, the ICD decision is evaluated particularly according to left ventricular ejection fraction and the patient's clinical status. Current guidelines recommend ICD in patients with reduced left ventricular ejection fraction due to ischemic or nonischemic cardiomyopathy who remain symptomatic despite appropriate medical therapy and have a meaningful life expectancy. The general approach is to consider ICD for primary prevention in NYHA class II–III patients with a left ventricular ejection fraction of $\leq 35\%$ if the risk persists despite optimal medical therapy. In ischemic cardiomyopathy, the decision for primary prevention ICD should be made at least 40 days after myocardial infarction. In patients who have undergone revascularization, left ventricular function should generally be reassessed at least 90 days after revascularization. After these periods have been completed and guideline-directed medical therapy has been optimized, ICD indication is evaluated if LVEF remains low (Heidenreich, et al., 2022: e895–e1032; McDonagh, et al., 2021: 3599–3726).

The ICD decision should not be reduced solely to ejection fraction. The patient's age, comorbidities, functional capacity, life

expectancy, arrhythmia burden, type of cardiomyopathy, and patient preference should be considered. In patients with advanced heart failure, severe comorbidities, or limited expected survival, the anticipated benefit from ICD may decrease. Therefore, before ICD implantation, the risk of death due to pump failure should be evaluated in addition to the risk of sudden death.

CRT Indication

CRT shows its strongest benefit in patients with heart failure in whom electrical dyssynchrony is prominent. CRT is strongly recommended particularly in patients with a left ventricular ejection fraction of $\leq 35\%$, persistent symptoms despite guideline-directed medical therapy, sinus rhythm, left bundle branch block morphology, and a QRS duration of ≥ 150 ms. CRT should also be evaluated in patients with LBBB morphology and a QRS duration of 130–149 ms. In contrast, in non-LBBB patterns, including RBBB, the expected benefit is more limited; in this group, CRT is mainly considered when QRS duration is ≥ 150 ms. In non-LBBB/RBBB patients with a QRS duration of 130–149 ms, the recommendation is weaker, and the decision should be individualized (Heidenreich, et al., 2022: e895–e1032; McDonagh, et al., 2021: 3599–3726).

When deciding on CRT, not only QRS duration but also QRS morphology, left ventricular ejection fraction, NYHA functional class, baseline rhythm, and adequacy of medical therapy should be evaluated together. CRT is not recommended in patients with a narrow QRS duration and no need for ventricular pacing. In contrast, CRT may be considered to prevent or reduce pacing-induced dyssynchrony in patients with a high need for ventricular pacing and reduced left ventricular function.

In heart failure patients with atrial fibrillation, the CRT decision should be made more carefully. In these patients, treatment success depends on achieving a high rate of effective biventricular

pacing. If an adequate biventricular pacing rate cannot be achieved with medications, AV node ablation may be considered in selected patients. This approach is particularly evaluated in patients with uncontrolled rapid ventricular response, symptomatic heart failure, and an expected benefit from CRT.

Cardiac Physiological Pacing

Cardiac physiological pacing is an approach that aims to provide ventricular activation in a manner closer to the native conduction system. His-bundle pacing and left bundle branch area pacing are the main methods of this strategy. This approach is becoming increasingly important in patients with heart failure or at risk of developing heart failure. Avoiding conventional right ventricular pacing is particularly important in patients expected to have a high ventricular pacing burden.

Current cardiac physiological pacing guidelines state that cardiac physiological pacing may be considered in patients who require permanent pacemaker implantation and are expected to have a high ventricular pacing burden. The aim is to reduce the risk of pacing-induced cardiomyopathy. This approach is particularly important in patients with reduced, borderline, or at-risk left ventricular function. However, the feasibility of His-bundle pacing and left bundle branch area pacing depends on the center's experience, the patient's anatomy, and the likelihood of technical success (Chung, et al., 2023: e17–e91).

CRT-P, CRT-D, and Patient Selection

In patients planned for CRT, it should also be determined whether the device will be CRT-P, which provides only resynchronization, or CRT-D, which includes defibrillator capability. If the patient also has an ICD indication, CRT-D may be preferred. CRT-P may be more appropriate in patients with a low risk of sudden

cardiac death, advanced age, severe comorbidities, or limited expected benefit from defibrillator therapy. This decision should be made through a shared decision-making process with the patient.

Before device therapy is planned, optimization of guideline-directed medical therapy is essential. SGLT2 inhibitors, beta-blockers, renin-angiotensin system inhibitors or ARNI, and mineralocorticoid receptor antagonists constitute the foundation of therapy in eligible patients. The device decision should be made after medical therapy has been initiated and left ventricular function has been reassessed. Exceptions to this are clinical conditions requiring urgent pacing or ICD for secondary prevention (Heidenreich, et al., 2022: e895–e1032; McDonagh, et al., 2021: 3599–3726).

In conclusion, device therapy in heart failure is based on three main questions: Does the patient require pacing because of bradycardia or conduction disturbance? Is the risk of sudden cardiac death high enough to require ICD? Can electrical or pacing-induced dyssynchrony be corrected with CRT or cardiac physiological pacing? The answers to these questions should be evaluated together with left ventricular ejection fraction, QRS duration and morphology, rhythm status, expected pacing burden, comorbidities, and patient preference.

Comparison of ESC and ACC/AHA Guidelines

ESC and ACC/AHA guidelines are largely based on similar fundamental principles regarding pacemaker, ICD, and CRT indications. In both approaches, device therapy is not planned solely according to electrocardiographic findings. The presence of symptoms, the relationship between rhythm disturbance and symptoms, reversible causes, left ventricular function, expected ventricular pacing burden, and the risk of sudden cardiac death are evaluated together. However, while ESC guidelines provide a more algorithmic and detailed classification in some areas,

ACC/AHA/HRS guidelines place greater emphasis on clinical context, symptom correlation, and shared decision-making (Glikson, et al., 2021: 3427–3520; Kusumoto, et al., 2019: 932–987).

Sinus Node Dysfunction

In sinus node dysfunction, ESC and ACC/AHA/HRS recommendations are generally consistent. Both guidelines accept that asymptomatic sinus bradycardia alone does not constitute an indication for permanent pacemaker implantation. The ACC/AHA/HRS guideline uses a clearer statement on this issue and notes that there is no established absolute minimum heart rate or pause duration for permanent pacing. The ESC guideline similarly emphasizes that the decision should be based on the relationship between bradycardia and symptoms. Therefore, the difference between the two guidelines is more a nuance in emphasis than a difference in principle (Glikson, et al., 2021: 3427–3520; Kusumoto, et al., 2019: 932–987).

Atrioventricular Blocks

The approach of the two guidelines to atrioventricular blocks is largely similar. If there is no reversible or physiological cause, permanent pacemaker implantation is recommended regardless of symptoms in Mobitz type II AV block, high-grade AV block, and third-degree AV block. In first-degree AV block and Mobitz type I AV block, both guidelines are more selective. In this group, the pacemaker decision usually depends on demonstrating that symptoms are related to AV block, the clinical impact of marked PR prolongation, or suspicion of infranodal block. The ESC guideline discusses the determination of the block level and the role of electrophysiological evaluation in greater detail, whereas the ACC/AHA/HRS guideline places symptom-rhythm correlation more prominently (Glikson, et al., 2021: 3427–3520; Kusumoto, et al., 2019: 932–987).

Bifascicular and Trifascicular Blocks

In bifascicular blocks, the ESC and ACC/AHA approaches are similar in that they do not support routine pacemaker implantation in asymptomatic patients. The difference becomes more apparent in patients with unexplained syncope. The ESC guideline presents electrophysiological study, implantable loop recorder, and empirical pacing in selected cases in a more algorithmic manner. The ACC/AHA/HRS approach also does not consider bundle branch block alone as an indication; however, the indication for pacemaker implantation becomes stronger in the presence of documented high-grade AV block, infranodal conduction disease, or alternating bundle branch block. Therefore, in both guidelines, the decision is based not only on surface ECG findings, but also on the history of syncope and evidence of advanced conduction system disease (Glikson, et al., 2021: 3427–3520; Kusumoto, et al., 2019: 932–987).

Atrial Fibrillation and Bradycardia

The ESC and ACC/AHA approaches are generally consistent regarding atrial fibrillation and bradycardia. In both approaches, the presence of atrial fibrillation alone does not constitute an indication for pacemaker implantation. Permanent pacing is evaluated in clinical conditions such as symptomatic slow ventricular response, long pauses, or tachycardia-bradycardia syndrome. Drug effect is also specifically considered in both guidelines. Both guidelines recommend reviewing dose adjustment and alternative treatment options before making a device decision if treatments used for rate or rhythm control increase bradycardia. The guidelines also follow a similar rationale in AV node ablation and pacing strategy. In selected symptomatic patients with atrial fibrillation whose ventricular rate cannot be controlled with medications, both guidelines recommend

permanent pacing together with AV node ablation (Van Gelder, et al., 2024: 3314–3414).

Ventricular Tachycardias

The ESC and ACC/AHA approaches to ventricular tachycardias are largely similar. Both guidelines address the ICD decision by distinguishing between secondary and primary prevention. ICD implantation should be considered for secondary prevention. after cardiac arrest, ventricular fibrillation, or sustained ventricular tachycardia not caused by a reversible cause. In primary prevention, the decision is made according to left ventricular function, underlying cardiomyopathy, scar burden, history of syncope, and disease-specific risk markers (Al-Khatib, et al., 2018: e210–e271; Zeppenfeld, et al., 2022: 3997–4126).

The 2022 ESC guideline recommends catheter ablation as one of the first-line options in symptomatic idiopathic VT/PVCs, particularly those originating from the RVOT or left fascicle; in other foci, ablation or flecainide may be evaluated in selected patients. The 2017 ACC/AHA/HRS guideline also addresses monomorphic VT without structural heart disease under the heading of idiopathic VT and emphasizes symptoms, arrhythmia focus, response to medical therapy, and ablation options in treatment (Al-Khatib, et al., 2018: e210–e271; Zeppenfeld, et al., 2022: 3997–4126).

Non-sustained ventricular tachycardia alone is not an indication for ICD; however, risk stratification is required in the presence of structural heart disease or a high-risk genetic background. The ESC guideline emphasizes genetic and imaging-based risk markers in greater detail, whereas the ACC/AHA approach highlights secondary prevention and primary prevention criteria based on reduced ejection fraction (Al-Khatib, et al., 2018: e210–e271; Zeppenfeld, et al., 2022: 3997–4126).

Carotid Sinus Syndrome and Neurocardiogenic Syncope

In reflex syncope, the ESC guideline defines pacing indications in more detail than the ACC/AHA/HRS approach. The ESC guideline recommends considering pacing particularly in patients over 40 years of age with severe, recurrent, unpredictable reflex syncope carrying a risk of trauma. For this indication, demonstration of a spontaneous or provoked asystolic cardioinhibitory response is important. The ACC/AHA/HRS syncope guideline uses more cautious wording. It states that dual-chamber pacing may be reasonable in selected patients aged 40 years or older with recurrent vasovagal syncope when a prolonged spontaneous pause has been documented. The common point in both approaches is that the benefit of pacemaker therapy is considered limited in patients in whom the vasodepressor component is predominant (Brignole, et al., 2018: 1883–1948; Shen, et al., 2017: e60–e122).

Congenital Heart Diseases

In congenital heart diseases, ESC and ACC/AHA approaches are similar in that standard bradycardia and conduction disturbance indications should be adapted according to congenital anatomy. In both approaches, postoperative AV block, congenital complete AV block, sinus node dysfunction, and a history of complex surgery are important in device decision-making. ESC guidelines address technical details such as congenital anatomy, venous access, the need for epicardial systems, and systemic ventricular morphology more explicitly. The ACC/AHA approach emphasizes multidisciplinary evaluation and individualized decision-making in adult congenital heart disease. CRT and ICD decisions are evaluated in both approaches based on ventricular function, dyssynchrony, and sudden cardiac death risk rather than the congenital diagnosis itself

(Baumgartner, et al., 2021: 563–645; Stout, et al., 2019: e698–e800; Writing Committee, et al., 2021: 1888–1924).

Cardiomyopathies

In cardiomyopathies, ESC and ACC/AHA guidelines adopt a similar approach in that the ICD decision should not be reduced solely to left ventricular ejection fraction. ESC guidelines discuss genetic, phenotypic, and imaging-based risk markers in greater detail. High-risk genetic variants such as LMNA, PLN, FLNC, and RBM20, cardiac magnetic resonance findings, and disease-specific arrhythmic risk are particularly important in ICD decision-making. The ACC/AHA approach also considers disease-specific risk factors; however, in heart failure and ICD decision-making, LVEF, NYHA class, optimal medical therapy, and life expectancy have a more central role. In both approaches, the pacemaker decision is based on concomitant bradycardia or conduction disturbance rather than the diagnosis of cardiomyopathy itself (Arbelo, et al., 2023: 3503–3626; Ommen, et al., 2024: e1239–e1311).

Channelopathies

In channelopathies, ESC and ACC/AHA approaches are similar in terms of their basic principles. In long QT syndrome, Brugada syndrome, catecholaminergic polymorphic ventricular tachycardia, and short QT syndrome, the device decision is based not on the diagnosis itself, but on the history of arrhythmic events and the risk of sudden cardiac death. The ESC guideline presents disease-specific risk stratification in channelopathies in greater detail. Beta-blocker therapy in long QT syndrome, avoidance of adrenergic triggers and appropriate pharmacological therapy in CPVT, and early treatment of fever and avoidance of triggering drugs in Brugada syndrome are emphasized. The ACC/AHA approach also bases the ICD decision on high-risk clinical conditions such as cardiac arrest, documented malignant ventricular arrhythmia, and arrhythmic

syncope. In both approaches, the role of pacemaker therapy is limited and is generally restricted to concomitant bradycardia or pause-dependent arrhythmias (Al-Khatib, et al., 2018: e210–e271; Priori, et al., 2013: 1932–1963; Zeppenfeld, et al., 2022: 3997–4126).

Heart Failure

In heart failure, ESC and ACC/AHA guidelines use largely similar criteria for ICD and CRT indications. The main approach for ICD is reduced left ventricular ejection fraction, symptomatic heart failure, persistent risk despite optimal medical therapy, and meaningful life expectancy. In ischemic cardiomyopathy, the decision for primary prevention ICD should be made at least 40 days after myocardial infarction and generally at least 90 days after revascularization. This approach is consistent with both guideline pathways (Heidenreich, et al., 2022: e895–e1032; McDonagh, et al., 2021: 3599–3726).

For CRT, the strongest common indication is in patients with LVEF $\leq 35\%$, persistent symptoms despite guideline-directed medical therapy, sinus rhythm, LBBB morphology, and QRS duration ≥ 150 ms. The ESC guideline also recommends evaluating CRT in patients with LBBB morphology and a QRS duration of 130–149 ms. In non-LBBB patterns, including RBBB, the expected benefit is more limited. In this group, CRT is mainly considered when QRS duration is ≥ 150 ms; at shorter QRS durations, the recommendation is weaker. The ACC/AHA/HFSA guideline similarly gives the strongest recommendation for patients with LBBB and QRS ≥ 150 ms. In non-LBBB morphology, the CRT decision is more selective (Heidenreich, et al., 2022: e895–e1032; McDonagh, et al., 2021: 3599–3726).

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CARDIAC PACING TECHNOLOGY AND HARDWARE

SEFA ERDİ ÖMÜR¹

Introduction

Permanent cardiac pacing systems are considered one of the most important technological advances in modern cardiology. Since the introduction of the first implantable pacemaker into clinical practice in 1958, substantial progress has been achieved in device technology. Today, pacing systems are used not only for the treatment of symptomatic bradycardia but also in the management of heart failure, cardiac resynchronization therapy (CRT), conduction system pacing, and remote patient monitoring (Glikson, et al., 2021: 3427–3520).

The primary objective of cardiac pacing is to maintain adequate cardiac output and reduce symptoms by ensuring an appropriate heart rate in situations where spontaneous impulse generation or cardiac conduction is impaired. Contemporary devices are capable of much more than delivering electrical stimulation; they also provide advanced telemetry systems, intracardiac electrogram

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storage, arrhythmia detection algorithms, and remote monitoring capabilities (Chung, et al., 2023: e17–e91).

In recent years, major paradigm shifts have occurred in the field of cardiac pacing, particularly with the development of conduction system pacing techniques, including His Bundle Pacing (HBP) and Left Bundle Branch Area Pacing (LBBAP), leadless pacemaker technologies, and MRI-conditional systems. These innovations have enabled more physiological ventricular activation, reduced device-related complications, and improved patient quality of life (Chung, et al., 2023: e17–e91; Kusumoto, et al., 2019: e382–e482).

Permanent pacing systems (table 1) consist primarily of two major components: the pulse generator and the lead system. The pulse generator contains the energy source, electronic circuitry, and microprocessor architecture, whereas the leads provide electrical communication between the generator and the myocardium (Cazeau, et al., 2004: S42–48). Advanced software algorithms incorporated into modern devices facilitate individualized pacing strategies and optimize energy consumption according to patient-specific requirements (Ellison, Sharma, & Trohman, 2017: 429–440).

This chapter reviews the fundamental components of permanent cardiac pacing systems, including generator architecture, battery technologies, lead systems, connector standards, and emerging technological developments that continue to shape the future of cardiac rhythm management.

Generator Structure and Components

The pulse generator constitutes the central component of a permanent cardiac pacing system (figure 1). It is a complex electronic unit that houses the energy source, microprocessor,

memory systems, and telemetry modules responsible for device operation (Cazeau, et al., 2004: S42–48).

The outer casing of modern pulse generators is typically manufactured from titanium alloy. Titanium has become the standard material for implantable cardiac devices because of its excellent biocompatibility, corrosion resistance, and mechanical durability (Cazeau, et al., 2004: S42–48). In addition, titanium enclosures provide effective electromagnetic shielding, thereby enhancing the reliability and stability of internal electronic circuits.

Table 1: Major Indications for Permanent Cardiac Pacing (ESC 2021)

Clinical Condition	Class of Recommendation	Level of Evidence	Clinical Recommendation
Symptomatic sinus node dysfunction	I	B	Permanent pacing is recommended
Advanced atrioventricular block	I	B	Permanent pacing is recommended
Complete atrioventricular block	I	B	Permanent pacing is recommended
Alternating bundle branch block	I	C	High risk of progression to advanced conduction disease

Although contemporary generators are substantially smaller than first-generation devices, they offer significantly greater computational capacity. Advances in microprocessor technology have enabled modern devices to execute sophisticated algorithms in

real time while storing millions of cardiac events within their internal memory systems (Ellison, Sharma, & Trohman, 2017: 429–440).

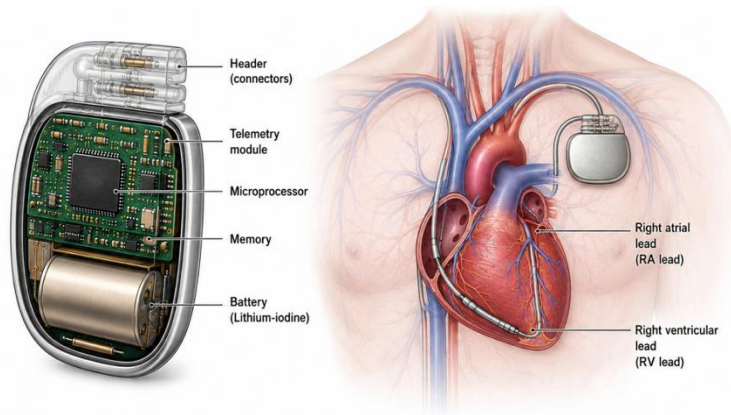


Figure 1: Basic components of a permanent cardiac pacing system. Schematic representation of a conventional dual-chamber pacemaker system consisting of a pulse generator, right atrial lead and right ventricular lead.

Microprocessor Systems

The microprocessor serves as the control center of the pulse generator. Electrical signals detected by the leads are continuously analyzed to determine the presence or absence of intrinsic cardiac activity (Cazeau, et al., 2004: S42–48).

The principal functions of the microprocessor include:

- Detection and processing of sensing signals
- Control of pacing timing intervals
- Arrhythmia analysis and classification
- Optimization of energy consumption
- Management of telemetry communication
- Interpretation of sensor-derived information

Through advanced microprocessor technology, modern devices can adapt heart rate according to patient activity levels and maintain efficient energy utilization while preserving device longevity (Ellison, Sharma, & Trohman, 2017: 429–440).

Memory Systems

Contemporary implantable devices possess substantial data storage capabilities. Device memory can store information regarding atrial and ventricular arrhythmias, intracardiac electrograms, lead performance parameters, battery status, and patient activity profiles (Ellison, Sharma, & Trohman, 2017: 429–440).

These data provide valuable clinical information during routine device interrogation and remote follow-up assessments. Device memory has become particularly important for the detection of subclinical or silent atrial fibrillation episodes that may otherwise remain unrecognized (Chung, et al., 2023: e17–e91).

Telemetry Systems

Telemetry systems enable bidirectional communication between the implanted device and the external programmer. Whereas early-generation systems relied primarily on inductive communication, radiofrequency-based wireless technologies have become the standard approach in modern devices (Ellison, Sharma, & Trohman, 2017: 429–440).

Contemporary telemetry systems facilitate remote device interrogation, early detection of potential device-related problems, and more efficient longitudinal patient management. As a result, remote monitoring has become an integral component of modern cardiac device follow-up programs (Chung, et al., 2023: e17–e91).

Battery Technologies and Longevity Calculations

Battery technology plays a critical role in the long-term success of permanent pacing systems. An ideal battery should provide long service life, high reliability, biocompatibility, and excellent energy density while maintaining stable performance throughout its operational lifespan (Cazeau, et al., 2004: S42–48).

Although early pacemakers utilized nickel-cadmium and mercury-zinc energy sources, modern implantable cardiac devices have transitioned almost entirely to lithium-based battery technologies (Ellison, Sharma, & Trohman, 2017: 429–440). The introduction of lithium batteries has significantly prolonged device longevity and reduced the frequency of generator replacement procedures.

Lithium-Iodine Batteries

Lithium-iodine batteries represent the most widely used energy source in contemporary pacemaker systems.

Their principal advantages include:

- Low self-discharge rate
- Extended operational lifespan
- High reliability
- Stable voltage output

These characteristics have made lithium-iodine technology the standard energy source for permanent pacemakers (Cazeau, et al., 2004: S42–48).

Depending on pacing dependency, pacing burden, programmed output settings, and device utilization, the average battery longevity of contemporary pacemakers ranges from approximately 8 to 15 years (Ellison, Sharma, & Trohman, 2017: 429–440).

Batteries Used in ICD and CRT-D Systems

Implantable cardioverter-defibrillators (ICDs) and CRT-D systems require substantially greater energy reserves than conventional pacemakers. Consequently, these devices utilize lithium-silver vanadium oxide and lithium-carbon monofluoride battery technologies (Cazeau, et al., 2004: S42–48).

These battery systems are capable of delivering high-energy defibrillation shocks while maintaining reliable long-term performance and acceptable device longevity (Ellison, Sharma, & Trohman, 2017: 429–440).

Factors Influencing Battery Longevity

Several factors influence battery consumption and overall device longevity, including:

- Daily pacing percentage
- Programmed pacing output voltage
- Pulse width settings
- Lead impedance
- Sensor utilization
- Frequency of telemetry communication
- Percentage of CRT pacing

Battery depletion is particularly accelerated in systems requiring high-output pacing or frequent delivery of therapeutic interventions (Cazeau, et al., 2004: S42–48).

Elective Replacement Indicator (ERI)

The Elective Replacement Indicator (ERI) represents a stage at which battery capacity has begun to decline but the device continues to function safely and reliably. At this stage, generator replacement should be planned, and follow-up intervals should

generally be shortened to ensure timely intervention (Ellison, Sharma, & Trohman, 2017: 429–440).

End of Service (EOS)

End of Service (EOS) indicates that battery capacity has reached a critical threshold. In pacemaker-dependent patients, generator replacement before reaching EOS is of paramount importance, as battery depletion may result in serious clinical consequences (Cazeau, et al., 2004: S42–48; Ellison, Sharma, & Trohman, 2017: 429–440).

Lead Engineering and Structure

Leads constitute the fundamental components that provide electrical communication between the pulse generator and the myocardium in permanent cardiac pacing systems. Delivery of pacing impulses to the myocardium and detection of intrinsic cardiac electrical activity are both accomplished through the lead system. Consequently, long-term device performance and reliability are highly dependent on lead integrity and function (Wilkoff, et al., 2009: 1085–1104).

Modern pacing leads consist of four principal components: the connector, conductor system, insulation material, and electrode. Each of these components directly influences the electrical performance, mechanical durability, and long-term reliability of the pacing system (Mond & Proclemer, 2011: 1013–1027; Wilkoff, et al., 2009: 1085–1104).

Advances in lead technology have significantly improved implantation success rates and reduced complications such as lead fracture, insulation failure, and electrical dysfunction (Mond & Proclemer, 2011: 1013–1027).

Conductor Systems

The conductor system is responsible for transmitting electrical energy from the pulse generator to the electrode. Materials commonly used in contemporary lead construction include MP35N alloy, Elgiloy, and platinum-iridium alloys (Liew, et al., 2025: 1403–1413).

These materials provide excellent tensile strength, corrosion resistance, flexibility, and long-term electrical stability, making them suitable for chronic implantation (Liew, et al., 2025: 1403–1413).

Electrode–Myocardial Interface

The electrode–myocardial interface is one of the most critical determinants of lead performance. Following lead implantation, local inflammatory reactions, fibrosis, and encapsulation may develop around the electrode tip, potentially affecting pacing thresholds and sensing performance (Mehta, Bossone, & Eagle, 2000: 47–60).

The introduction of steroid-eluting electrode technology has significantly reduced inflammatory responses and helped maintain low chronic pacing thresholds, thereby improving device efficiency and battery longevity (Mehta, Bossone, & Eagle, 2000: 47–60).

Sensing and Capture

Sensing refers to the ability of the device to detect intrinsic cardiac electrical activity, whereas capture describes successful myocardial depolarization in response to a pacing stimulus (Cazeau, et al., 2004: S42–48).

Inadequate sensing may result in undersensing, while excessive detection of non-cardiac signals can lead to oversensing. Both conditions may adversely affect device performance and

patient safety (Cazeau, et al., 2004: S42–48; Mond, et al., 2014: 1232–1249).

Unipolar and Bipolar Leads

Pacing systems can be classified as unipolar or bipolar (figure 2) according to the configuration of the electrical circuit used for stimulation and sensing (Cazeau, et al., 2004: S42–48).

Unipolar Leads

In unipolar pacing systems, the cathode is located at the lead tip, while the pulse generator casing functions as the anode. Although these systems possess a relatively simple design, they are more susceptible to electromagnetic interference (EMI) and myopotential oversensing (Mond & Proclemer, 2011: 1013–1027).

Historically, unipolar leads were widely used; however, their clinical application has markedly declined with the advancement of bipolar technology.

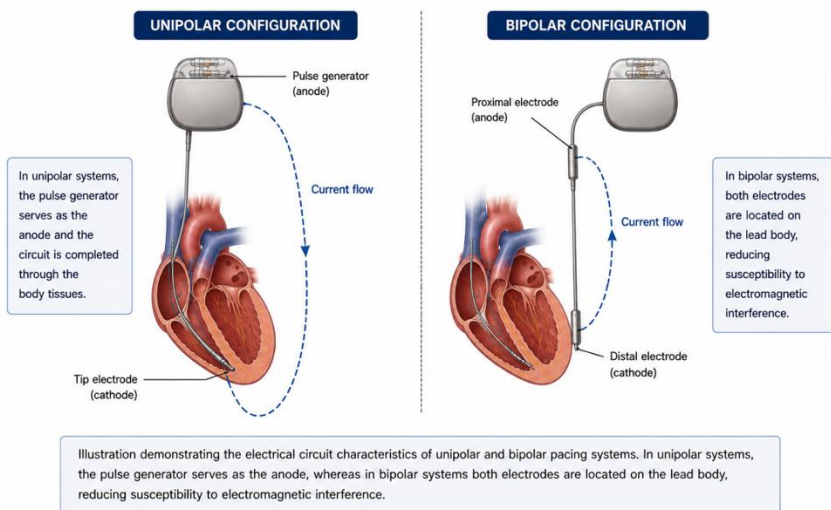


Figure 2: Comparison of unipolar and bipolar pacing lead configurations

Bipolar Leads

In bipolar pacing systems, both the cathode and anode are located on the lead itself (table 2). This design provides a shorter sensing circuit, resulting in improved signal quality and reduced susceptibility to electromagnetic interference (Mond & Proclemer, 2011: 1013–1027).

Because of their superior sensing performance and greater resistance to electrical noise, bipolar leads have become the standard configuration in contemporary pacing systems (Mond & Proclemer, 2011: 1013–1027).

Table 2: *Comparison of Unipolar and Bipolar Leads*

Feature	Unipolar	Bipolar
Sensing performance	Lower	Higher
EMI susceptibility	High	Low
Myopotential oversensing	More frequent	Less frequent
Current clinical use	Limited	Standard approach

Active and Passive Fixation Systems

Adequate lead stability is essential for successful long-term pacing therapy. Modern pacing leads utilize either active or passive (figure 3) fixation mechanisms to achieve stable myocardial attachment (Wilkoff, et al., 2009: 1085–1104).

Active Fixation Leads

Active fixation leads incorporate a retractable or extendable helical screw mechanism at the distal electrode tip. This screw is actively deployed into the myocardium, providing secure fixation (Hiruma, et al., 2021: 1105–1107).

Major advantages of active fixation systems include:

- Ease of repositioning
- Suitability for septal implantation
- Reduced risk of lead dislodgement
- Compatibility with conduction system pacing techniques

These characteristics have contributed to their widespread adoption in contemporary pacing practice (Hiruma, et al., 2021: 1105–1107).

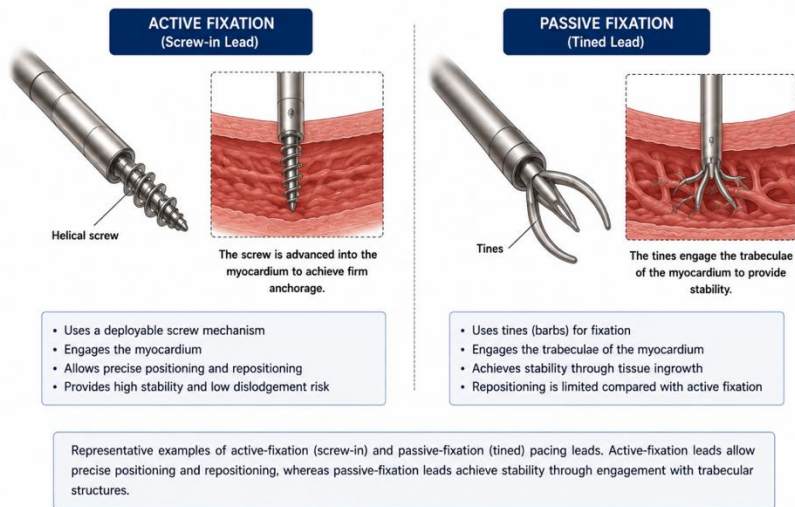


Figure 3: Active and passive fixation pacing leads

Passive Fixation Leads

Passive fixation leads utilize flexible tines located at the distal tip (table 3). These tines become anchored within the trabecular structures of the heart, thereby maintaining lead stability (Hiruma, et al., 2021: 1105–1107).

Although passive fixation leads are generally easy to implant, repositioning after deployment may be more challenging compared with active fixation systems (Hiruma, et al., 2021: 1105–1107).

Table 3: *Comparison of Active and Passive Fixation Leads*

Feature	Active Fixation	Passive Fixation
Repositioning	Easy	More difficult
Septal implantation	Suitable	Limited
HBP/LBBAP compatibility	Suitable	Generally unsuitable
Perforation risk	Slightly higher	Lower

Lead Extraction

Lead extraction may become necessary in cases of device-related infection, lead fracture, venous occlusion, lead malfunction, or system revision. In leads that have remained implanted for prolonged periods, fibrotic adhesions frequently develop, increasing procedural complexity and technical difficulty (Wilkoff, et al., 2009: 1085–1104).

Current international consensus documents strongly recommend complete system removal in patients with cardiac implantable electronic device (CIED)-related infections (Wilkoff, et al., 2009: 1085–1104).

Modern laser-assisted and mechanical extraction systems have substantially improved procedural success rates, allowing experienced centers to achieve high extraction success with acceptable complication rates (Wilkoff, et al., 2009: 1085–1104).

Lead Materials and Insulation Technologies

Because pacing leads are exposed to continuous mechanical stress throughout their lifespan, insulation materials must provide

long-term durability while maintaining electrical integrity (Liew, et al., 2025: 1403–1413).

Silicone Insulation

Silicone is one of the most commonly used insulation materials in pacing leads. Its major advantages include excellent biocompatibility, flexibility, and long-term stability (Hua, et al., 2022: 1162–1174).

However, silicone insulation may be more susceptible to mechanical abrasion than polyurethane under certain circumstances (Hua, et al., 2022: 1162–1174).

Polyurethane Insulation

Polyurethane offers superior mechanical strength and abrasion resistance. Its favorable mechanical properties allow the production of thinner leads without compromising structural integrity (Hua, et al., 2022: 1162–1174).

Consequently, polyurethane has been widely incorporated into contemporary lead designs (Hua, et al., 2022: 1162–1174).

Hybrid Insulation Systems

Many modern manufacturers employ hybrid insulation technologies that combine the favorable characteristics of both silicone and polyurethane. Such designs aim to maximize biocompatibility while improving mechanical durability and long-term performance (Hua, et al., 2022: 1162–1174).

Connector Standards

Connector systems (table 4) provide the mechanical and electrical interface between the lead and the pulse generator (figure 4). Historically, differences in connector design among manufacturers significantly limited compatibility between devices.

Consequently, international standardization efforts led to the development of universal connector systems (Haqqani & Mond, 2009: 1336–1353).

Standardized connectors improve compatibility among devices, facilitate implantation procedures, and reduce connection-related complications (Haqqani & Mond, 2009: 1336–1353).



Figure 4: Connector standards used in contemporary cardiac implantable electronic devices

IS-1 Standard

IS-1 (International Standard-1) is currently the most widely used pacing lead connector standard. It was specifically developed for unipolar and bipolar pacing leads (Haqqani & Mond, 2009: 1336–1353).

Major advantages include:

- Universal compatibility
- Reliable electrical contact
- Ease of implantation
- Low complication rates

These features have established IS-1 as the standard connector system for modern pacemakers (Haqqani & Mond, 2009: 1336–1353).

Table 4: *Connector Standards Used in Contemporary Cardiac Implantable Electronic Devices*

Standard	Primary Application	Characteristics
IS-1	Pacemakers	Standard pacing connector
DF-1	ICDs	Separate shock connectors
DF-4	Modern ICDs	Integrated single-connector system
IS-4	CRT systems	Multipolar LV lead connector

DF-1 Standard

The DF-1 connector was developed primarily for implantable cardioverter-defibrillator systems. In this design, pacing and defibrillation terminals are separated into distinct connectors (Sticherling & Burri, 2012: 1081–1086).

Although highly reliable, the requirement for multiple connections may increase procedural complexity and implantation time (Sticherling & Burri, 2012: 1081–1086).

DF-4 Standard

The DF-4 connector represents a major technological advancement in ICD design. In this system, pacing and defibrillation connections are integrated into a single connector (Sticherling & Burri, 2012: 1081–1086).

Advantages of DF-4 systems include:

- Smaller generator size
- Shorter implantation procedures

- Reduced connection errors
- Improved cosmetic outcomes

IS-4 Standard

The IS-4 standard was developed specifically for multipolar left ventricular leads used in cardiac resynchronization therapy. This system enables multiple pacing vector configurations and greater programming flexibility (Sticherling & Burri, 2012: 1081–1086).

Multipolar pacing can reduce phrenic nerve stimulation and facilitate selection of optimal pacing configurations, thereby improving CRT effectiveness (Sticherling & Burri, 2012: 1081–1086).

Sensor Technologies

Under normal physiological conditions, heart rate varies according to exercise, emotional stress, and metabolic demand. In patients with chronotropic incompetence, this adaptive response is impaired, resulting in reduced exercise capacity and diminished quality of life (Dell'Orto, Valli, & Greco, 2004: 137–145).

Rate-responsive pacing technologies were developed to restore physiological heart rate adaptation according to the patient's metabolic requirements (Dell'Orto, Valli, & Greco, 2004: 137–145).

Activity Sensors

Activity sensors represent the most widely used rate-responsive pacing technology in contemporary cardiac devices. These systems utilize accelerometers to detect body movement and adjust pacing rate according to physical activity levels (Dell'Orto, Valli, & Greco, 2004: 137–145).

The principal advantages of activity sensors include:

- Rapid response to changes in physical activity

- Low energy consumption
- Simple design
- Reliable performance

Because they primarily detect motion rather than metabolic demand, activity sensors may not accurately reflect physiological requirements in all clinical situations, particularly during emotional stress or isometric exercise (Dell'Orto, Valli, & Greco, 2004: 137–145).

Minute Ventilation Sensors

Minute ventilation sensors assess respiratory activity by measuring changes in transthoracic impedance associated with respiration. These systems evaluate both respiratory rate and tidal volume, providing a more direct estimation of metabolic demand than activity-based sensors (Occhetta, Bortnik, & Marino, 2011: 925653).

As a result, minute ventilation sensors often produce a more physiological heart rate response during exercise and daily activities (Occhetta, Bortnik, & Marino, 2011: 925653).

QT-Based Sensors

Certain pacing systems utilize variations in the QT interval to guide rate adaptation. Because QT duration is influenced by autonomic tone, these sensors can indirectly reflect changes in sympathetic nervous system activity (Occhetta, Bortnik, & Marino, 2011: 925653).

Although QT-based sensors can provide physiological rate responsiveness, their clinical application has remained limited because they may be influenced by medications, electrolyte abnormalities, ischemia, and other factors affecting ventricular repolarization (Occhetta, Bortnik, & Marino, 2011: 925653).

Dual-Sensor Technologies

Modern cardiac devices frequently combine activity sensors and minute ventilation sensors within a single system. This dual-sensor approach integrates the advantages of both technologies and improves rate-adaptive performance (Bristow, et al., 2004: 2140–2150).

Potential benefits include:

- Faster onset of rate response
- More accurate assessment of metabolic demand
- Improved exercise tolerance
- Higher patient satisfaction

By integrating multiple physiological signals, dual-sensor systems provide a more individualized and physiological pacing strategy (Bristow, et al., 2004: 2140–2150).

Next-Generation Sensor Technologies

Recent advances in artificial intelligence and multiparametric sensor systems have led to the development of increasingly sophisticated rate-responsive pacing technologies. These systems simultaneously analyze heart rate variability, activity level, respiratory parameters, and additional physiological signals to optimize pacing behavior (Cleland, et al., 2005: 1539–1549).

Future pacing systems are expected to employ advanced machine learning algorithms capable of continuously adapting device settings according to the patient's physiological status and clinical needs. Such developments may serve as the foundation for fully personalized pacing therapies in the coming decades (Cleland, et al., 2005: 1539–1549).

Cardiac Resynchronization Therapy (CRT)

Cardiac resynchronization therapy (CRT) is an advanced pacing modality developed to correct mechanical dyssynchrony resulting from ventricular conduction abnormalities (figure 5). CRT has become a cornerstone therapy for selected patients with heart failure and ventricular conduction delay (Moss, et al., 2009: 1329–1338).

Numerous clinical trials (table 5) have demonstrated that CRT reduces mortality, decreases heart failure-related hospitalizations, improves functional capacity, and enhances quality of life in appropriately selected patients with reduced left ventricular ejection fraction and prolonged QRS duration (Moss, et al., 2009: 1329–1338; Tang, et al., 2010: 2385–2395).

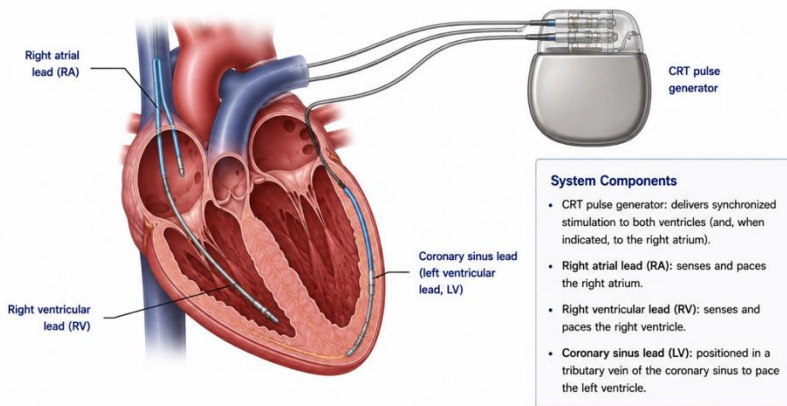


Figure 5: Components of a cardiac resynchronization therapy system

Fundamental Principles of CRT

Under normal physiological conditions, the right and left ventricles are activated synchronously through the His–Purkinje conduction system. In patients with left bundle branch block (LBBB), delayed activation of the left ventricle results in electrical

and mechanical dyssynchrony, which contributes to impaired ventricular function and progressive heart failure (Moss, et al., 2009: 1329–1338).

CRT restores ventricular synchrony (figure 6) through simultaneous or near-simultaneous stimulation of both ventricles, thereby improving cardiac efficiency and mechanical performance (Moss, et al., 2009: 1329–1338).

Table 5: *Landmark Randomized Clinical Trials of Cardiac Resynchronization Therapy*

Trial	Year	Number of Patients	Principal Findings
COMPANION	2004	1520	Reduced mortality and hospitalization
CARE-HF	2005	813	Improved survival
MADIT-CRT	2009	1820	Reduced heart failure events
RAFT	2010	1798	Reduced mortality and heart failure hospitalization

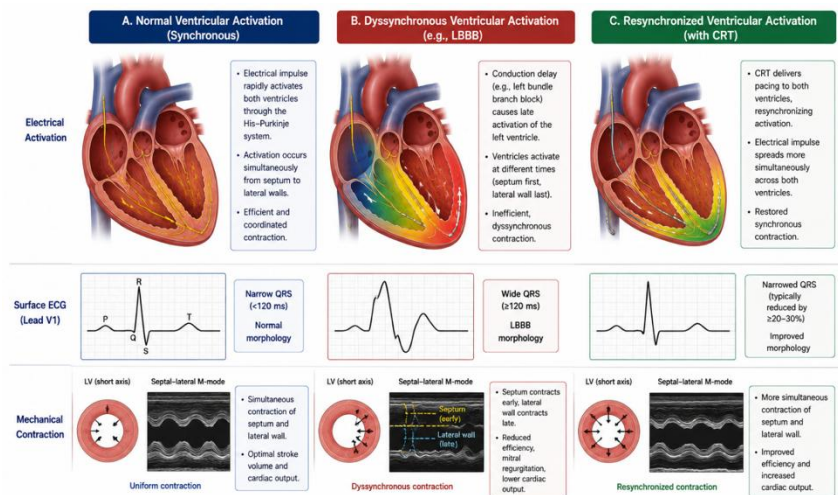


Figure 6: Normal vs. dyssynchronous vs. resynchronized ventricular activation

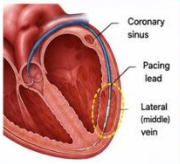
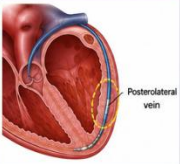
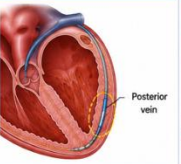
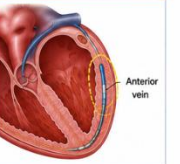
Components of a CRT System

A conventional CRT system typically consists of three leads:

- Right atrial lead
- Right ventricular lead
- Left ventricular lead

The left ventricular lead (figure 7) is generally positioned within a lateral or posterolateral branch of the coronary sinus venous system (Tang, et al., 2010: 2385–2395).

This configuration enables (figure 8) coordinated stimulation of both ventricles and promotes restoration of ventricular synchrony.

Pacing Location	Lateral (Mid-Lateral)	Posterolateral	Posterior	Anterior
				
Typical Lead Position	Mid-lateral wall of the LV via a lateral vein.	Posterolateral (inferolateral) wall of the LV.	Directly posterior wall of the LV.	Anterior wall of the LV via an anterior vein.
Physiologic Rationale	Targets latest activated region in most LBBB patients.	Often close to latest activation in many patients.	May capture latest activation when lateral veins are not available.	Alternative when lateral or posterior veins are not accessible.
Advantages	• Strong evidence for reverse remodeling and clinical benefit. • Associated with greatest improvement in ventricular synchrony.	• Good alternative when mid-lateral veins are not available. • Can provide substantial clinical response.	• Useful when lateral/posterolateral veins are unavailable. • May still achieve resynchronization in selected patients.	• Provides an option in patients with limited suitable veins. • Technically feasible in many anatomies.
Limitations	• Venous anatomy may limit access. • Phrenic nerve stimulation possible.	• May be more proximal with less optimal electrical delay in some patients. • Phrenic nerve stimulation possible.	• Less robust evidence compared with lateral pacing. • May require more lead manipulation.	• Hemodynamically less favorable in some studies. • Often associated with higher capture thresholds.

Comparison of left ventricular pacing locations in CRT. Mid-lateral pacing is preferred and associated with the best clinical outcomes in most patients. Posterolateral, posterior, and anterior pacing are alternative sites when lateral veins are not available or feasible.

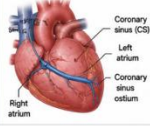
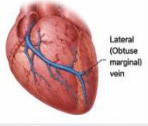
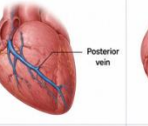
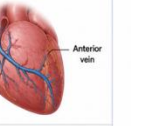
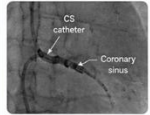
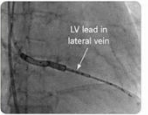
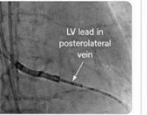
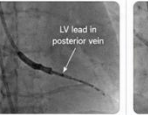
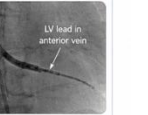
Figure 7: Left ventricular pacing locations in cardiac resynchronization

Clinical Effectiveness of CRT

The COMPANION and CARE-HF trials demonstrated significant reductions in mortality and heart failure-related hospitalization among patients treated with CRT (Moss, et al., 2009: 1329–1338; Tang, et al., 2010: 2385–2395).

Subsequently, the MADIT-CRT and RAFT studies expanded the evidence base by demonstrating clinical benefits in patients with less advanced symptoms and earlier stages of heart failure (Tang, et al., 2010: 2385–2395).

These landmark studies established CRT as a guideline-directed therapy for appropriately selected patients with heart failure and electrical dyssynchrony.

	1. Coronary Sinus Overview	2. Lateral (Obtuse Marginal) Vein	3. Posterolateral Vein	4. Posterior Vein	5. Anterior Vein
Coronary Sinus Anatomy					
Typical Venous Branches	- Coronary sinus runs in the atrioventricular groove. - Receives multiple tributaries draining the LV myocardium. - Primary target for LV lead placement.	- Courses along the lateral wall of the LV. - Most common and preferred target for LV lead. - Typically has a straight course and suitable caliber.	- Runs over the posterolateral surface of the LV. - Alternative when lateral vein is not available. - Often larger caliber.	- Courses on the posterior (inferior) surface of the LV. - Used when lateral and posterolateral veins are unsuitable or absent.	- Courses on the anterior surface of the LV. - Alternative pathway via anterior cardiac veins. - Useful in selected anatomies.
Fluoroscopic Appearance (RAD View)					
Key Points	- CS is the main route for LV lead delivery. - Cannulation performed via right atrial approach.	- Associated with best electrical delay and clinical outcomes. - May provide the most resynchronization benefit.	- Good alternative target. - May be more proximal and result in less optimal delay in some patients.	- May still achieve resynchronization. - Evidence less robust than lateral pacing.	- Feasible in many patients. - Hemodynamically less favorable in some studies.

The coronary sinus and its venous branches provide access to the left ventricular myocardium for lead placement in CRT. Lateral (obtuse marginal) vein is the preferred target, while posterolateral, posterior, and anterior veins are important alternatives.

Figure 8: Coronary sinus anatomy and left ventricular lead pathways in CRT

CRT Non-Response

Despite substantial clinical benefits, approximately 30% of patients undergoing CRT fail to achieve meaningful clinical improvement. This phenomenon is commonly referred to as CRT non-response (Moss, et al., 2009: 1329–1338).

The most frequently reported causes include:

- Myocardial scar burden
- Suboptimal lead positioning
- Atrial fibrillation
- Inadequate biventricular pacing percentage

Identification and correction of these factors remain essential for maximizing CRT effectiveness.

CRT-P versus CRT-D Selection

Patients receiving cardiac resynchronization therapy may be treated with either a CRT-P (Cardiac Resynchronization Therapy–Pacemaker) or a CRT-D (Cardiac Resynchronization Therapy–Defibrillator) system. Device selection should be individualized based on life expectancy, comorbid conditions, risk of sudden cardiac death, and underlying cardiomyopathy etiology (Moss, et al., 2009: 1329–1338; Tang, et al., 2010: 2385–2395).

Patients with ischemic cardiomyopathy generally carry a higher risk of ventricular arrhythmias and are therefore more likely to benefit from CRT-D implantation. In contrast, elderly patients with multiple comorbidities and a lower arrhythmic risk profile may be adequately managed with CRT-P alone (Moss, et al., 2009: 1329–1338).

Recent studies suggest that the incremental benefit of defibrillator therapy may be less pronounced in certain older patient populations, highlighting the importance of individualized decision-making (Tang, et al., 2010: 2385–2395).

Management of CRT Non-Responders

Approximately one-third of CRT recipients experience inadequate clinical improvement despite successful implantation. Management of CRT non-responders requires a systematic evaluation of potentially reversible causes (Moss, et al., 2009: 1329–1338).

Common contributors to non-response include:

- Suboptimal left ventricular lead position
- Myocardial scar tissue
- Atrial fibrillation
- Low biventricular pacing percentage

- Inadequate AV or VV interval optimization

When non-response is identified, device programming should be reassessed, biventricular pacing percentage optimized, and lead revision considered when appropriate.

Multipoint Pacing

Multipoint pacing (MPP) refers to the delivery of pacing stimuli from multiple electrodes located on the left ventricular lead during a single cardiac cycle (Tang, et al., 2010: 2385–2395).

The primary objectives of multipoint pacing are:

- Accelerated left ventricular activation
- Improved electrical synchrony
- Enhanced CRT response

Several studies have suggested that multipoint pacing may be particularly beneficial in patients at high risk for CRT non-response (Tang, et al., 2010: 2385–2395).

Relationship Between Conduction System Pacing and CRT

His Bundle Pacing (HBP) and Left Bundle Branch Area Pacing (LBBAP) are increasingly recognized as complementary or alternative strategies to conventional cardiac resynchronization therapy (Vijayaraman, et al., 2025: 1512–1522).

Particularly with LBBAP, studies have demonstrated:

- Narrower QRS duration
- Lower pacing thresholds
- More physiological ventricular activation

Compared with conventional pacing strategies (Vijayaraman, et al., 2025: 1512–1522).

Emerging evidence suggests that LBBAP may provide outcomes comparable to or superior to traditional CRT in selected patient populations. However, additional randomized clinical trials are required before definitive conclusions can be drawn (Vijayaraman, et al., 2025: 1512–1522).

MRI-Conditional Cardiac Implantable Electronic Devices

Magnetic resonance imaging (MRI) has become one of the most widely utilized advanced imaging modalities in modern medicine. Because patients with cardiac implantable electronic devices (CIEDs) frequently require MRI examinations during their lifetime, the development of MRI-compatible device technology has represented a major milestone in the field of cardiac pacing (Indik, et al., 2017: e97–e153).

Historically, MRI examinations were considered contraindicated in patients with pacemakers or implantable cardioverter-defibrillators due to concerns regarding electromagnetic interference, lead tip heating, inappropriate pacing behavior, device malfunction, and unintended delivery of therapy (Indik, et al., 2017: e97–e153; Nazarian, et al., 2017: 2555–2564).

The introduction of MRI-conditional systems has significantly reduced these risks, allowing MRI examinations to be performed safely under appropriate conditions and standardized protocols (Nazarian, et al., 2017: 2555–2564).

Potential Risks Associated with MRI

Potential complications associated with MRI exposure include:

- Lead tip heating
- Device reprogramming
- Temporary sensing abnormalities

- Inappropriate pacing behavior
- Changes in battery performance

These risks are generally more pronounced in older-generation devices that were not specifically designed for MRI compatibility (Indik, et al., 2017: e97–e153).

Characteristics of MRI-Conditional Systems

MRI-conditional systems incorporate several technological modifications, including:

- Specialized lead designs
- Reduced ferromagnetic content
- Advanced filtering systems
- Dedicated MRI safety software

These features minimize electromagnetic interactions and improve patient safety during MRI examinations.

Contemporary Clinical Approach

Current guidelines support MRI examinations in appropriately selected patients when compatible devices and standardized safety protocols are available (Indik, et al., 2017: e97–e153; Nazarian, et al., 2017: 2555–2564).

Before MRI scanning, the following steps should be performed:

- Device interrogation
- Battery assessment
- Lead evaluation
- Activation of MRI mode

Close collaboration between electrophysiology and radiology teams remains essential for ensuring procedural safety.

Leadless Pacemaker Systems

Lead-related complications and device pocket infections have historically represented important limitations of conventional pacing therapy. To overcome these challenges, leadless pacemaker systems were developed, eliminating both transvenous leads and subcutaneous generator pockets (Reynolds, et al., 2016: 533–541).

In leadless systems, the entire device is contained within a single capsule that is implanted directly into the right ventricle (Reynolds, et al., 2016: 533–541).

Fundamental Design

Leadless pacemaker systems incorporate:

- Battery
- Microprocessor
- Electrode system
- Telemetry module

within a compact self-contained device (Reynolds, et al., 2016: 533–541).

The most widely used leadless pacing platforms currently include the Micra and Aveir systems (Kumar, et al., 2021: 19–24).

Advantages

Major advantages of leadless pacing systems include (Kumar, et al., 2021: 19–24; Reynolds, et al., 2016: 533–541):

- Elimination of pocket infections
- Elimination of lead fracture risk
- Improved cosmetic outcomes
- Reduced risk of pneumothorax

These benefits are particularly relevant in patients at increased risk of infection or vascular access complications (Kumar, et al., 2021: 19–24).

Limitations

Despite their advantages, leadless pacemakers have several limitations (Kumar, et al., 2021: 19–24):

- Limited atrial pacing capabilities
- Inability to provide conventional CRT
- Challenges associated with device retrieval
- Higher cost

These factors currently restrict their application to carefully selected patient populations.

Clinical Outcomes

Multicenter studies have demonstrated high implantation success rates and low complication rates with leadless pacing systems (Kumar, et al., 2021: 19–24; Reynolds, et al., 2016: 533–541).

Long-term follow-up data suggest lower rates of lead-related complications compared with conventional transvenous pacing systems (Kumar, et al., 2021: 19–24).

New-generation systems such as Micra AV and Aveir DR provide atrioventricular synchrony and represent important steps toward dual-chamber leadless pacing. In addition, wireless left ventricular pacing technologies such as WiSE-CRT have shown promising results for completely leadless cardiac resynchronization therapy (El-Chami, et al., 2022: 1207–1215; Kumar, et al., 2021: 19–24).

Conduction System Pacing (CSP)

Conventional right ventricular apical pacing may produce ventricular dyssynchrony during long-term follow-up. Consequently, pacing strategies that directly utilize the native His–Purkinje conduction system have emerged as physiologically attractive alternatives (Chinitz, et al., 2017: 2639–2641).

Conduction system pacing (CSP) currently represents one of the most important developments in physiological pacing and has gained widespread clinical interest (Chinitz, et al., 2017: 2639–2641).

His Bundle Pacing (HBP)

His Bundle Pacing aims to deliver pacing stimuli directly to the His bundle, thereby preserving physiological ventricular activation through the native conduction system (Chinitz, et al., 2017: 2639–2641; Vijayaraman, et al., 2018: 460–468).

Major advantages include (Vijayaraman, et al., 2018: 460–468):

- Physiological ventricular activation
- Narrow QRS complexes
- Preservation of left ventricular function

These characteristics have established HBP as an important physiological pacing strategy.

Left Bundle Branch Area Pacing (LBBAP)

Left Bundle Branch Area Pacing has rapidly emerged as a promising pacing modality. Direct stimulation of the left bundle branch region enables low pacing thresholds and high implantation success rates (Vijayaraman, et al., 2025: 1512–1522).

Several studies have suggested that LBBAP provides greater electrical stability and more favorable chronic pacing parameters than HBP (Liu, et al., 2021: 630399).

CSP in Heart Failure

Recent investigations have suggested that CSP may serve as an alternative to conventional CRT (table 6) in selected patients with heart failure (Zimerman, et al., 2026: 360–368).

The role of LBBAP in heart failure management remains an area of intense clinical research and may significantly influence future pacing strategies (Zimerman, et al., 2026: 360–368).

Selective and Non-Selective His Bundle Pacing

His Bundle Pacing may be classified according to whether pacing activates only the His bundle or both the His bundle and adjacent myocardium (Sharma, et al., 2018: 413–420; Vijayaraman, et al., 2018: 927–947).

Table 6: Comparison of CRT and Conduction System Pacing

Feature	CRT	LBBAP/CSP
Number of leads	3	1
QRS narrowing	High	Very high
Physiological activation	Partial	More physiological
Coronary sinus requirement	Yes	No
Future potential	High	Very high

Selective His Bundle Pacing

In selective His Bundle Pacing, only the His bundle is captured.

Characteristics include (Sharma, et al., 2018: 413–420):

- Preservation of physiological ventricular activation

- Maintenance of native QRS morphology
- Absence of direct myocardial capture

Non-Selective His Bundle Pacing

In non-selective His Bundle Pacing, both the His bundle and adjacent septal myocardium are stimulated.

As a result, a pseudo-delta wave may be observed at the onset of the QRS complex (Sharma, et al., 2018: 413–420).

Both selective and non-selective HBP have demonstrated favorable clinical outcomes.

Left Bundle Branch Area Pacing and Stim-LVAT

One of the most important parameters used to evaluate successful LBBAP implantation is the Stimulus-to-Left Ventricular Activation Time (Stim-LVAT) (Liu, et al., 2021: 630399).

Stim-LVAT is defined as the interval between:

- Delivery of the pacing stimulus
- Peak R-wave activation in leads V5–V6

Short and stable Stim-LVAT values are generally considered indicators of successful left bundle branch capture.

Criteria for Left Bundle Branch Capture

Several electrocardiographic criteria have been proposed to confirm successful left bundle branch capture, including (Liu, et al., 2021: 630399):

- Narrow QRS duration
- Right bundle branch block-like morphology
- Stable Stim-LVAT
- Confirmation through programmed pacing maneuvers

These criteria have become standard tools for evaluating successful LBBAP implantation.

2023 HRS/APHRS/LAHS Guideline Recommendations

The 2023 HRS/APHRS/LAHS Guideline on Cardiac Physiologic Pacing recognizes conduction system pacing as a valuable therapeutic option in multiple clinical scenarios (Chung, et al., 2023: e17–e91).

Particularly, HBP and LBBAP should be considered in:

- Patients requiring substantial ventricular pacing
- Individuals at risk of pacing-induced cardiomyopathy
- Candidates for CRT
- Patients with CRT non-response

These recommendations highlight the expanding role of physiological pacing strategies in contemporary clinical practice.

Remote Monitoring

Remote monitoring has become an integral component of modern cardiac device management (Slotwiner, et al., 2015: e69–100).

Through internet-based communication platforms, device data can be transmitted directly from the patient to healthcare providers, enabling continuous surveillance and more efficient clinical follow-up.

Advantages of Remote Monitoring

Remote monitoring offers several clinical advantages (Slotwiner, et al., 2015: e69–100):

- Earlier detection of complications
- Reduced outpatient clinic visits

- Faster clinical intervention
- Improved patient satisfaction

Arrhythmia Surveillance

Modern devices are capable of automatically detecting and recording numerous arrhythmias, particularly atrial fibrillation.

Remote monitoring systems facilitate early review of these recordings and may contribute to stroke prevention through earlier diagnosis and treatment initiation (Varma & Ricci, 2013: 1885–1895).

Heart Failure Monitoring

Certain contemporary devices continuously evaluate parameters such as:

- Thoracic impedance
- Heart rate variability
- Physical activity level

These measurements may help identify impending heart failure decompensation before overt clinical deterioration occurs (Varma & Ricci, 2013: 1885–1895).

Such technologies are expected to play an increasingly important role in proactive heart failure management.

Artificial Intelligence, Digital Health, and Future Perspectives

Permanent cardiac pacing systems have evolved beyond simple electrical therapeutic devices and increasingly function as sophisticated digital health platforms capable of generating large volumes of physiological data. Artificial intelligence (AI) and machine learning technologies are becoming increasingly important in the interpretation of these data streams (Johnson, et al., 2018: 2668–2679).

Modern devices continuously record numerous parameters, including activity levels, heart rate variability, arrhythmia burden, thoracic impedance, and sleep-related metrics. AI algorithms can analyze these large datasets and support clinical decision-making processes (Herman, et al., 2026: 145–156; Johnson, et al., 2018: 2668–2679).

AI-Assisted Arrhythmia Analysis

Artificial intelligence has achieved significant advances in arrhythmia detection and classification.

Contemporary systems can identify atrial fibrillation, ventricular tachycardia, and other rhythm disturbances with high diagnostic accuracy (Herman, et al., 2026: 145–156).

Potential clinical applications include:

- Early detection of silent atrial fibrillation
- Stroke risk assessment
- Reduction of inappropriate device therapies

Early Prediction of Heart Failure Deterioration

One of the major goals of modern device technology is the early identification of heart failure worsening.

AI-supported algorithms can simultaneously evaluate:

- Thoracic impedance trends
- Physical activity levels
- Heart rate variability
- Nocturnal heart rate

and generate alerts before overt decompensation develops (Singhal & Cowie, 2020: 125–132). Such strategies may contribute to reductions in heart failure hospitalization rates.

Personalized Pacing Strategies

Future pacing systems are expected to operate according to highly individualized physiological profiles.

AI algorithms may optimize pacing parameters for each patient, potentially enabling (Krittanawong, et al., 2017: 2657–2664):

- Reduced energy consumption
- Longer battery longevity
- More physiological ventricular activation

Digital Twin Technologies

Digital twin technology refers to the creation of a virtual cardiac model that accurately represents an individual patient's anatomy and physiology.

Different pacing strategies can be simulated within this virtual environment to identify the most effective therapeutic approach before clinical implementation (Corral-Acero, et al., 2020: 4556–4564).

This technology may become particularly valuable in complex electrophysiological cases.

Fully Wireless Cardiac Devices

The continuing evolution of leadless pacing technologies has stimulated the development of entirely wireless cardiac device systems.

Future platforms may enable wireless communication among atrial, ventricular, and left ventricular components, facilitating completely leadless cardiac rhythm management (El-Chami, et al., 2022: 1207–1215).

Potential advantages include:

- Reduced infection risk
- Fewer mechanical complications
- Improved patient comfort

Biological Pacemakers

Biological pacemaker technology aims to create naturally functioning impulse-generating tissue through genetic engineering and cellular therapies (Rajesh & Francis, 2006: 1–5).

Although experimental studies have produced promising results, further research is required before biological pacemakers can be incorporated into routine clinical practice (Rajesh & Francis, 2006: 1–5).

Conclusion

Permanent cardiac pacing systems have undergone extraordinary technological evolution over the past six decades. From the first-generation pacemakers to today's sophisticated digital platforms, remarkable advances have been achieved in device reliability, battery longevity, lead technology, and patient monitoring (Vijayaraman, et al., 2025: 1512–1522).

Modern pacing systems have become essential tools not only for the treatment of symptomatic bradycardia but also for cardiac resynchronization therapy, conduction system pacing, remote patient monitoring, and arrhythmia management.

The development of MRI-conditional devices, leadless pacemakers, and conduction system pacing techniques has introduced safer and more physiological therapeutic options. Furthermore, artificial intelligence–assisted analytics and digital health technologies have substantially enhanced the diagnostic and prognostic value of cardiac implantable electronic devices (Herman, et al., 2026: 145–156; Johnson, et al., 2018: 2668–2679).

Future innovations—including fully wireless cardiac systems, biological pacemakers, and AI-guided personalized pacing strategies—are expected to transform clinical practice even further. In light of these developments, permanent cardiac pacing systems remain one of the most dynamic and rapidly evolving fields within contemporary cardiovascular medicine (Jastrzebski, et al., 2022: 4161–4173).

Recent advances in conduction system pacing, leadless technologies, and remote monitoring have transformed pacing systems into tools that are not only therapeutic but also diagnostic and prognostic. The integration of artificial intelligence and digital health applications is expected to further expand the role of personalized and physiological pacing strategies in the years ahead. (Chung, et al., 2023: e17–e91; Jastrzebski, et al., 2022: 4161–4173; Johnson, et al., 2018: 2668–2679; Slotwiner, et al., 2015: e69–100).

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CARDIAC PACING MODES, THE NBG CODE SYSTEM, AND CONDUCTION MANAGEMENT ALGORITHMS

VOLKAN YILMAZ¹

Introduction

Cardiac pacing technology has evolved from simple electrical stimulators designed solely to prevent bradycardia into complex microcomputer systems that integrate with the autonomic nervous system, optimize hemodynamics, and prevent pathological arrhythmias. In this chapter, the fundamental operating principles and modes of pacemakers, their hemodynamic effects, sensor technologies, and advanced management algorithms aimed at minimizing unnecessary ventricular pacing will be comprehensively discussed.

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Evolution and Structure of the NBG (NASPE/BPEG) Code System

In modern cardiac pacing technology, defining the functional capacities of devices through a standardized terminology has become essential following the acquisition of multi-chamber pacing and physiological sensing capabilities by pacemaker systems. In response to this requirement, the North American Society of Pacing and Electrophysiology (NASPE) and the British Pacing and Electrophysiology Group (BPEG) established a joint committee in 1987 and developed the "NBG" (NASPE/BPEG Generic) code system (Bernstein, et al., 1987: 794–799).

Subsequently, advancing technology, increased microprocessor capacities, and particularly the integration of cardiac resynchronization therapy (CRT) into clinical practice for heart failure management necessitated a revision of this system. The "2002 Revised NBG Code," approved in October 2001 and implemented in 2002, consists of a standardized five-position (letter) structure capable of more comprehensively articulating the contemporary capabilities of these devices (Bernstein, et al., 2002: 260–264).

Position I (Chamber Paced): O (None), A (Atrium), V (Ventricle), D (Dual - A+V).

Position II (Chamber Sensed): O (None), A (Atrium), V (Ventricle), D (Dual).

Position III (Response to Sensing): O (None), I (Inhibited - pacing is withheld upon sensing an intrinsic event), T (Triggered - pacing is triggered in response to a sensed event), D (Dual - both triggered and inhibited).

Position IV (Rate Modulation): O (None), R (Rate-Responsive). This position indicates the capability of the device to

automatically adjust the pacing rate in response to physical exertion or metabolic demands.

Position V (Multisite Pacing): O (None), A (Atrium), V (Ventricle), D (Dual). Scenarios involving pacing from multiple sites within the same chamber, such as biventricular pacing (CRT), are denoted in this position.

Basic Pacing Modes and Their Hemodynamic Effects

The optimal selection of the pacing mode is the most critical factor concerning the electrical compatibility between the patient's intrinsic conduction system and the device. Inappropriate mode selection can predispose the patient to recurrent syncope episodes or the triggering of secondary heart failure.

AAI Mode (Atrial Demand Pacing): It performs sensing and pacing exclusively at the atrial level. The device inhibits pacing upon sensing an intrinsic P wave. By preserving the natural conduction pathways through the atrioventricular (AV) node, His bundle, and Purkinje system, it provides maximum contribution to left ventricular filling, making it the most physiological mode from a hemodynamic perspective. However, due to the absence of ventricular sensing and pacing capabilities, it leaves the patient vulnerable to the risk of fatal asystole in the event of developing AV block (Kuniewicz, et al., 2023).

VVI Mode (Ventricular Demand Pacing): The electrode is positioned at the right ventricular apex or septum. Pacing is inhibited upon sensing an intrinsic R wave. It is hemodynamically disadvantageous as it completely abolishes AV synchronization. Apical or septal pacing from the right ventricle leads to a left bundle branch block (LBBB)-like activation pattern, causing electrical and mechanical dyssynchrony; this condition can lead to the deterioration of left ventricular systolic functions over time.

Additionally, "Pacemaker Syndrome," characterized by impaired venous return and reduced cardiac output as a result of the atria contracting against closed tricuspid and mitral valves, may develop. In clinical practice, it is predominantly preferred in patients with permanent atrial fibrillation (AF) (Glikson, et al., 2021: 3427–3520; Sweeney, et al., 2003: 2932–2937).

DDD Mode (Dual-Chamber Pacing): It possesses sensing and pacing functions in both chambers. Following a sensed or paced atrial event, the device initiates the programmed "AV delay" interval. If intrinsic ventricular conduction does not occur within this period, it paces the ventricle, ensuring optimal AV synchronization. Its primary disadvantage is the potential for high atrial rates to be transmitted to the ventricle in a 1:1 ratio during atrial tachyarrhythmias, leading to hemodynamically dangerous tachycardias. In contemporary devices, this is prevented through advanced automatic mode switch algorithms (Kumagai, et al., 2004: 2281–2289).

VDD Mode: It operates with a single lead placed in the right ventricle, harboring "floating" ring electrodes corresponding to the atrial level. It has the capacity to sense atrial activity but cannot perform atrial pacing. It offers the possibility of physiological AV synchronization with a single electrode for patients with preserved sinus node function but who have AV block. Although procedure-related complication rates are relatively low, it will be insufficient to meet clinical needs if the patient develops sinus bradycardia in subsequent years, as it cannot pace the atrium (Gillis, et al., 2006: 697–705).

Rate-Responsive Pacing and Sensor Technologies (The Letter "R")

In a significant proportion of patients with sinus node dysfunction (SND), "chronotropic incompetence," a condition

characterized by the inability of the heart rate to reach physiological limits (age- and sex-specific targets) during exertion, is observed. To optimize exercise capacity in this patient group, sensor systems (R adaptation) that detect the metabolic demands of the organism and modulate the pacing rate accordingly are utilized (Dell'Orto, Valli, & Greco, 2004: 137–145).

Activity Sensors (Accelerometer): These rely on the physical movements, mechanical vibrations, and acceleration of the body. They provide an extremely rapid response to the initial phase of exercise. Their primary limitation is their dependence on physical motion; they cannot generate an adequate chronotropic response during exertions where the torso remains relatively stable, such as on a bicycle ergometer or during isometric exercises, or in situations of mental stress (Dell'Orto, Valli, & Greco, 2004: 137–145; Glikson, et al., 2021: 3427–3520).

Minute Ventilation (MV) Sensor: It determines metabolic demand by calculating the respiratory rate and tidal volume via intrathoracic impedance measurements. Transthoracic impedance decreases during inspiration and increases with expiration. It provides a highly physiological heart rate response during the peak phase of exercise and the recovery period (Dell'Orto, Valli, & Greco, 2004: 137–145; Glikson, et al., 2021: 3427–3520).

Myocardial Contractility Sensor (Closed Loop Stimulation - CLS): This is an advanced sensor technology capable of directly evaluating the effects of the autonomic nervous system on the inotropic state of the heart. The system measures regional myocardial impedance changes in the early systolic phase via the right ventricular electrode. As the contraction rate (dP/dt) and force of the myocardium increase, the blood volume at the electrode tip decreases and tissue contact increases; this results in an elevation of local impedance. Through this mechanism, it responds with a

simultaneous physiological rate increase not only to physical activity but also to clinical situations that generate autonomic discharge, such as acute mental stress, emotional reactions, and fever. Additionally, in patients with a history of vasovagal syncope, it demonstrates high efficacy in preventing syncopal episodes by detecting the compensatory myocardial hypercontractility that develops immediately prior to the vasodepressor response at an early stage, thereby increasing the pacing rate and breaking the hypotension-bradycardia cascade (Dell'Orto, Valli, & Greco, 2004: 137–145; Galderisi, Esposito, & Trimarco, 2017: 1717–1719).

Atrial Tachyarrhythmia Management: Automatic Mode Switching

In devices programmed in DDD or VDD modes, the conduction of atrial tachyarrhythmias, such as atrial fibrillation (AF) or atrial flutter, to the ventricle at high rates can compromise the patient's hemodynamic stability. To prevent this hemodynamic deterioration, "Automatic Mode Switch" (AMS) algorithms have been developed.

The fundamental rationale of these algorithms is to switch the device to an asynchronous mode (e.g., DDI or VVI)—where atrial activity tracking (P-wave tracking) is suspended—upon the detection of a pathological atrial rhythm, and to ensure it reverts to a synchronous (DDD) mode once the arrhythmia terminates. While executing this transition, pacemaker systems utilize complex mathematical filtering mechanisms to avoid being influenced by electrical noise, premature atrial complexes (PACs), or physiological sinus tachycardias. For instance, rather than directly measuring consecutive P-P intervals, many contemporary devices calculate a dynamic "Filtered Atrial Rate Interval (FARI)." If the sensed intrinsic atrial cycle length is shorter than the calculated FARI value, the FARI value is decremented by a specific number of milliseconds

(e.g., 39 ms); if the intrinsic cycle is longer, the FARI value is incrementally increased (e.g., 23 ms). Through this dynamic window, isolated atrial extrasystoles are prevented from abruptly elevating the filtered rate (Glikson, et al., 2021: 3427–3520; Laperche, et al., 1999: 336–341).

When this calculated filtered rate exceeds the device's programmed "Atrial Tachycardia Detection Rate," the system transitions to a safe asynchronous mode. To preclude the development of symptomatic bradycardia secondary to a precipitous drop in ventricular rate during mode switching, the ventricular pacing rate is gradually reduced (e.g., by adding milliseconds to each cardiac cycle) to the programmed base rate. Once the atrial tachyarrhythmia terminates, the device automatically reverts to the synchronous (DDD) mode. In most modern devices, "Post-Mode Switch Overdrive Pacing (PMOP)" algorithms are activated to prevent post-AF bradycardia symptoms that may emerge following the termination of an AF episode; following the transition to the synchronous mode, this system paces the heart at a rate above the programmed base rate for a brief duration (e.g., 10 minutes), thereby preventing potential sinus pauses (Glikson, et al., 2021: 3427–3520; Laperche, et al., 1999: 336–341).

Atrial Fibrillation (AF) Prevention Algorithms

Atrial pacing modes can proactively suppress the triggering of atrial tachyarrhythmias when programmed with appropriate parameters, rather than merely treating bradycardia (Glikson, et al., 2021: 3427–3520). Contemporary pacemaker systems incorporate specific algorithms developed for this purpose:

Atrial Overdrive Pacing: The device suppresses the atrial tissue by continuously applying pacing (overdrive pacing) at a rate a few beats above the patient's intrinsic sinus rate. Through this mechanism, the formation of premature atrial complexes (PACs),

which play a triggering role in atrial tachyarrhythmias, is suppressed (Glikson, et al., 2021: 3427–3520).

PAC Pause Suppression: Many atrial fibrillation (AF) episodes are triggered as a consequence of a prolonged "compensatory pause" (short-long-short cycle) occurring subsequent to an atrial extrasystole. Upon detecting premature atrial activity, this algorithm prevents the occurrence of the aforementioned long pause period by instantaneously increasing the pacing rate, thereby stabilizing the cardiac rhythm (Glikson, et al., 2021: 3427–3520).

Ventricular Rate Stabilization in Conducted AF: During an AF episode, impulses conducted via the atrioventricular (AV) node result in the manifestation of highly irregular R-R intervals (long and short cycles). By continuously calculating these cycle length fluctuations, the system adapts the ventricular pacing rate to the mean intrinsic ventricular rate; thus, it optimizes cardiac output by minimizing R-R irregularity (Glikson, et al., 2021: 3427–3520).

The AAI vs. DDD Pacing Controversy and Clinical Realities

In patients diagnosed with isolated sinus node dysfunction (SND) and intact atrioventricular (AV) conduction, the adequacy of the AAI pacing mode alone has been one of the fundamental topics of debate in the electrophysiology literature for many years. The AAI mode was theoretically considered an ideal option due to its preservation of physiological AV conduction via a single electrode and its prevention of the mechanical dyssynchrony that unnecessary right ventricular pacing could induce.

However, the randomized DANPACE (*Danish Multicenter Randomized Study on Single Lead Atrial Pacing vs. Dual Chamber Pacing*) trial, which evaluated SND patients, demonstrated that there was no statistically significant difference between the AAI and DDD groups in terms of long-term mortality, development of heart failure,

or risk of stroke. Conversely, it was shown that the incidence of paroxysmal atrial fibrillation (AF) was significantly higher in the AAIR group and, more importantly, that more than 20% of the patients (at an annual rate of approximately 1.7%) were required to undergo reoperation to upgrade the device mode to DDDR as a consequence of AV block developing over time (Nielsen, et al., 2011: 686–696).

In the extended 8.9-year long-term follow-up of the DANPACE cohort using national registries, it was also confirmed that the rate of transition (upgrade) to the DDDR mode among patients initially implanted with an AAI device reached 4.5% annually, and that this risk increased exponentially as the follow-up duration prolonged (Brandt, et al., 2017: 1981–1987). Similar findings were reported in the long-term Kraków retrospective cohort analysis exceeding 12-15 years; it was observed that approximately 40% of the patients who initially received an isolated AAI implant required revision (upgrade) surgery in the ensuing period due to the development of AF (approximately 21%) or high-degree AV block (approximately 16%). The procedure of adding a new ventricular lead to the system via a secondary surgical intervention resulted in total occlusion of the subclavian vein in 11% of the cases and dramatically increased the risk of device infection (Kuniewicz, et al., 2023).

In light of the acquired evidence-based data, isolated AAI implantation has been largely abandoned in modern cardiology practice; primary dual-chamber (DDD/R) device implantation as a proactive approach against progressive conduction system diseases in SND patients has become the gold standard in contemporary guidelines (Gillis, et al., 2006: 697–705).

Pacing Mode Selection and Decision Algorithms in Light of Clinical Trials

In modern cardiology practice, device and mode selection is built upon evidence-based strategies aimed not only at correcting the current bradycardia presentation but also at minimizing the long-term risks of developing heart failure and atrial tachyarrhythmias.

Sinus Node Dysfunction (SND): In SND patients with intact atrioventricular (AV) conduction, the primary choice is the DDD(R) mode. However, since it has been proven that unnecessary right ventricular (RV) apical pacing impairs left ventricular systolic functions and significantly increases the risk of atrial fibrillation (AF), algorithms that strictly "minimize ventricular pacing" must be activated within the device. It has been clearly demonstrated in the literature that this proactive strategy reduces the incidence of AF development by up to 40% compared to conventional pacing (Sweeney, et al., 2007: 1000–1008).

Atrioventricular (AV) Block: In patients with preserved sinus rhythm and permanent or intermittent (paroxysmal) 2nd- and 3rd-degree AV block, the standard approach to maintain physiological AV synchronization is the DDD(R) mode. Even in complex patient populations where intrinsic conduction returns intermittently, the use of algorithms that minimize ventricular pacing is highly safe from a clinical standpoint and effectively eliminates the unnecessary RV pacing burden (Thibault, et al., 2015).

Pacing in the Setting of Heart Failure: In patients with a reduced left ventricular ejection fraction (LVEF <40%) who are anticipated to be subjected to a high burden (>20%) of right ventricular pacing (RV pacing) due to bradycardia or conduction block, conventional RV pacing may deepen (exacerbate) the clinical presentation of heart failure. Since large-scale clinical trials have demonstrated that the risk of heart failure-related hospitalization

rises linearly as the cumulative right ventricular pacing burden increases, it is strongly recommended that these patients be primarily directed toward Cardiac Resynchronization Therapy (CRT) or conduction system pacing (His bundle / left bundle branch area pacing) to prevent cardiac mechanical dyssynchrony (Sweeney, et al., 2003: 2932–2937).

AV Block and Permanent AF: In atrial fibrillation presentations where the atria have irreversibly (permanently) lost both their electrical and mechanical functions, atrial pacing or sensing capabilities do not provide a hemodynamic benefit. Therefore, the application of the VVIR (rate-adaptive ventricular pacing) mode with a single ventricular electrode is indicated in this patient group.

Algorithms Preventing Unnecessary Ventricular Pacing

Although conventional dual-chamber (DDD) pacing optimally provides AV synchronization, programmed fixed AV delay intervals may prevent the emergence of the patient's intrinsic conduction. A high burden (cumulatively $\geq 20\%$) of right ventricular apical pacing can lead to inter-ventricular electrical and mechanical dyssynchrony, causing deterioration in left ventricular systolic functions and adverse myocardial remodeling, and significantly increases the risk of secondary atrial fibrillation (AF) (Sweeney, et al., 2003: 2932–2937). To prevent this, "advanced management algorithms" have been designed that operate the device primarily in the AAI mode and provide ventricular pacing only when a critical conduction block develops (Gillis, et al., 2006: 697–705). Clinical trials have proven that these proactive algorithms reduce the cumulative ventricular pacing burden from the 90% range down to 1-10% levels (e.g., the SAVE-PACe, ANSWER, and CAN-SAVE R trials) and decrease the risk of AF development by approximately 40% (Sweeney, et al., 2007: 1000–1008; Thibault, et al., 2015).

These algorithms fundamentally operate based on three main electrophysiological principles (Casavant & Belk, 2021: 4625–4632; Chen, et al., 2014: 1595–1602):

Dynamic Mode-Switching (AAI ↔ DDD) Algorithms: The device monitors the patient's intrinsic rhythm in the physiological AAI/R mode. In cases where intrinsic AV conduction is interrupted, the system does not immediately transition to a permanent DDD mode. For instance, following a non-conducted isolated atrial activation, the device delivers a life-saving "backup" pacing to the ventricle with a very short AV delay (e.g., 80 milliseconds). In the event of progression of the conduction block (e.g., block observed in 2 out of the last 4 cardiac cycles or the detection of consecutive blocked atrial waves), the device makes a full transition to the permanent dual-chamber DDD/R mode to ensure patient safety. Even while operating in the DDD mode, the system periodically (e.g., every 100 beats, at specific hours, or at time intervals extending from 1 minute to 16 hours) tests for the resolution (return) of intrinsic conduction by temporarily inhibiting ventricular pacing. If conduction is detected, it immediately reverts to the physiological AAI mode. Furthermore, these algorithms can also monitor marked 1st-degree AV block (excessively prolonged PR intervals) and pathological ventricular pauses using specific parameters.

AV Hysteresis (AV Interval Extension) Algorithms: The device continuously operates in the DDD/R mode at baseline. However, to allow the emergence of the patient's intrinsic His-Purkinje conduction, it periodically extends the programmed AV delay interval up to 400-450 milliseconds. When an intrinsic R wave is sensed within this extended "conduction search window," the device inhibits ventricular pacing, permitting the utilization of intrinsic AV conduction. If conduction fails to occur, the system reverts to the standard AV delay interval and delivers pacing.

Low-Rate Backup VVI Pacing: Rather than making an immediate transition to the DDD mode upon the loss of intrinsic conduction, algorithms exist that provide pacing in the VVI mode at a very low rate (e.g., 15 beats/minute below the programmed lower rate limit) for a transient period. This slow backup pacing (e.g., at a rate of 35 bpm) protects the patient from the risk of syncope while simultaneously providing a physiological time window for the heart to recover its intrinsic rhythm and autonomic conduction. If intrinsic AV conduction does not return within the specified timeframe, the device permanently transitions to the DDD mode.

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PACEMAKER IMPLANTATION TECHNIQUES

VELİ AKIN¹

Introduction and Scope

Permanent pacemaker implantation is a cornerstone therapy for symptomatic bradyarrhythmias, yet the procedural details of implantation remain decisive determinants of pocket hematoma, lead dislodgement, venous complications, infection, and long-term lead survival (Burri, et al., 2021: 983–1008; Glikson, et al., 2021: 3427–3520). Contemporary guidance therefore treats pacemaker implantation not as a simple hardware insertion, but as a structured surgical-electrophysiological intervention that begins with preprocedural risk stratification and ends only after stable acute electrical performance and an uncomplicated wound course are secured (Baddour, et al., 2024: e201–e216; Glikson, et al., 2021: 3427–3520).

Infection prevention provides the conceptual framework for modern implantation technique because most clinically relevant device infections originate from perioperative contamination or from re-entry into previously manipulated pockets, and because

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reoperations, pocket hematoma, temporary pacing, renal dysfunction, diabetes, and prior device infection consistently increase risk.[3-6] This perspective explains why high-quality implantation technique emphasizes meticulous patient selection, minimization of bleeding, adherence to full sterile standards, careful choice of venous access, precise lead fixation, and disciplined postoperative surveillance rather than focusing narrowly on fluoroscopic lead positioning alone (Glikson, et al., 2021: 3427–3520; Polyzos, Konstantelias, & Falagas, 2015: 767–777).

The present chapter addresses conventional transvenous pacemaker implantation in adults and then separately discusses pediatric and epicardial implantation, where body size, congenital anatomy, future growth, and lifetime lead burden materially alter the operative strategy. The in-text citations are numbered in Vancouver style, and the full reference list at the end identifies the corresponding source and PubMed identifier for each reference (Burri, et al., 2021: 983–1008; Glikson, et al., 2021: 3427–3520; Shah, et al., 2021: 1738–1769).

Preoperative assessment and antithrombotic planning

Preoperative evaluation and preparation

Preoperative assessment should first reconfirm the pacing indication, define the required pacing mode, and determine whether the patient needs a single-chamber, dual-chamber, or alternative system, because each additional intracardiac component incrementally increases procedural complexity and complication burden.[1,2] The same evaluation should identify factors that may favor a nonstandard strategy, such as absent superior venous access, prior device infection, end-stage renal disease, hemodialysis dependence, complex congenital anatomy, prior tricuspid surgery, or anticipated need to avoid a transvenous system altogether (Baddour,

et al., 2024: e201–e216; Blomstrom-Lundqvist & Ostrowska, 2021: iv11–19; Glikson, et al., 2021: 3427–3520).

A thorough history and examination should specifically document prior central venous instrumentation, previous pacemaker or ICD procedures, ipsilateral breast or thoracic surgery, current temporary pacing, indwelling central lines, chronic skin disease, diabetes, chronic obstructive pulmonary disease, renal insufficiency, immunosuppressive therapy, and any evidence of fever or systemic infection, because these variables shape both access planning and infection-prevention strategy (Blomstrom-Lundqvist & Ostrowska, 2021: iv11–19; Polyzos, Konstantelias, & Falagas, 2015: 767–777). Suspected venous occlusion of the subclavian or innominate system warrants targeted preprocedural imaging with venography or chest computed tomography, which may avert failed puncture attempts, arterial injury, or an unplanned change in approach after sterile preparation has already begun (Blomstrom-Lundqvist & Ostrowska, 2021: iv11–19; Glikson, et al., 2021: 3427–3520).

Active infection is a contraindication to elective implantation, and the procedure should be postponed until the patient has been afebrile for at least 24 hours and the infectious focus has been addressed, because preprocedural fever is independently associated with subsequent device infection (Baddour, et al., 2024: e201–e216; Blomstrom-Lundqvist & Ostrowska, 2021: iv11–19). Temporary transvenous pacing should be avoided whenever feasible because it roughly doubles infection risk, and, when temporary support is unavoidable, alternatives such as pharmacologic chronotropic support, transthoracic pacing, or a jugular rather than femoral temporary route deserve consideration in selected cases (Blomstrom-Lundqvist & Ostrowska, 2021: iv11–19; Glikson, et al., 2021: 3427–3520).

Complex revisions, upgrades, and difficult first implants are best planned with explicit consideration of operator experience and institutional volume, because procedural duration, early re-intervention, and lower-volume environments correlate with higher device infection rates (Blomstrom-Lundqvist & Ostrowska, 2021: iv11–19; Polyzos, Konstantelias, & Falagas, 2015: 767–777). In practical terms, a technically demanding pacemaker implantation is often safer when performed or directly supervised by an experienced implanter than when repeated failed attempts by a less experienced operator prolong tissue trauma, fluoroscopy, and the interval from incision to closure (Blomstrom-Lundqvist & Ostrowska, 2021: iv11–19; Burri, et al., 2021: 983–1008).

For patients with very high risk of infection or with impossible or undesirable upper-extremity venous access, the preoperative discussion should include alternative systems such as leadless pacing or epicardial pacing, because preventing a difficult or infected transvenous implant is preferable to rescuing one later by extraction and reimplantation. This decision is particularly relevant in patients with severe renal disease, prior device infection, hostile venous anatomy, or anticipated repeated interventions over a long lifetime horizon (Baddour, et al., 2024: e201–e216; Blomstrom-Lundqvist & Ostrowska, 2021: iv11–19; Glikson, et al., 2021: 3427–3520; Shah, et al., 2021: 1738–1769).

Anticoagulant and Antiplatelet Management

Management of anticoagulant and antiplatelet therapy is central to pacemaker implantation because clinically significant pocket hematoma is not merely a nuisance complication but a major driver of later device infection. In BRUISE CONTROL, clinically significant pocket hematoma independently increased the risk of later device infection, and contemporary guidance accordingly treats hematoma avoidance as one of the most important perioperative

objectives (Baddour, et al., 2024: e201–e216; Birnie, et al., 2013: 2084–2093; Glikson, et al., 2021: 3427–3520).

For patients receiving a vitamin K antagonist, uninterrupted warfarin within the therapeutic INR range is generally superior to interruption with heparin bridging, because BRUISE CONTROL showed a marked reduction in clinically significant pocket hematoma with continued warfarin compared with bridging. Heparin bridging should therefore be avoided in routine pacemaker surgery unless an exceptional situation exists that materially changes the balance of risk (Birnie, et al., 2013: 2084–2093; Blomstrom-Lundqvist & Ostrowska, 2021: iv11–19; Glikson, et al., 2021: 3427–3520).

For direct oral anticoagulants, the evidence supports a more individualized strategy, because BRUISE CONTROL-2 and the combined BRUISE CONTROL analyses demonstrated similarly low hematoma rates with either continued or briefly interrupted DOAC therapy, rather than clear superiority of one universal approach. In practice, the decision should incorporate renal function, the specific DOAC, concomitant antiplatelet therapy, procedural bleeding risk, and whether the case is a straightforward first implant or a higher-risk revision or upgrade (Birnie, et al., 2018: 3973–3979; Essebag, et al., 2019: e007545; Glikson, et al., 2021: 3427–3520)

Dual antiplatelet therapy substantially increases pocket hematoma risk, particularly when a P2Y₁₂ inhibitor is continued through the procedure. When clinically permissible, clopidogrel is generally discontinued at least 5 days before surgery, ticagrelor at least 3 days before surgery, and prasugrel at least 7 days before surgery, while aspirin is often continued, especially for low-bleeding-risk first implants (Blomstrom-Lundqvist & Ostrowska, 2021: iv11–19; Glikson, et al., 2021: 3427–3520).

The most challenging scenario is a patient with a recent coronary stent or recent acute coronary syndrome who still carries high thrombotic risk, because elective pacemaker implantation may need to be postponed rather than forcibly performed during the highest-risk DAPT interval. When postponement is impossible, the case should be approached with explicit multidisciplinary agreement, meticulous hemostasis, and the recognition that bleeding and thrombotic hazards have both been amplified by necessity rather than by choice (Blomstrom-Lundqvist & Ostrowska, 2021: iv11–19; Glikson, et al., 2021: 3427–3520).

Operative Environment and Venous Access

Surgical Setup and Sterilization

Pacemaker implantation should be performed in an environment that satisfies the sterility standards required for other implanted surgical devices, whether the procedure occurs in an operating room or in an electrophysiology laboratory that has been configured and maintained to equivalent infection-control standards. Adequate room cleaning, proper ventilation, positive-pressure air handling, filtered air exchange, controlled traffic, and restricted access are not peripheral administrative details but integral components of the sterile chain that protects the pocket and leads from inoculation (Blomstrom-Lundqvist & Ostrowska, 2021: iv11–19).

Out-of-hours implantation, when avoidable, should be minimized because it has been associated with higher infection risk, probably reflecting a convergence of fatigue, staffing variation, and institutional workflow rather than a single isolated technical factor. By the same logic, complex cases benefit from a deliberate setup that includes functioning fluoroscopy, a pacing system analyzer, a full lead and sheath inventory, backup venous-access tools, temporary pacing capability, and a pre-agreed bailout plan before skin incision

is made (Blomstrom-Lundqvist & Ostrowska, 2021: iv11–19; Burri, et al., 2021: 983–1008).

Systemic intravenous antibiotic prophylaxis is the standard of care and should be administered before incision, because randomized evidence demonstrated a significant reduction in device infection with preprocedural antibiotics (Blomstrom-Lundqvist & Ostrowska, 2021: iv11–19; de Oliveira, et al., 2009: 29–34; Glikson, et al., 2021: 3427–3520). In routine adult pacemaker implantation, cefazolin 1–2 g intravenously or an equivalent anti-staphylococcal agent is typically given within 30–60 minutes before incision, whereas vancomycin, when indicated by severe beta-lactam allergy or institutional MRSA epidemiology, should be started earlier, usually 90–120 minutes before incision (Blomstrom-Lundqvist & Ostrowska, 2021: iv11–19; Glikson, et al., 2021: 3427–3520).

Routine postoperative prophylactic antibiotics do not reduce infection after pacemaker implantation and should not substitute for correct timing of preprocedural prophylaxis, meticulous tissue handling, and careful hemostasis. Antibiotic stewardship is therefore fully consistent with optimal device care, because prolonged postoperative antibiotics expose patients to unnecessary drug effects without correcting technical causes of infection such as hematoma, re-entry, or contamination (Blomstrom-Lundqvist & Ostrowska, 2021: iv11–19; Glikson, et al., 2021: 3427–3520; Lee, et al., 2017: 559–565)

Skin antisepsis should preferentially use chlorhexidine-alcohol rather than povidone-iodine-alcohol, consistent with current guideline recommendations and broader surgical evidence favoring chlorhexidine-based preparation. If hair removal is required, electric clipping rather than razor shaving should be used to reduce skin microabrasions and bacterial burden at the incision field.

(Blomstrom-Lundqvist & Ostrowska, 2021: iv11–19; Glikson, et al., 2021: 3427–3520).

Venous Access

The three standard venous routes for transvenous pacemaker lead implantation are the cephalic vein, the axillary vein, and the subclavian vein, and the optimal choice depends on anatomy, operator expertise, device type, and the balance among immediate access success, pleuropulmonary safety, and long-term lead durability (Burri, et al., 2021: 983–1008; Glikson, et al., 2021: 3427–3520). No single route is ideal in every patient, but contemporary evidence has shifted practice away from routine blind intrathoracic subclavian puncture and toward extrathoracic axillary access or direct-vision cephalic access whenever feasible (Benz, et al., 2019: 121–129; Glikson, et al., 2021: 3427–3520).

The cephalic approach is attractive because it allows lead introduction under direct vision and largely avoids pneumothorax, hemothorax, arterial puncture, and brachial plexus injury associated with needle-based Seldinger puncture. Meta-analytic data indicate that cephalic cutdown is associated with less pneumothorax and less lead failure than subclavian puncture, supporting its continued value as a low-complication access strategy (Benz, et al., 2019: 121–129).

The principal limitation of cephalic access is technical failure, particularly in obese patients, in those with small or tortuous veins, and when multiple leads must be introduced through a vein of modest caliber. In the ESC guideline summary of comparative data, cephalic access had a lower success rate than axillary or subclavian access, and this limitation explains why many operators favor a hybrid strategy in which cephalic cutdown is attempted first and supplemented by axillary puncture if necessary (Atti, et al., 2020: 661–671; Chan, Kwong, & Cheong, 2017: 1193–1197).

Subclavian puncture remains familiar and efficient, but it traverses the intrathoracic pleural region and the costoclavicular space, which explains its higher rates of pneumothorax and later lead damage from mechanical compression. Indeed, the ESC guideline cites a 7.8-fold increased risk of pneumothorax with subclavian access, and long-term observational data identify subclavian puncture as a predictor of pacemaker lead failure relative to axillary access (Chan, Kwong, & Cheong, 2017: 1193–1197; Glikson, et al., 2021: 3427–3520).

The axillary route has emerged as the preferred puncture-based technique because it is extrathoracic, reduces pleural complications, and appears to improve long-term lead preservation by avoiding the costoclavicular crush zone (Atti, et al., 2020: 661–671; Chan, Kwong, & Cheong, 2017: 1193–1197). Randomized and observational studies of ultrasound-guided axillary access have shown high success rates, low complication rates, and shorter venous-access times than cephalic cutdown, while maintaining the safety advantages expected from direct vessel visualization (Charles, et al., 2023: 4847–4858).

The practical implication of current evidence is that ultrasound-guided axillary puncture should be strongly considered whenever the operator is trained in the technique, particularly for dual-lead implants, difficult body habitus, or when cephalic cutdown is unlikely to be successful (Atti, et al., 2020: 661–671; Charles, et al., 2023: 4847–4858). Cephalic access remains excellent when a suitable vein is readily identified, whereas intrathoracic subclavian puncture should be reserved for situations in which safer extrathoracic options are impractical or have failed (Charles, et al., 2023: 4847–4858; Glikson, et al., 2021: 3427–3520).

Pocket Creation and Transvenous Lead Implantation

Pocket Creation Techniques

The standard pacemaker pocket is a left or right prepectoral infraclavicular subcutaneous pocket created bluntly and sharply over the pectoral fascia, sized to accommodate the generator without undue tension but without leaving excessive dead space (Burri, et al., 2021: 983–1008; Glikson, et al., 2021: 3427–3520). Subcutaneous pockets are appropriate for most patients, while submuscular pockets may be preferred in very thin individuals, in patients with prior Twiddler-type manipulation or cosmetic concerns, and in selected reoperative scenarios where tissue coverage is limited (Glikson, et al., 2021: 3427–3520).

Pocket location and pocket handling matter because the pocket itself is a major source of complications, especially hematoma and infection.[1,5] For this reason, careful dissection along stable tissue planes and meticulous point-by-point hemostasis are more important than speed, and the implanter should not proceed to generator insertion until even minor venous oozing has been controlled (Baddour, et al., 2024: e201–e216; Burri, et al., 2021: 983–1008; Glikson, et al., 2021: 3427–3520).

No randomized trial has established a universal superiority of subcutaneous over submuscular pockets in terms of major outcomes, but submuscular implantation may require deeper sedation and can make later generator replacement more painful and technically demanding (Glikson, et al., 2021: 3427–3520). Accordingly, pocket depth should be individualized rather than ritualized, with the overriding aim of achieving secure tissue coverage while minimizing bleeding, discomfort, and future re-entry difficulty (Burri, et al., 2021: 983–1008; Glikson, et al., 2021: 3427–3520).

Pocket irrigation with sterile saline at the end of the procedure is reasonable because it removes debris and dilutes residual contamination, but adding antibiotics to the irrigant has not been shown to reduce device infection (Glikson, et al., 2021: 3427–3520). This distinction is clinically important, because irrigation can support sound wound preparation, whereas antibiotic pocket bathing should not be used as a surrogate for inadequate sterile technique or for poorly controlled bleeding (Baddour, et al., 2024: e201–e216; Glikson, et al., 2021: 3427–3520).

In selected high-risk cases, particularly replacement, revision, and upgrade procedures, an absorbable antibacterial envelope may reduce major CIED infection. However, the pacemaker subgroup benefit in WRAP-IT was not clearly established, so envelope use in standard pacemaker implantation should remain targeted rather than routine and should be reserved for patients with a compelling aggregate risk profile such as renal failure, diabetes, chronic lung disease, or repeated pocket re-entry (Burri, et al., 2021: 983–1008; Glikson, et al., 2021: 3427–3520; Tarakji, et al., 2019: 1895–1905).

Lead Placement and Threshold Testing

For atrial pacing, the right atrial appendage remains the preferred conventional site because it usually provides stable lead seating and satisfactory sensing and pacing characteristics (Burri, et al., 2021: 983–1008; Glikson, et al., 2021: 3427–3520). Alternative atrial sites can be used when anatomy or prior surgery demands it, but lateral atrial placement may provoke phrenic nerve capture, and nonstandard atrial pacing sites have not shown consistent routine benefit in preventing atrial fibrillation (Glikson, et al., 2021: 3427–3520).

For ventricular pacing, the right ventricular apex remains a reproducible and technically straightforward target, whereas mid-

septal or other nonapical sites may be selected to reduce dyssynchrony or to avoid specific anatomic constraints (Burri, et al., 2021: 983–1008; Glikson, et al., 2021: 3427–3520) When septal placement is intended, multiple fluoroscopic projections are essential because conventional fluoroscopy and ECG criteria alone are only moderately accurate in distinguishing true septal from anterior or free-wall positions (Pang, et al., 2014: 495–504).

This limitation is not trivial because a lead that appears “septal” on a single projection may ultimately be demonstrated by computed tomography or three-dimensional echocardiography to occupy a different right ventricular surface. Therefore, right atrial and right ventricular leads should be assessed in at least orthogonal fluoroscopic views, and the operator should retain a low threshold for revising lead position when the electrogram, paced QRS morphology, or mechanical behavior is discordant with the intended site (Burri, et al., 2021: 983–1008; Glikson, et al., 2021: 3427–3520; Pang, et al., 2014: 495–504).

Active-fixation leads facilitate selective site pacing and are particularly useful when septal or nonappendage atrial positions are desired, whereas passive-fixation leads remain suitable for conventional appendage or apical placement (Glikson, et al., 2021: 3427–3520; Kistler, et al., 2005: 903–909). Active fixation, however, requires greater awareness of atrial wall fragility and potential perforation, especially when a lead is directed toward the thin right atrial free wall (Burri, et al., 2021: 983–1008; Glikson, et al., 2021: 3427–3520).

Once the helix has been deployed, the lead should not be judged solely by the first instantaneous threshold reading because both ventricular and atrial active-fixation leads may show rapid early improvement in capture threshold and sensing over the first several minutes. Studies of acute lead behavior have shown that screw-in

leads can display an initially higher threshold that falls promptly, while P-wave and R-wave amplitudes often improve during the first 20–30 minutes after fixation, making premature repositioning occasionally unnecessary (Kistler, et al., 2005: 903–909).

Current of injury is a useful adjunct during active-fixation lead implantation because it reflects tissue engagement and predicts acute lead stability. In right atrial active-fixation implantation, combining a preserved current of injury with adequate P-wave sensing improved prediction of optimized chronic performance, reinforcing the value of waiting briefly after fixation rather than making immediate binary judgments (Saxonhouse, Conti, & Curtis, 2005: 412–417).

Threshold testing itself should be performed in a standardized fashion, commonly at a pulse width of 0.4 ms, by progressively lowering output until loss of consistent capture and then re-establishing an appropriate safety margin above the measured threshold. Stable fluoroscopic position, secure lead slack, reproducible sensing, and absence of diaphragmatic capture should be confirmed before the lead is accepted, because good electrical numbers alone do not compensate for poor mechanical seating or excessive tension (de Buitelir, et al., 1990: 999–1003; Kistler, Liew, & Mond, 2006: 226–230).

Acute Measurements: Threshold, Impedance, and R/P-wave Amplitude

The three acute electrical variables that matter at implantation are capture threshold, lead impedance, and intrinsic sensing amplitude, because together they assess tissue contact, conductor continuity, and the device's ability to recognize native myocardial depolarization. None of these variables should be interpreted in isolation, and the implanter should evaluate them as a functional triad integrated with fluoroscopic appearance and lead

stability (Burri, et al., 2021: 983–1008; Chen, et al., 2019: 1279–1286).

Although acceptable acute targets vary somewhat by chamber, lead design, and manufacturer, contemporary practical targets for active-fixation leads commonly include an atrial P-wave of at least 2 mV, atrial threshold of 1.0 V or less, and impedance between roughly 300 and 1000 ohms, whereas ventricular leads are commonly accepted when R-wave amplitude exceeds 5 mV and impedance lies within approximately 300–1500 ohms together with a low capture threshold. These values are best understood as pragmatic implant goals rather than immutable biologic cutoffs, but failure to achieve them should prompt re-examination of position, helix engagement, lead connection, or possible perforation (Chen, et al., 2019: 1279–1286).

Acute sensing behavior is dynamic, and de Buitelir and colleagues demonstrated that both atrial and ventricular sensing amplitudes may improve during the first 30 minutes after implantation, particularly when baseline signals are suboptimal but mechanically satisfactory. For this reason, a lead that is electrically borderline but fluoroscopically excellent may justify brief observation and repeat measurement before the operator commits to additional manipulation (de Buitelir, et al., 1990: 999–1003; Kistler, et al., 2005: 903–909).

Lead impedance also changes early after implantation, typically declining from initial values over the first hours to weeks as the electrode–tissue interface matures. This expected early fall underscores why marked outlier values are more concerning than modest temporal drift and why trend interpretation is more informative than any single isolated impedance number during early follow-up (Kistler, Liew, & Mond, 2006: 226–230).

A useful procedural synthesis is that the “best” implant site is not merely the site with the lowest threshold at one moment, but the site where all acute variables are concordant, the lead is mechanically secure, current of injury behaves appropriately if relevant, and the operator can create durable slack without kinking or undue tension. This integrated view reduces unnecessary repositioning while also avoiding the opposite error of accepting a seemingly satisfactory lead that later fails because its electrical adequacy was achieved at the expense of mechanical instability (Chen, et al., 2019: 1279–1286; Saxonhouse, Conti, & Curtis, 2005: 412–417).

Closure and Postoperative Management

Wound Closure Techniques

After all leads have been connected and final testing has been completed, the pocket should be reinspected carefully for bleeding, because even minor residual oozing can expand into a clinically significant postprocedural hematoma once anticoagulation is resumed or blood pressure rises after sedation wears off. Hemostasis, not the choice of skin suture alone, is therefore the most important determinant of early wound evolution (Baddour, et al., 2024: e201–e216; Glikson, et al., 2021: 3427–3520).

Evidence comparing skin-closure methods in pacemaker implantation remains limited, and available studies have not shown a clear reduction in infection or hematoma with one routine suture strategy over another. In a large observational study, continuous and interrupted closure techniques yielded similar pocket infection rates, and in the PRO-PACE randomized trial, absorbable and non-absorbable skin sutures produced comparable cosmetic and clinical outcomes (Abboud, et al., 2022: 203–208; Datta, 2020: 44–48).

Accordingly, layered closure with careful obliteration of dead space, a tension-free skin line, and surgeon familiarity with the chosen material is more defensible than dogmatic adherence to a single named suture technique. The purpose of closure is to support healing biology after good surgery rather than to rescue poor hemostasis or an oversized pocket through tighter stitching (Abboud, et al., 2022: 203–208; Datta, 2020: 44–48).

Postoperative Care

Immediate postoperative management should include rhythm and device interrogation, hemodynamic observation, assessment of the wound for swelling or expanding ecchymosis, and reevaluation of pacing and sensing parameters before discharge (Archontakis, et al., 2023: 471–481; Edwards, Varma, & Pitcher, 2005: 92–96, discussion 96–97). Patient education at this stage is essential and should explicitly cover the warning signs of infection, hematoma, lead-related symptoms, and the timeline for wound review and device follow-up (Baddour, et al., 2024: e201–e216; Blomstrom-Lundqvist & Ostrowska, 2021: iv11–19).

Routine chest radiography after uncomplicated pacemaker implantation is not universally necessary, particularly when venous access was cephalic or clearly extrathoracic and intraoperative parameters are fully satisfactory. Nevertheless, chest imaging remains appropriate when subclavian or axillary puncture has been difficult, when pleural injury is suspected, when there is respiratory compromise, or when lead course or final position is uncertain (Burri, et al., 2021: 983–1008; Edwards, Varma, & Pitcher, 2005: 92–96, discussion 96–97)

Selected patients can be discharged the same day after elective device implantation, provided that bleeding is controlled, electrical performance is stable, postprocedural observation is uneventful, and an organized pathway for urgent recontact and early

follow-up exists. Meta-analytic and contemporary observational data indicate that same-day discharge is feasible and safe in appropriately selected patients, although frailty, social limitations, difficult access, early hematoma, or pacing dependence may justify overnight monitoring.

The traditional advice of prolonged arm immobilization after pacemaker implantation has become less rigid because available evidence suggests that early mobilization does not meaningfully increase lead displacement when the lead is well fixed and the implant itself is mechanically sound. This does not eliminate the need for prudent activity modification, but it supports a more balanced recommendation centered on avoiding extreme repetitive shoulder stress rather than promoting unnecessary fear of all ipsilateral arm movement (Archontakis, et al., 2023: 471–481).

Pediatric and Epicardial Implantation

Pediatric Transvenous Implantation

Pacemaker implantation in children differs fundamentally from adult implantation because the operator must anticipate somatic growth, small-caliber veins, congenital heart disease, altered chamber geometry, future surgeries, and the cumulative burden of decades of lead management. The 2021 PACES consensus therefore emphasizes individualized system choice based not only on the immediate rhythm indication, but also on patient size, venous reserve, anatomy, and long-term strategy (Shah, et al., 2021: 1738–1769).

In larger children and adolescents with suitable anatomy, transvenous pacing is often feasible and may provide favorable pacing thresholds and easier generator management, but it carries a long-term risk of venous occlusion, thrombosis, and valvular interaction that becomes especially relevant in the smallest patients.

Long-term data from children weighing less than 10 kg show that transvenous pacing can be performed successfully in specialized centers, yet subclavian vein occlusion remains a meaningful late complication and explains why many teams still prefer an epicardial approach in infants and very small children (Kwak, Cho, & Kim, 2019: 1127–1133; Shah, et al., 2021: 1738–1769).

When a pediatric transvenous system is chosen, ultrasound-guided axillary access is particularly attractive because it may reduce pneumothorax and hemothorax while preserving a controlled extrathoracic venous entry. Clark and colleagues showed that ultrasound-guided axillary venous access is feasible for pediatric and adult congenital lead implantation, providing a useful extension of contemporary adult access principles into congenital practice (Clark, et al., 2019: 166–170).

Pediatric and Epicardial Implantation

Epicardial pacing remains the preferred strategy in neonates, infants, many small children, and patients with complex congenital anatomy or absent safe transvenous routes. This preference reflects not only vessel size but also the desire to preserve central venous pathways and avoid long-term transvenous complications during growth and future surgery (Konta, et al., 2016: e003422; Shah, et al., 2021: 1738–1769)

Epicardial implantation is performed surgically and may use sternotomy, thoracotomy, subxiphoid, thoroscopic, or subcostal approaches depending on anatomy and surgical context, with the generator commonly placed in a subcostal or abdominal location in smaller children to provide soft-tissue coverage. The left subcostal approach has been described as a simpler alternative to thoracotomy in selected children and can yield acceptable thresholds with less extensive chest-wall disruption (Kwak, Cho, & Kim, 2019: 1127–1133).

Historically, epicardial pacing was associated with higher lead failure and poorer thresholds than endocardial pacing, but the advent of steroid-eluting epicardial leads substantially improved performance and longevity. Even so, pediatric series continue to show that lead revision and generator replacement are common over time, meaning that every epicardial implant should be planned with future re-entry in mind rather than as a one-time operation (Kwak, Cho, & Kim, 2019: 1127–1133; Odum, et al., 2008: 1412–1416).

Cohen and colleagues reported 1-, 2-, and 5-year epicardial lead survival rates of 96%, 90%, and 74%, respectively, in pediatric patients, while more contemporary infant and neonatal series confirm acceptable mid- and long-term outcomes but a persistent need for repeat surgery as the child grows or hardware reaches end of life. The practical consequence is that electrode site selection, lead routing, generator-pocket security, and excess lead management should all be optimized at the first operation because revision in a growing child is not a remote possibility but an expected component of lifetime care (Kwak, Cho, & Kim, 2019: 1127–1133; Zhao, et al., 2022: 825–833).

A balanced modern view is therefore that epicardial pacing is not an inferior fallback but an anatomically appropriate primary strategy for small children and many congenital cases, whereas transvenous pacing becomes progressively more attractive as body size increases and venous risk decreases. The best pediatric implantation technique is the one that secures dependable pacing today while preserving the greatest number of safe procedural options for tomorrow (Odum, et al., 2008: 1412–1416; Shah, et al., 2021: 1738–1769).

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CARDIAC DEVICE PROGRAMMING AND FOLLOW-UP A PRACTICAL OVERVIEW FOR CLINICIANS

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Introduction

Cardiac implantable electronic devices (CIEDs) play a central role in the management of patients with bradyarrhythmias, tachyarrhythmias, and heart failure. Over the past decades, advances in device technology have significantly improved patient survival, symptom control, and quality of life. Modern devices are capable not only of delivering pacing therapy but also of monitoring cardiac rhythms, storing diagnostic information, and providing life-saving treatments for malignant ventricular arrhythmias (Glikson, et al., 2021: 3427–3520).

The long-term success of device therapy depends not only on proper implantation but also on appropriate programming and regular follow-up. Device programming should be individualized according to the patient's clinical condition, underlying rhythm disorder, and therapeutic goals. Similarly, systematic follow-up is

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essential to ensure proper device function, identify complications, and optimize therapy throughout the lifespan of the device (Varma, et al., 2010: 325–332).

Device Types and Basic Components

Cardiac implantable electronic devices include permanent pacemakers, implantable cardioverter-defibrillators (ICDs), and cardiac resynchronization therapy (CRT) systems. Permanent pacemakers are primarily used for the treatment of symptomatic bradycardia resulting from sinus node dysfunction or atrioventricular conduction abnormalities. ICDs are designed to detect and terminate potentially fatal ventricular arrhythmias. CRT devices improve ventricular synchrony in selected patients with heart failure and conduction disturbances.

All devices consist of two major components: the pulse generator and the leads. The pulse generator contains the battery, microprocessor, memory, and telemetry systems. It functions as the control center of the device, continuously analyzing cardiac activity and determining whether therapy is required. The leads establish communication between the generator and the heart, allowing the delivery of pacing impulses and the detection of intrinsic electrical signals (F. M. Kusumoto, et al., 2019: e382–e482).

Understanding the interaction between these components is fundamental for effective programming and follow-up.

Principles of Device Programming

Device programming refers to the adjustment of specific parameters that determine how the device responds to intrinsic cardiac activity. The primary objectives of programming are to maintain adequate heart rate, preserve physiological cardiac function, avoid unnecessary pacing, and maximize battery longevity.

One of the most important parameters is the lower rate limit. This setting defines the minimum heart rate maintained by the device. If the patient's intrinsic heart rate falls below this value, pacing is initiated. Most patients are programmed between 50 and 70 beats per minute, although individual requirements may vary (Ferrick, et al., 2023: e92–e144).

Another critical parameter is the upper tracking rate. In dual-chamber devices, this setting determines the highest ventricular rate that can follow sensed atrial activity. An inappropriately low upper tracking rate may limit exercise capacity, whereas excessively high settings may increase the risk of rapid ventricular pacing.

The atrioventricular (AV) delay represents the interval between atrial activation and ventricular pacing. Proper AV timing is essential for maintaining optimal ventricular filling and preserving cardiac output. Programming decisions should balance physiological timing with the need to minimize unnecessary ventricular pacing (Ferrick, et al., 2023: e92–e144).

Modern devices incorporate sophisticated algorithms that automatically adapt to changing physiological conditions. These algorithms may promote intrinsic conduction, reduce right ventricular pacing, improve rate responsiveness, and optimize battery performance.

Sensing and Capture

The effectiveness of any pacing system depends on adequate sensing and capture. Sensing refers to the device's ability to detect intrinsic electrical activity within the heart. Accurate sensing allows the device to appropriately distinguish native cardiac events from periods requiring pacing support.

Sensing amplitudes are generally evaluated during every follow-up visit. Typical atrial sensing values exceed 1 mV, while

ventricular sensing amplitudes are usually greater than 5 mV. Reduced sensing may result from lead displacement, fibrosis at the electrode-tissue interface, or lead malfunction (Varma, et al., 2010: 325–332).

Capture occurs when a pacing stimulus successfully depolarizes the myocardium and produces a cardiac contraction. Capture thresholds represent the minimum amount of energy required to achieve consistent myocardial depolarization. Since thresholds may change over time due to lead maturation, medications, metabolic disturbances, or disease progression, periodic assessment is necessary.

Key parameters routinely evaluated during follow-up include in:

- Atrial sensing amplitude

- Ventricular sensing amplitude

- Atrial pacing threshold

- Ventricular pacing threshold

- Lead impedance

- Battery status

Appropriate safety margins should always be maintained when programming pacing outputs to ensure reliable capture under varying physiological condition (Hayes, Asirvatham, & Friedman, 2021).

Pacemaker Follow-Up

Routine follow-up is essential for maintaining device performance and patient safety. The first post-implant assessment is usually performed within several weeks of implantation. During this

visit, clinicians evaluate wound healing, confirm lead stability, and reassess pacing thresholds.

Subsequent follow-up intervals depend on device type, patient characteristics, and manufacturer recommendations. Most pacemaker patients undergo device interrogation every six to twelve months. More frequent evaluations may be necessary in patients with complex programming requirements or nearing battery depletion.

A standard follow-up visit includes review of several important parameters as well as:

- Battery longevity estimates

- Lead impedance measurements

- Sensing performance

- Capture thresholds

- Percentage of pacing

- Stored arrhythmia episodes

- Device alerts

Device diagnostics provide valuable information regarding rhythm disturbances, pacing burden, and changes in device performance. These data often assist clinicians in making therapeutic decisions beyond simple device management (Ellenbogen, et al., 2011).

Remote monitoring has become an increasingly important component of follow-up care. Continuous transmission of device information allows earlier identification of lead problems, battery depletion, atrial fibrillation, and other clinically significant events. Numerous studies have demonstrated improved clinical outcomes and reduced healthcare utilization with remote monitoring programs.

ICD Programming and Follow-Up

Implantable cardioverter-defibrillators are designed to prevent sudden cardiac death by detecting and treating ventricular tachyarrhythmias. Programming strategies aim to maximize arrhythmia detection while minimizing inappropriate therapies.

ICDs typically classify arrhythmias into different detection zones according to heart rate. Slower ventricular tachycardias may be treated with anti-tachycardia pacing (ATP), whereas faster ventricular arrhythmias often require high-energy shock therapy.

Appropriate ICD programming includes careful consideration of:

- Detection rate thresholds

- Detection duration

- ATP sequences

- Shock energy settings

- Redetection criteria

- Discrimination algorithms

One of the most important goals of modern ICD programming is reducing inappropriate shocks. Inappropriate therapies may result from atrial fibrillation, sinus tachycardia, lead noise, electromagnetic interference, or oversensing. Such shocks are associated with reduced quality of life and increased morbidity.

During follow-up, stored electrograms should be reviewed carefully to determine the appropriateness of delivered therapies and identify opportunities for programming optimization (Ellenbogen, 2022).

Cardiac Resynchronization Therapy

Cardiac resynchronization therapy has become a cornerstone of treatment for selected patients with heart failure and ventricular dyssynchrony. CRT improves coordination between the right and left ventricles, leading to improved cardiac performance and symptom relief.

Successful CRT therapy depends not only on patient selection and lead placement but also on appropriate device programming. AV and VV timing optimization may enhance ventricular filling and improve hemodynamic performance (Ellenbogen, 2022).

Follow-up evaluations focus on several important areas:

Percentage of biventricular pacing

Lead performance

Heart failure symptoms

Echocardiographic response

Arrhythmia burden

A high percentage of effective biventricular pacing is essential for achieving optimal clinical benefit. Factors that reduce CRT delivery, such as atrial fibrillation or frequent premature ventricular contractions, should be identified and treated appropriately.

Troubleshooting Common Device Problems

Device-related complications may occur despite appropriate implantation and programming. Early recognition of these issues is essential to prevent adverse outcomes.

Loss of capture occurs when pacing stimuli fail to depolarize the myocardium. Potential causes include lead dislodgement, battery

depletion, metabolic abnormalities, or rising pacing thresholds. Management depends on identifying and correcting the underlying cause (F. Kusumoto, 2021).

Undersensing refers to failure of the device to detect intrinsic cardiac activity. This may result in inappropriate pacing despite the presence of native cardiac rhythm. Conversely, oversensing occurs when non-cardiac signals are incorrectly interpreted as intrinsic cardiac activity, potentially leading to inappropriate inhibition of pacing or unnecessary ICD therapies.

Lead-related complications remain an important concern during long-term follow-up. Significant changes in lead impedance may suggest lead fracture or insulation failure. Sudden alterations in sensing or pacing thresholds should prompt further investigation.

Clinicians should remain alert for symptoms suggesting device malfunction, including:

- Syncope

- Presyncope

- Dizziness

- Palpitations

- Worsening heart failure symptoms

- Unexpected ICD shocks

Prompt evaluation of such symptoms is necessary to ensure patient safety.

Battery Management and Generator Replacement

Battery longevity is influenced by multiple factors, including pacing burden, programmed outputs, lead characteristics, and device type. Modern devices provide estimates of remaining battery life based on current usage patterns.

As battery depletion progresses, devices typically enter an elective replacement indicator (ERI) phase. During this period, device replacement should be planned before progression to end-of-service status. Timely generator replacement prevents interruption of therapy and reduces the risk of emergency procedures (F. Kusumoto, 2021).

Careful monitoring of battery status is therefore an essential component of routine follow-up.

Future Directions

The field of cardiac rhythm management continues to evolve rapidly. Leadless pacemakers have emerged as an alternative to traditional transvenous systems in selected patients. Conduction system pacing, including His bundle pacing and left bundle branch area pacing, offers the potential for more physiological ventricular activation.

Advances in remote monitoring, artificial intelligence, and automated device algorithms are expected to further improve patient care. These innovations may allow earlier detection of clinical deterioration, more personalized programming strategies, and improved long-term outcomes (Dubner, et al., 2012: 278–293).

Conclusion

Cardiac device programming and follow-up are essential components of contemporary cardiovascular care. Successful management requires a thorough understanding of device function, programming principles, sensing and capture assessment, arrhythmia management, and troubleshooting techniques. Regular follow-up, combined with appropriate use of remote monitoring and individualized programming strategies, ensures optimal device performance and maximizes clinical benefit for patients living with cardiac implantable electronic devices.

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CARDIAC RESYNCHRONIZATION THERAPY

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Introduction

Cardiac resynchronization therapy (CRT) is a strongly evidence-based device therapy that provides symptomatic improvement, reverses left ventricular (LV) remodeling, reduces heart failure hospitalizations, and decreases mortality by achieving ventricular synchronization in selected patients with heart failure (HF)-associated ventricular dyssynchrony. Alongside the conventional biventricular pacing (BiV-CRT) approach, physiological conduction system pacing (CSP) modalities—such as His bundle pacing (HBP) and left bundle branch area pacing (LBBAP)—have rapidly evolved in recent years, establishing their role in clinical practice as alternatives that more closely replicate the natural ventricular activation pattern compared to traditional CRT. In this chapter, we will comprehensively address the subject based on the scientific literature, encompassing the pathophysiological foundations of CRT, patient selection, implantation techniques,

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optimization, management of non-responders, and future perspectives.

Pathophysiology of Heart Failure and Dyssynchrony

In heart failure, ventricular dyssynchrony is divided into electrical and mechanical discordance. Electrical dyssynchrony is most commonly associated with left bundle branch block (LBBB) morphology and is characterized by the prolongation of the QRS duration (typically ≥ 130 -150 ms). In LBBB, while the septal region of the left ventricle activates early, the lateral and posterolateral walls demonstrate significant delay. This delay leads to an intraventricular conduction disturbance and results in inhomogeneous ventricular depolarization. Mechanical dyssynchrony, on the other hand, is the condition in which the lateral wall has not yet contracted or contracts late during the contraction of the early-activated septal segments. This discordance reduces the effective stroke volume of the LV, exacerbates mitral regurgitation, and creates heterogeneity in regional wall stress (Chung, et al., 2023: e17–e91; Glikson, et al., 2021: 3427–3520).

While myocardial workload decreases in early-activated regions, wall stress increases in late-activated regions. This condition leads to an increase in myocardial oxygen consumption, a decrease in contractile reserve, and progressive LV dilatation. As demonstrated in animal models and clinical studies, chronic dyssynchrony triggers neurohumoral activation (the renin-angiotensin-aldosterone system and sympathetic nervous system), activates inflammatory pathways, and accelerates myocardial fibrosis. Consequently, LV ejection fraction (LVEF) declines, heart failure symptoms worsen, and the risk of mortality increases (Chung, et al., 2023: e17–e91).

Similar "pacing-induced cardiomyopathy" mechanisms come into play in situations where right ventricular (RV) pacing is

utilized at a high rate (over 20-40%). RV apical pacing bypasses the physiological His-Purkinje system, leading to an abnormal activation pattern. This, in turn, has been associated with long-term LV dysfunction and HF. By correcting this dyssynchrony through biventricular stimulation, CRT synchronizes ventricular contraction, reduces mitral regurgitation, decreases LV end-systolic volume, and promotes reverse remodeling. Reverse remodeling manifests itself as an increase in LVEF, a reduction in LV dimensions, and an enhancement in myocardial efficiency. These effects directly contribute to symptomatic relief (improvement in NYHA class) and prognostic benefit (reduction in mortality and hospitalizations) (Dan, 2021: e55).

At the pathophysiological level, the cellular effects of dyssynchrony are also significant. Heterogeneous stress leads to impairments in calcium handling, gap junction remodeling, and alterations in action potential duration. When synchronization is achieved with CRT, these cellular abnormalities partially resolve, and myocardial gene expression (e.g., SERCA2a, phospholamban) approaches normal. These molecular-level improvements explain the long-term duration of the clinical benefit. Chronic dyssynchrony also accelerates HF progression by leading to myocardial perfusion heterogeneity and subendocardial ischemia. Dyssynchrony also paves the way for irreversible remodeling by increasing myocardial apoptosis and fibrosis (Moss, et al., 2009: 1329–1338).

CRT Indications and Patient Selection

The 2021 ESC Guidelines on Cardiac Pacing and CRT have clearly classified CRT indications. In patients with symptomatic heart failure (NYHA class II-IV), LVEF $\leq 35\%$, sinus rhythm with LBBB morphology, and a QRS duration ≥ 150 ms, CRT is a Class I indication (level of evidence A). There is a Class IIa recommendation for LBBB morphology with a QRS duration of

130-149 ms. For non-LBBB morphology (RBBB or non-specific intraventricular conduction delay) with a QRS $\geq$ 150 ms, it is a Class IIa indication; in narrower QRS durations, the benefit is limited and it is not routinely recommended. The EchoCRT study demonstrated that CRT may be potentially harmful in patients with a QRS <130 ms (Tang, et al., 2010: 2385–2395).

The most critical point in patient selection is the administration of optimal medical therapy (Guideline-Directed Medical Therapy - GDMT) for at least 3 months. GDMT should include an ARNI (or ACEi/ARB), beta-blockers, mineralocorticoid receptor antagonists (MRA), SGLT2 inhibitors, and, if necessary, ivabradine or other agents. Reversible causes of HF (ischemia, valvular disease, uncontrolled tachyarrhythmias, toxic agents) must be ruled out. Comorbidities (chronic kidney disease, COPD, diabetes, AF), life expectancy, frailty, and patient preference should be taken into consideration (Bristow, et al., 2004: 2140–2150).

Women, patients with non-ischemic cardiomyopathy, a wider QRS (>150 ms), and more pronounced mechanical dyssynchrony respond better to CRT. In patients with atrial fibrillation, an AV junction ablation strategy is a Class IIa recommendation to ensure adequate biventricular pacing (over 95-98%). The 2023 HRS/APHRS/LAHRS Guideline on Physiologic Pacing also emphasizes conduction system pacing alternatives and states that, in addition to conventional BiV-CRT, CSP can be utilized in cases of anatomical challenges or inadequate response (Ruschitzka, et al., 2013: 1395–1405).

Multimodality assessment is recommended in patient selection: ECG (QRS morphology and duration), echocardiography (mechanical dyssynchrony parameters: septal flash, apical rocking, strain imaging), cardiac MRI (scar burden), and occasionally nuclear imaging. The response rate is lower in ischemic patients with a high

scar burden. CRT should be avoided in patients with advanced comorbidities and a life expectancy of <1 year (Vijayaraman, et al., 2023: 228–241).

The Importance of QRS Morphology and Duration

QRS duration and morphology are among the strongest predictors of CRT response. The highest clinical and echocardiographic response rates are observed with true LBBB morphology, as defined by the Strauss criteria, and a QRS ≥ 150 ms. In these patients, the reduction in mortality, the decrease in hospitalizations, and the rate of super-responders (an increase in LVEF to >50% or an improvement to NYHA class I) are pronounced. In non-LBBB morphologies (RBBB, non-specific), the response rate decreases to 30-40%; however, there may still be a limited benefit when the QRS is ≥ 150 ms (Gerra, et al., 2025: 159–169).

Significant benefit has been demonstrated in patients with LBBB and a wide QRS in landmark trials such as MADIT-CRT, RAFT, COMPANION, and CARE-HF. The long-term follow-up results of the RAFT trial have confirmed that CRT-D reduces mortality. QRS narrowing (paced QRS <130-140 ms) is considered a surrogate for a good response. The EchoCRT trial demonstrated that CRT may be futile or potentially harmful in patients with a narrow QRS (<130 ms). The benefit increases as the QRS duration increases; at ≥ 150 ms, the response rate is over 70%. The combination of morphology and duration is the most practical and cost-effective criterion in patient selection. The observation that women can derive benefit even at narrower QRS durations has brought sex-specific approaches to the forefront (Wijesuriya, et al., 2023: 1054095).



QRS duration ≥ 120 ms, Dominant S wave in lead V1, Broad monophasic R wave in lateral leads (I, aVL, V5-6), Absence of Q waves in lateral leads, Prolonged R wave peak time > 60 ms in leads V5-6

Left Ventricular Lead Implantation and Coronary Sinus Anatomy

The LV lead is classically placed epicardially via the coronary sinus (CS) and cardiac veins. The coronary sinus is a venous structure coursing in the posterior atrioventricular groove, with its ostium located in the posteroseptal region of the right atrium near the Thebesian valve. Individual variations in venous anatomy are very common: lateral and posterolateral veins are ideal targets, but tortuosity, valvular structures, stenosis, or absence can complicate implantation. Venography is an indispensable part of implantation (Sapp, et al., 2024: 212–220).

The optimal LV lead position should be the late-activated lateral or posterolateral wall (basal-mid segment). Apical or anterior placement should be avoided because these reduce hemodynamic benefit and may increase mortality. A Q-LV interval (the time from the LV lead to the onset of the QRS) of >95 - 110 ms is targeted; this correlates with an increase in hemodynamic indices (dP/dt max). Quadripolar leads reduce the risk of phrenic nerve stimulation, high

thresholds, and dislocation by offering multiple pacing vectors (Cleland, et al., 2005: 1539–1549).

In the event of implantation failure (5-10%), a surgical epicardial lead, an endocardial LV lead, or a transition to CSP may be considered. During the procedure, radiation exposure, contrast use, and complication risks (dislocation, coronary sinus dissection, tamponade) must be minimized. A multidisciplinary team approach enhances success.

His Bundle and Left Bundle Branch Pacing Alternatives

Conduction system pacing (CSP) has emerged as a physiological alternative to conventional BiV-CRT. His bundle pacing (HBP) provides physiological ventricular activation by directly stimulating the His bundle. However, high pacing thresholds, sensing issues, lead stability, and a 70-80% success rate in correcting LBBB pose limitations. Left bundle branch area pacing (LBBAP) offers more stable threshold values, a narrow paced QRS, and high implantation success (>90%) by capturing the left bundle branch from the interventricular septum (Glikson, et al., 2021: 3427–3520).

Observational studies and randomized trials (e.g., I-CLAS) demonstrate that LBBAP is associated with a narrower QRS, better LVEF improvement, and fewer deaths/HF hospitalizations compared to BiV-CRT. Particularly in patients with true LBBB, LBBAP increases the super-responder rate. The 2023 HRS guidelines recommend CSP as a Class IIa indication in cases of anatomical or functional failure of conventional CRT. The long-term lead durability and extraction safety of LBBAP are still in the maturation phase but are promising (Morcos, et al., 2025: 2028–2037).

HBP and LBBAP are also superior in preventing pacing-induced cardiomyopathy. Future randomized trials will determine

whether these modalities will become the standard of care (Herweg, et al., 2024: 379–390).

CRT Optimization (Echocardiographic and Device-Based)

To achieve the maximum benefit from CRT, optimization of the AV (atrioventricular) and VV (interventricular) delays is necessary. Echocardiographic optimization (AV delay via mitral inflow Doppler, VV delay via aortic VTI or tissue Doppler) is the classical method, but it is time-consuming and operator-dependent. Simplified protocols are utilized in practice (Shroff, et al., 2024: 893–900).

Device-based algorithms (e.g., AdaptivCRT, SmartDelay, SonR) preserve intrinsic AV conduction, perform dynamic VV adjustment, and optimize BiV capture during AF. AdaptivCRT increases the response rate, reduces the incidence of AF, and prolongs battery longevity. Electrical optimization (paced QRS narrowing) is the simplest and most effective surrogate. Whether routine optimization is necessary in all patients is controversial; however, it is mandatory in non-responders or in cases of a suboptimal pacing percentage. Multipolar leads and MultiPoint pacing (MPP) provide better synchronization through multiple LV pacing sites (Chen, et al., 2026: 352–359).

CRT Non-Response and Management

The clinical response rate in CRT is 60-70%, whereas the echocardiographic response (a $\geq 15\%$ reduction in LVESV or an increase in LVEF) is more variable. The prognosis is significantly worse in non-responders (high mortality and hospitalizations). The main causes of non-response are suboptimal patient selection (narrow QRS, non-LBBB, high scar burden), poor LV lead position, inadequate BiV pacing percentage ($<95\%$), ongoing arrhythmias

(AF with rapid ventricular response), insufficient GDMT, comorbidities, and myocardial scar tissue (Varma, 2016).

Management should be algorithmic. The first step is device interrogation (pacing percentage, thresholds, impedance, arrhythmia logs) and echocardiographic reassessment. Options such as optimization, lead revision, MPP activation, CSP upgrade, or LV endocardial pacing are evaluated. Response rates can be increased with a multidisciplinary "CRT optimization clinic" approach (HF specialist, EP, imaging). Although the prognosis is poor in non-responders, improvement can be achieved in many patients with aggressive management (Zareba, 2010: 543–548).

CRT-P vs. CRT-D Selection

The choice between CRT-P (pacemaker only) and CRT-D (with defibrillator) is made based on the risk of sudden cardiac death (SCD), patient profile, and shared decision-making. CRT-D is generally preferred in patients with a primary prevention ICD indication (LVEF $\leq 35\%$, NYHA II-III). However, CRT-P is a reasonable alternative in the presence of advanced age (>75 -80), advanced comorbidities, non-ischemic etiology, limited life expectancy, or a high risk of infection (Sudesh, 2024).

The 2021 ESC guidelines emphasize individualized risk assessment and patient preference. Although meta-analyses demonstrate that CRT-D reduces SCD, a clear superiority over CRT-P in overall mortality has not always been proven. CRT-P may be more frequently preferred in women and the elderly. During device replacements, battery life, infection risk, and patient status should be reassessed (Leclercq, et al., 2023).

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IMPLANTABLE CARDIOVERTER- DEFIBRILLATORS (ICD)

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INTRODUCTION

Sudden cardiac death (SCD) is a catastrophic public health problem that affects approximately 4–5 million people worldwide annually and accounts for 50% of all cardiovascular deaths. The vast majority of SCD cases stem from ventricular fibrillation (VF) or hemodynamically intolerated ventricular tachycardia (VT). This fact brings a critical urgency both in terms of understanding arrhythmic mechanisms and developing effective intervention strategies.

The transvenous ICD was first applied in humans by Michel Mirowski in 1980. Since then, the technology has undergone a radical transformation with small capacitors, advanced sensing algorithms, biphasic waveforms, and remote monitoring systems. Today, implantable cardioverter-defibrillators (ICDs) are developed to prevent sudden cardiac death secondary to sustained VT or VF. These devices are the only proven device therapy effective in

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preventing sudden cardiac death by automatically recognizing and terminating life-threatening ventricular arrhythmias. Randomized controlled trials conducted over the last two decades have demonstrated that ICD implantation significantly reduces total mortality in appropriate patient groups (Kadish, et al., 2004: 2151–2158).

INDICATIONS

Indications for Primary Prevention

Primary prevention refers to the implantation of an Implantable Cardioverter-Defibrillator (ICD) to prevent sudden cardiac death (SCD) in patients who have no prior history of life-threatening ventricular arrhythmias (ventricular tachycardia or ventricular fibrillation) but are identified as having a high risk of SCD due to an underlying heart disease or genetic predisposition.

The efficacy of ICD therapy in primary prevention has been established by numerous randomized controlled trials. Today, recommendations regarding ICD implantation are largely based on the results of these trials and the guidelines for the prevention of SCD published by the European Society of Cardiology (ESC) in 2022 and the AHA/ACC in 2017.

Ischemic Cardiomyopathy

In patients with a history of myocardial infarction (MI) and left ventricular systolic dysfunction, the development of non-sustained VT is associated with a 2-year mortality rate of approximately 30–35% (Bigger, et al., 1984: 250–258). The first major study conducted in this patient population was the Multicenter Automatic Defibrillator Implantation Trial-I (MADIT-I) (Moss, et al., 1996: 1933–1940). This study enrolled patients with a history of MI, an ejection fraction (EF) $\leq 35\%$, and episodes of non-sustained VT; at the end of a mean follow-up period of 27 months, a 54%

relative risk reduction was observed in the ICD group compared to conventional medical therapy. In the Multicenter Automatic Defibrillator Implantation Trial-II (MADIT-II), patients with ischemic cardiomyopathy and an $EF \leq 30\%$ were randomized into ICD and medical therapy arms. Following a mean follow-up of 20 months, a 31% relative risk reduction in mortality was detected in the ICD group (Moss, et al., 2002: 877–883). In the Defibrillator in Acute Myocardial Infarction (DINAMIT) trial, patients with recent MI and an $EF \leq 35\%$ were assigned to either ICD implantation or standard medical therapy within 6–40 days post-MI. At the end of a 30-month follow-up period, although SCD was reduced in the ICD arm, all-cause mortality did not show a decrease. This study forms the clinical basis for the 40-day waiting period mandated by current guidelines for primary prevention ICD implantation.

ICD implantation is not recommended during the early phase following an acute myocardial infarction. The primary reason for this is that ventricular functions may recover over time and the early arrhythmic risk can be transient.

The DINAMIT and IRIS trials demonstrated that although ICD implantation within the first weeks following a myocardial infarction reduces sudden cardiac death rates, it does not lower all-cause mortality (Hohnloser, et al., 2004: 2481–2488; Steinbeck, et al., 2009: 1427–1436). For this reason, current guidelines recommend a waiting period of:

At least 40 days after a myocardial infarction,

At least 90 days after coronary revascularization (Zeppenfeld, et al., 2022: 3997–4126).

Non-Ischemic Cardiomyopathy

The Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation (DEFINITE) trial randomized 458 patients

with non-ischemic dilated cardiomyopathy, NYHA Class I–III symptoms, an LVEF 35%, and more than 10 premature ventricular contractions per hour or episodes of non-sustained VT into optimal medical therapy or ICD groups. At the end of a 2-year follow-up period, a 35% relative risk reduction in mortality was observed in the ICD group (Strickberger, et al., 2003: 1707–1712). In the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT), 2,521 patients with an LVEF 35% and symptomatic NYHA Class II–III heart failure were enrolled. The clinical benefit of ICD therapy was found to be similar in patients with both ischemic and non-ischemic cardiomyopathy (Moss, et al., 2002: 877–883).

Hypertrophic Cardiomyopathy

Preventing sudden cardiac death is one of the primary therapeutic goals in hypertrophic cardiomyopathy (HCM). In high-risk patients, ICD implantation is the most effective method for preventing sudden cardiac death. American and European cardiology societies have published a consensus statement regarding risk stratification in patients with HCM, incorporating major and potential risk factors (Maron, et al., 2003: 1687–1713). Primary prevention ICD is specifically recommended for high-risk patients.

ICD implantation is recommended (Class IIa) in the presence of at least one of the following clinical features:

- Maximum left ventricular wall thickness ≥ 30 mm

- Unexplained syncope suspected to be of arrhythmic origin

- A family history of HCM-related sudden cardiac death

- Presence of a left ventricular apical aneurysm

- Left ventricular ejection fraction $< 50\%$

Conversely, findings such as non-sustained ventricular tachycardia (NSVT) and extensive late gadolinium enhancement

(LGE) do not constitute strong standalone indications; however, an ICD may be considered in these cases based on individual risk assessment (Class IIb).

Arrhythmogenic Right Ventricular Cardiomyopathy

Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) predominantly affects the right ventricle and is a major cause of SCD in young individuals and athletes (Gaine & Calkins, 2023). ICD implantation is recommended as a Class I indication for patients with a history of hemodynamically unstable sustained VT or VF, or those presenting with severe systolic dysfunction of the right ventricle, left ventricle, or both.

An ICD should also be considered in patients who do not meet the aforementioned indications but possess risk factors such as VT inducibility during an electrophysiology (EP) study, episodes of NSVT, or syncope suspected to be of arrhythmic origin after a comprehensive sudden cardiac arrest risk assessment. However, prophylactic implantation is not recommended for healthy gene carriers or asymptomatic patients without risk factors (Towbin, et al., 2019: e301–e372).

Left Ventricular Non-Compaction

Left ventricular non-compaction is a rare congenital disorder characterized by excessive trabeculation and deep intertrabecular recesses within the left ventricular myocardium (Priori, et al., 2001: 1374–1450). Sudden cardiac death has been reported in up to 18% of adults and between 0% and 13% of children with this condition (Weiford, Subbarao, & Mulhern, 2004: 2965–2971). ICD implantation is recommended for patients presenting with life-threatening arrhythmias (Caliskan, et al., 2011: 898–904).

The following table summarizes the indications for implantable cardioverter-defibrillator (ICD) implantation for primary prevention (Table 1).

Primary Prevention Indications for Implantable Cardioverter-Defibrillator (ICD) Implantation

Cardiomyopathies

Table 1: Primary Prevention Indications for Implantable Cardioverter Defibrillator (ICD) Implantation in Cardiomyopathies

Class & Level of Evidence	Clinical Condition / Indication Criteria
I, A	Patients with NYHA Class II or III heart failure and LVEF $\leq 35\%$, at least ≥ 40 days post-MI (Myocardial Infarction) and at least 90 days post-revascularization.
I, B	Patients with NICM (Non-Ischemic Cardiomyopathy), NYHA Class II or III heart failure, and LVEF $\leq 35\%$.
I, A	Patients with NYHA Class I heart failure and LVEF $\leq 30\%$, at least 40 $\geq$ days post-MI and at least 90 days post-revascularization.
I, B	Patients with a history of MI presenting with NSVT (Non-Sustained Ventricular Tachycardia), an LVEF $\leq 40\%$, and inducible sustained VT or VF during an EPS (Electrophysiological Study).
IIb, C	Patients with NICM, NYHA Class I heart failure, and LVEF $\leq 35\%$.

Table 2: Ion Channelopathies

Class & Level of Evidence	Clinical Condition / Indication Criteria
I, B	Brugada syndrome presenting with a spontaneous type 1 pattern and a history of cardiac arrest, sustained VT, or recent syncope suspected to be of arrhythmic origin.
I, B	Long QT syndrome in patients with a history of syncope or sustained VT, where beta-blocker (BB) or BB + Mexiletine therapy has been ineffective.
IIa, B	Patients with Long QT syndrome who develop syncope and/or VT while under beta-blocker therapy.
IIa, C	Patients with Brugada syndrome who have a history of syncope.
IIa, C	Patients with Brugada syndrome who have documented sustained VT but no prior history of SCD (Sudden Cardiac Death).
IIb, B	Patients with Long QT syndrome who possess risk factors for SCD.
IIb, B	Patients under beta-blocker therapy who present with Long QT and a resting QTc > 500 ms.

Table 3: Special Clinical Conditions

Class & Level of Evidence	Clinical Condition / Indication Criteria
I, B	Cardiac Sarcoidosis in patients with a history of sustained VT or SCD, or presenting with an LVEF $\leq$ 35%.
I, B	ARVC (Arrhythmogenic Right Ventricular Cardiomyopathy) patients presenting with resuscitated SCA (Sudden Cardiac Arrest), sustained VT, or an RVEF or LVEF $\leq$ 35% along with $\geq$ 1 major SCD risk factor.
IIa, C	HCM (Hypertrophic Cardiomyopathy) patients presenting with $\geq$ 1 major SCD risk factor (left ventricular wall thickness $\geq$ 3 cm, recent unexplained syncope, or a family history of SCD in a first-degree relative).
IIa, C	HCM patients presenting with NSVT or an abnormal blood pressure response to exercise, in combination with additional risk factors.
IIa, B	ARVC patients with a history of syncope suspected to be secondary to VT/VF.
IIa, B	Cardiac Sarcoidosis in patients with an LVEF $\geq$ 35% and/or evidence of myocardial scar on cardiac MRI/PET, and/or inducible sustained ventricular arrhythmias, and/or a requirement for a PPM (Permanent Pacemaker), and/or a history of syncope.
IIa, B	Non-Ischemic Cardiomyopathy secondary to Lamin A/C mutation in the presence of $\geq$ 2 risk factors (NSVT, LVEF $<$ 45%, non-missense mutation, and male sex).
IIa, B	Patients with Emery-Dreifuss or limb-girdle type 1B muscular dystrophy demonstrating progressive cardiac involvement.
IIb, C	Familial cardiomyopathy associated with SCD.
IIb, B	HCM patients presenting with NSVT or an abnormal blood pressure response to exercise, without additional risk factors.
IIb, B	Heart transplant recipients presenting with severe allograft vasculopathy in combination with LV (Left Ventricular) dysfunction.
IIb, B	Patients with Myotonic Dystrophy Type 1 who have an indication for a PPM.

BB: Beta-blocker; BP: Blood pressure; EPS: Electrophysiological study; LVEF: Left ventricular ejection fraction; HCM: Hypertrophic cardiomyopathy; MI: Myocardial infarction; NICM: Non-ischemic cardiomyopathy; NSVT: Non-sustained ventricular tachycardia; RVEF: Right ventricular ejection fraction; SCA: Sudden cardiac arrest; SCD: Sudden cardiac death; VT: Ventricular tachycardia

2.2 Secondary Prevention Indications

Secondary prevention refers to ICD (Implantable Cardioverter-Defibrillator) implantation aimed at preventing SCD (Sudden Cardiac Death) in patients who have experienced symptomatic sustained VT (Ventricular Tachycardia) and VF (Ventricular Fibrillation), or who have been successfully resuscitated following cardiac arrest. There are 3 major randomized controlled trials investigating ICDs in the secondary prevention of SCD (Kuck, et al., 2000: 748–754).

The Antiarrhythmics Versus Implantable Defibrillators (AVID) trial was terminated early due to positive findings in favor of the ICD (Kuck, et al., 2000: 748–754). This study reported a significant 31% reduction in mortality with ICD therapy.

The Canadian Implantable Defibrillator Study (CIDS) enrolled 659 patients at high risk for SCD who had either suffered cardiac arrest due to VT-VF or had documented VT (17). Patients were randomized into amiodarone and ICD arms. A 32.8% reduction in arrhythmic deaths and a 19.7% reduction in all-cause mortality were observed in the ICD arm.

The Cardiac Arrest Study Hamburg (CASH) was designed to compare ICD, amiodarone, metoprolol, and propafenone in patients who had undergone resuscitation due to cardiac arrest and had documented ventricular arrhythmias (Kuck, et al., 2000: 748–754). The propafenone arm was discontinued after a 61% increase in mortality was detected compared to the ICD arm (Siebels, et al., 1993: 552–558). In the ICD arm, a 23% reduction in mortality was

found compared to the combined amiodarone and metoprolol arms. Secondary prevention indications are shown in the table 4.

Table 4: Secondary Prevention Indications for Implantable Cardioverter-Defibrillator (ICD)

Clinical Scenario	Description	ESC 2022 Class / Level	AHA/ACC/HRS Class / Level
Survivors of cardiac arrest (VF or hemodynamically unstable VT)	High-risk patients (especially structural heart disease)	Class I, Level A	Class I, Level A
Hemodynamically unstable sustained VT	Syncope, hypotension, or shock	Class I	Class I
Structural heart disease with spontaneous sustained VT	Independent of LVEF	Class I	Class I
Recurrent VT/VF episodes	Despite optimal medical therapy	Class I	Class I
Unexplained syncope with suspected ventricular arrhythmia	High-risk patients (especially structural heart disease)	Class IIa	Class IIa
Genetic or inherited arrhythmia syndromes with VT/VF	HCM, ARVC, channelopathies	Class I	Class I
Inflammatory or infiltrative heart disease with VT/VF	e.g., myocarditis, sarcoidosis (post-acute phase)	Class IIa	Class IIa

Hemodynamically tolerated monomorphic VT	Selected patients	Class IIa–IIb	Class IIa
Reversible causes of VT/VF	Acute ischemia (<48h MI), electrolyte imbalance, drug toxicity	Not recommended	Not recommended
Limited life expectancy (<1 year)	Due to comorbid conditions	Not recommended	Not recommended

ICD = Implantable Cardioverter-Defibrillator; VT = Ventricular Tachycardia; VF = Ventricular Fibrillation; LVEF = Left Ventricular Ejection Fraction; HCM = Hypertrophic Cardiomyopathy; ARVC = Arrhythmogenic Right Ventricular Cardiomyopathy.

ICD HARDWARE: PHYSICAL AND ELECTROPHYSIOLOGICAL BASIS

Shock Coils, Capacitor, and Sensing

Implantable cardioverter-defibrillators (ICDs) are high-tech devices used for the recognition and treatment of malignant ventricular arrhythmias. The efficacy of an ICD system depends not only on software algorithms but also on the correct design and integration of its hardware components.

Shock coils (defibrillation electrodes) are conductive electrodes that deliver high-energy defibrillation shocks to the myocardium. They are typically localized in the:

Right ventricle (RV coil)

Superior vena cava (SVC coil)

In some systems, a single-coil or a dual-coil configuration may be preferred. Dual-coil systems feature lower defibrillation thresholds (DFT); however, due to the difficulty associated with lead extraction, single-coil configurations are mostly preferred today.

Coil positioning directly impacts shock success. By distributing the high-voltage energy generated by the device across a wide surface area into the cardiac tissue, the coils terminate ventricular fibrillation and provide synchronized cardioversion.

The Capacitor (Energy Storage System) is one of the most critical components of an ICD. It stores electrical energy and, when necessary, discharges it via the shock coils as a high-voltage shock within a very short duration.

Typical ICD capacitors:

Can store energy between 500–800 volts.

Can deliver a shock energy between 10–40 Joules.

Sensing Systems: One of the most vital functions of an ICD is accurately sensing the heart rhythm. The sensing system analyzes intracardiac electrograms (EGM) to differentiate between normal and abnormal rhythms.

The ICD sensing system is a sophisticated electronic infrastructure designed to reliably identify R waves from signal sources and provide the necessary data flow for therapy decisions. Its core components include:

A bandpass filter (typically between 10–40 Hz), which filters out high-frequency myopotentials and low-frequency T-wave components.

Automatic Gain Control (AGC), which dynamically adapts to changing signal amplitudes.

Blanking periods, which prevent the double-counting of pacing artifacts and T waves.

The clinical significance of AGC presents a double-edged sword: while it reduces far-field R-wave sensing and T-wave oversensing during sinus rhythm, it can also lead to the undersensing

of small-amplitude fibrillation wavelets during VF. This paradox makes the concept of a 'sensing margin' particularly critical, especially in S-ICD programming.

TACHYCARDIA DETECTION ALGORITHMS

Rate Zones and the NID Concept

The fundamental detection logic of modern ICDs relies on comparing the heart rate against programmed threshold values to define therapy zones. A typical configuration consists of three zones: the VT zone (usually 150–200 bpm), the fast VT zone (200–240 bpm), and the VF zone (>240 bpm). The type of therapy (monitoring, ATP, shock) and discrimination algorithms can be programmed independently for each zone.

The NID (Number of Intervals to Detect) parameter, which represents the number of consecutive intervals required for detection, sits at a clinically critical equilibrium point: increasing the NID reduces inappropriate therapies but increases detection delay; decreasing the NID increases speed but elevates the risk of inappropriate therapy due to SVT.

The MADIT-RIT trial (Schuger, et al., 2012: 176–185) empirically addressed this balancing issue. Groups programmed with a high-rate cutoff (≥ 200 bpm) or a long detection duration (≥ 60 -second delay) experienced a 79% reduction in inappropriate shocks compared to standard programming, and all-cause mortality was also significantly lower in these groups. This finding established the paradigm that "less aggressive programming can yield better outcomes."

The 2022 ESC Guidelines recommend programming the therapy zone to ≥ 188 bpm in primary prevention ICDs, adding ATP to all tachycardia zones, and keeping SVT/VT discrimination algorithms active up to 230 bpm.

ATP (Antitachycardia Pacing) and Shock Therapies

ATP is a non-shock therapeutic approach that stimulates the critical tissue of a tachycardia circuit to terminate re-entrant tachycardia. The primary mechanism involves sending timed pulses into the slow conduction zone of the tachycardia circuit to achieve 'entrainment,' which causes the arrhythmia to terminate when the pacing stops.

Burst ATP (successive stimulation at a fixed rate) and Ramp ATP (stimulation with progressively decrementing intervals) are the most commonly used methods. ATP protocols starting at 81–91% of the tachycardia cycle length are preferred; caution is required as excessively fast ATP can lead to acceleration and VF.

The PAIN-FREE Rx II trial demonstrated that ATP provides 72–78% efficacy during fast VT (188–250 bpm) and offers equivalent safety compared to shocks, while substantially causing less psychosocial trauma (Wathen, et al., 2004: 2591–2596). In light of these data, ATP is routinely recommended in all VT zones by current guidelines.

SVT-VT Discrimination Algorithms

To prevent inappropriate shocks, modern ICDs utilize multi-parametric algorithms to differentiate AF, sinus tachycardia, and other types of SVT from VT.

In single-chamber ICDs, evaluation is performed based on ventricular electrogram morphology. If the tachycardia is monomorphic and has a morphology similar to sinus rhythm, it is classified as SVT. If it exhibits variable morphology or slightly altered morphology from sinus rhythm, it is evaluated as sudden-onset VT or AF. If it is monomorphic but structurally distinct from sinus rhythm, it is classified as VT.

In dual-chamber ICDs, evaluation is based on ventricular and atrial rates. If the ventricular rate is faster than the atrial rate, it is VT. If the atrial rate equals the ventricular rate, it is either an SVT with 1:1 AV conduction or a VT with 1:1 ventriculoatrial (VA) conduction; differentiation is achieved by analyzing ventricular morphology, the atrioventricular (AV) interval, the chamber of arrhythmia onset, and the response to ATP. If the atrial rate is faster than the ventricular rate, it may indicate AF or atrial flutter $\pm$ VT. In this case, discrimination is made by assessing ventricular morphology, ventricular interval regularity, and AV association.

SUBCUTANEOUS ICD (S-ICD) SYSTEMS

The subcutaneous implantable cardioverter-defibrillator (S-ICD) fundamentally diverges from the traditional ICD because it lacks any intracardiac or transvenous components. The pulse generator is placed in the left axillary region, while a specialized tunneling electrode is positioned subcutaneously to the left of the sternum. The entire system is completely extravascular. This feature significantly reduces lead-related complications associated with transvenous systems, such as lead fracture, venous thrombosis, and systemic infection. The maximum shock energy is 80 J, which is approximately twice that of transvenous systems (30–40 J); this difference stems from increased tissue resistance.

Prior to S-ICD implantation, a screening test (SENSE algorithm) must be performed. This test verifies the patient's surface signal eligibility regarding the R/T amplitude ratio, QRS morphology, and noise profile to ensure S-ICD compatibility. Screening is of critical importance in mitigating the risk of T-wave oversensing.

WEARABLE CARDIOVERTER-DEFIBRILLATOR (WCD)

The wearable cardioverter-defibrillator (WCD) is a non-invasive protective system that provides continuous ECG recording and automatically delivers a shock during identified arrhythmic events.

The WCD system primarily consists of three main components:

Electrode System:

Contains surface electrodes placed around the circumference of the chest.

Functions to both sense ECG signals and deliver the defibrillation shock.

Typically features a multi-electrode array to ensure more reliable sensing.

Monitor and Control Unit:

A portable device worn on the patient's waist or shoulder.

Performs continuous ECG analysis.

Emits an alarm and initiates the treatment sequence upon detecting VT/VF.

Defibrillation System:

Capable of delivering a high-energy shock (typically up to 150 Joules).

Provides audible and vibratory warnings to the patient prior to shock delivery.

Allows a conscious patient to intervene and prevent an inappropriate shock.

The efficacy of the WCD has been demonstrated particularly in the early post-MI (myocardial infarction) period and in patients

facing transient risks. The VEST trial evaluated the impact of WCD use on sudden cardiac death and demonstrated a significant trend toward a reduction in all-cause mortality. The WCD serves as a crucial bridge-to-therapy option for patients who carry a risk of sudden cardiac death but are temporarily or permanently ineligible for permanent ICD implantation. Proper patient selection and patient compliance play a critical role in treatment success.

INAPPROPRIATE SHOCK: DEFINITION, ETIOLOGY, AND MANAGEMENT

An inappropriate shock is defined as any shock delivered by the ICD in the absence of VT or VF. Historically reported at a rate of 4–6% per year, this incidence has significantly decreased thanks to modern programming strategies (such as higher rate cutoffs, extended NID, and the active utilization of SVT discrimination algorithms).

An inappropriate shock is not merely a "distressing" side effect; it is a clinically severe complication. Documented consequences include troponin elevation (indicating myocardial injury), proarrhythmic effects (such as the induction of VF post-shock), the onset of PTSD, and paradoxically, an increase in mortality. In the ALTITUDE study, a large-scale registry database, patients who received inappropriate shocks exhibited a significantly increased mortality rate, though the direct causality remains a subject of debate.

Table 5: Causes and Management of Inappropriate Shocks

Cause	Identification Method	Management
SVT (AF, sinus tachycardia, accelerated SVT)	Atrial channel analysis on EGM; assessment of the V–A relationship	Rate control, optimize/strengthen SVT discrimination algorithms, catheter ablation
T-wave oversensing	Two deflections per QRS complex on EGM	Increase sensing threshold, adjust blanking period, perform software update
Lead fracture / insulation failure	High-frequency short artifacts; impedance changes	Lead revision or replacement
P-wave oversensing	Rare in dual-chamber devices; small deflections seen on EGM	Adjust sensing threshold or program a discrimination sensor/algorithm
Myopotential oversensing / EMI	Correlation with clinical context; association with physical activity or electrical interference	Device reprogramming; electrical safety education
Digital patient non-compliance	No corresponding event recorded in ICD memory	Patient education; remote monitoring

PSYCHOSOCIAL EFFECTS AND PATIENT EDUCATION

Approximately 20% of ICD recipients suffer from anxiety and depression, both of which are associated with increased mortality (Magyar-Russell, et al., 2011: 223–231). Psychological distress in ICD patients stems primarily from the fear of potentially receiving an ICD shock rather than having actually experienced one (Thylen, et al., 2016: 828–835). Therefore, it is recommended to evaluate ICD-related anxieties in all ICD patients before any shocks occur.

Communication must be established with all ICD recipients to clarify misconceptions regarding device function, discuss concerns regarding sexual function and driving restrictions, and propose an action plan in the event of shock therapy (Lane, et al., 2015: 1747–1769). When necessary, patients should be referred to mental health professionals (Sears, et al., 2007: 858–864).

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A NEW ERA IN CARDIAC PACING: THE HIS BUNDLE (HBP) AND THE LEFT BUNDLE BRANCH AREA (LBBAP) AND LEADLESS PACEMAKER TECHNOLOGY: DEVELOPMENT, CLINICAL APPLICATION, AND FUTURE

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Introduction

Conduction system pacing (CSP) offers a more physiological alternative to traditional methods for treating heart failure and arrhythmias by stimulating the heart's natural electrical pathways. The two main approaches in this context are His Bundle Pacing (HBP) and Left Bundle Branch Area Pacing (LBBAP).

His Bundle Pacing (HBP):

His Bundle Pacing is a method that transmits the electrical impulse directly to the His-Purkinje system, ensuring completely synchronized and the most natural (physiological) activation of both ventricles (Vijayaraman, et al., 2018: 927–947).

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Clinical Evidence: First demonstrated in 2000 by Deshmukh et al., this method has resulted in a significant increase in left ventricular ejection fraction (LVEF) and a reduction in ventricular size in patients with heart failure (Raymond-Paquin, Padala, & Ellenbogen, 2021: 241–243).

Advantages

It precisely mimics the heart's natural conduction pathway and maintains right ventricular synchronization at an excellent level.

Disadvantages and Limitations

The implementation of HBP is technically challenging, and pacing thresholds are generally high. Additionally, the amplitude of the detected R wave is low, and instability (increase) in pacing thresholds may occur over time (Zhang, Zhou, & Gold, 2019: 3039–3049).

Left Bundle Branch Area Pacing (LBBAP):

Left Bundle Branch Area Pacing is based on the principle of placing the electrode in the left septal subendocardial area—where the main trunk or branches of the left bundle branch are located—by passing it through the ventricular septum (Abdelrahman, et al., 2018: 2319–2330).

Clinical Efficacy

LBBAP yields more successful outcomes compared to traditional biventricular pacing (BiVP) in patients requiring cardiac resynchronization therapy (CRT). Meta-analyses have demonstrated that LBBAP results in a significant reduction in all-cause mortality and hospitalizations due to heart failure (Zhuo, et al., 2022: 849143).

Electrical Parameters

LBBAP offers much lower pacing thresholds and significantly higher R-wave detection sensitivity compared to HBP.

Use in Specific Populations

It has been documented that LBBAP can be successfully implanted in heart failure patients with right bundle branch block (RBBB) with an 88% success rate and results in a significant improvement in LVEF (Jastrzebski, et al., 2025: e06).

When compared, left bundle branch area pacing increasingly preferred in clinical use over his bundle pacing because of superior performance and stability (figure-1).

Comparison Criterion	His Bundle Pacing (HBP)	Left Bundle Branch Area Pacing (LBBAP)
 Physiological Activation	Gold standard physiological ventricular activation through direct His bundle capture.	Near-physiological activation with possible mild right ventricular conduction delay.
 Procedural Success Rate	Approximately 75–88%	Approximately 85–92%
 Pacing Threshold	Higher and less stable over long-term follow-up.	Lower and highly stable over time.
 R-wave Sensing Amplitude	Relatively low (<3.0 mV)	Excellent (>10.0 mV)
 Procedure Complexity and Duration	Technically demanding and generally associated with longer procedure times.	Easier implantation with shorter procedure times and a broader target area.
 Lead Performance	Greater risk of threshold rise and lead revision.	Superior long-term electrical performance and lead stability.
 Current Clinical Adoption	Less frequently used in routine practice.	Increasingly preferred in contemporary clinical practice.

Figure 1: This figure compares his bundle pacing and left bundle branch area pacing between key features of importance in clinical usage.

In conclusion, although HBP is physiologically the most optimal method, LBBAP is becoming more prevalent in clinical practice today due to its low threshold values, high detection amplitudes, and procedural ease (Li, et al., 2020: ii54–ii60). However, it should be noted that in LBBAP applications, placing the

electrode too close to the tricuspid valve may increase the risk of tricuspid regurgitation in the long term

Introduction and Historical Background

The field of cardiac pacing has been undergoing continuous innovation since the first transvenous implantation in 1958. Although traditional transvenous pacemakers (TVPs) remain the gold standard, the transvenous leads (wires) and subcutaneous generator pockets—often referred to as the system’s “Achilles’ heel”—carry significant risks of complications such as infection, lead fracture, vascular occlusion, and tricuspid valve insufficiency (Blank, El-Chami, & Wenger, 2023: 43–50). To address these challenges, leadless pacemakers (LP)—which are fully implanted within the heart and do not require leads—have been developed. First conceptualized by Dr. Spickler in the 1970s, this technology became a clinical reality starting in 2012, driven by advancements in battery power and miniaturization (Saleem-Talib, et al., 2025: 1979–1990).

Current Leadless Pacemaker Systems

Today, the market features systems from two main manufacturers:

Medtronic Micra System

Micra VR: Approved in 2016, this is a single-chamber (VVI) device measuring 25.9 mm in length and weighing less than 2 grams. It anchors to the myocardium using four nitinol tines (Blank, El-Chami, & Wenger, 2023: 43–50).

Micra AV and AV2: These models use an accelerometer-based algorithm to detect atrial mechanical activity and provide atrioventricular (AV) synchronization (VDD mode). The Micra AV2

offers a longer battery life and improved detection algorithms (Garweg & Willems, 2024: 4–6).

Abbott Aveir System

Aveir VR: Features an active helical fixation mechanism and is designed to be retrievable. It offers the advantage of performing electrical mapping prior to fixation (Perez Diez & Mosquera Perez, 2025: 438–440).

Aveir DR: The world’s first dual-chamber leadless system. It provides full DDD functionality through wireless communication via “i2i” (device-to-device) technology between two separate devices implanted in the right atrium and right ventricle (Perez Diez & Mosquera Perez, 2025: 438–440).

Clinical Benefits and Patient Selection

The primary advantage of leadless pacemakers over transvenous systems is a reduction in complication rates of approximately 50% (Tong & Sun, 2023).

Low Infection Risk: Since there is no subcutaneous pocket, the risk of device-related infection is virtually nonexistent. It is ideal for diabetic, immunocompromised, or patients who have previously experienced pacemaker infections (Blank, El-Chami, & Wenger, 2023: 43–50).

Vascular and Valvular Protection: The ability to implant via the femoral route is a significant advantage for patients with limited upper extremity venous access (e.g., dialysis patients). Additionally, since there is no lead passing through the tricuspid valve, the risk of valve damage and insufficiency is reduced (Blank, El-Chami, & Wenger, 2023: 43–50).

Cosmetic Benefits: There is no incision scar or implant bulge in the chest area (Trohman, 2025).

Ideal Candidates: Patients with persistent atrial fibrillation and a slow ventricular response, those with upper extremity vascular occlusion, those at high risk of infection, and elderly patients with a sedentary lifestyle are the most suitable candidates (Trohman, 2025).

Complications and Risk Management

Although LP devices are safe, they carry specific risks: **Cardiac Perforation and Tamponade:** The risk of perforation during LP implantation has been found to be slightly higher than with transvenous systems (less than approximately 1%). This typically occurs during device fixation or repositioning (Tam, et al., 2024).

Vascular Complications: Due to the use of a large sheath in the femoral region, hematoma, pseudoaneurysm, or arteriovenous fistula may occur (around 1–2%) (Ngo, et al., 2021: e019212).

Device Dislodgement: Although rare (<1%), there is a risk that the device may dislodge and migrate into the pulmonary artery (Knops, et al., 2023: 2360–2370).

Technological Evolution and Vision for the Future

Leadless pacing technology is evolving rapidly

Biventricular Communication: The Aveir DR system has paved the way for true physiological pacing through beat-by-beat wireless communication between the atrium and ventricle (Perez Diez & Mosquera Perez, 2025: 438–440).

Leadless CRT: Research is underway to integrate leadless pacemakers (LP) with systems like WiSE-CRT for cardiac resynchronization therapy (CRT) used in the treatment of heart failure.

S-ICD Integration: Research is ongoing (e.g., the EMPOWER system) into leadless pacemakers communicating with

subcutaneous ICD (S-ICD) systems to provide anti-tachycardia pacing (ATP) (Blank, El-Chami, & Wenger, 2023: 43–50).

Energy Harvesting: Work is underway on battery-free devices that generate electricity from the heart's own movement (kinetic energy), which could eliminate the need for battery replacement in the future (Tong & Sun, 2023).

Conclusion

Leadless pacemakers have revolutionized the field of cardiac pacing by eliminating lead and pocket complications associated with transvenous systems. Current data have demonstrated the long-term reliability of single-chamber systems, and as dual-chamber technologies become more widespread, the scope of leadless pacing is expected to expand further.

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THE DISSOLUTION OF THE LEAD: TOWARD A LIVING CARDIAC RHYTHM SYSTEM

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Introduction

Cardiac rhythm management (CRM) has revolutionized the prevention of sudden cardiac death and the treatment of bradyarrhythmias over the past five decades. Nevertheless, the conventional transvenous systems that constitute the cornerstone of this success are associated with substantial clinical limitations. Transvenous implantable cardioverter-defibrillators (TV-ICDs) are linked not only to acute procedural complications, including vascular injury, cardiac perforation, pneumothorax, and venous obstruction, but also to significant long-term adverse events. In particular, intravascular leads are susceptible to mechanical failure over time, such as conductor fracture and insulation defects, with approximately 20% of leads requiring intervention within 10 years of implantation (Toon, et al., 2026: e15). Furthermore, these systems predispose patients to life-threatening complications, including device-related infections and infective endocarditis. Extraction of

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infected leads carries considerable procedural risk, with reported in-hospital mortality rates approaching 0.9% (Friedman, et al., 2022: 1292–1302). The cumulative burden of these complications is particularly relevant in younger patients who are expected to remain device-dependent for several decades.

These challenges have driven the development of next-generation CRM technologies designed to minimize intravascular hardware, reduce procedural morbidity, and achieve a more physiological approach to rhythm management. Contemporary advances in electrophysiology are currently evolving along three major technological pathways:

Extravascular Implantable Cardioverter-Defibrillator (EV-ICD)

This technology places the defibrillation lead within the substernal space rather than inside the vascular system or cardiac chambers. By eliminating transvenous access while preserving antitachycardia pacing (ATP) capability and low-energy shock delivery, EV-ICD systems aim to overcome many limitations of conventional TV-ICDs (Crozier, et al., 2021: 2371–2378).

Modular Cardiac Rhythm Management Systems (mCRM)

Modular systems enable independent cardiac implantable electronic devices, such as a subcutaneous ICD and a leadless pacemaker, to communicate wirelessly and function as an integrated therapeutic platform. This architecture allows rhythm management strategies to be tailored according to evolving patient-specific clinical requirements (Knops, et al., 2024: 1402–1412).

Biological Pacemakers

Representing the most transformative concept in CRM, biological pacemakers seek to eliminate the need for permanent

hardware altogether. Through cellular reprogramming strategies utilizing transcription factors such as TBX18, native myocardial cells can be converted into pacemaker-like cells capable of generating spontaneous electrical activity and establishing a physiological rhythm source (Choi, et al., 2025: H978–H990).

Together, these emerging technologies illustrate the ongoing transition from conventional lead-based systems toward fully extravascular, modular, and biologically integrated approaches to cardiac rhythm management (Figure 1)

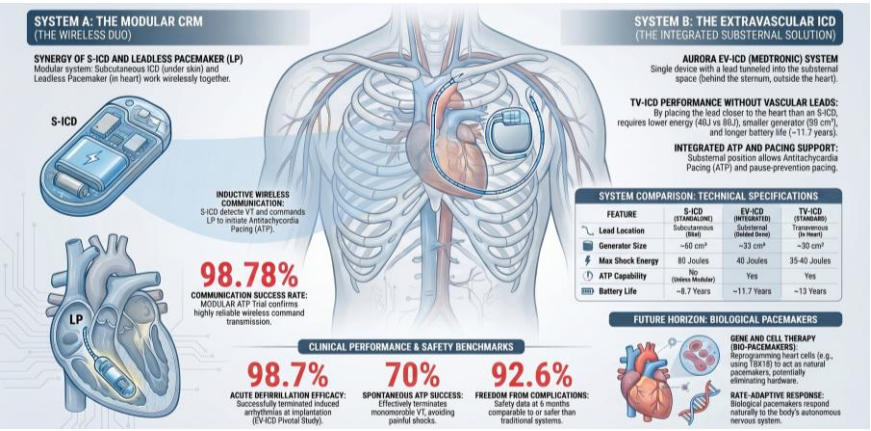


Figure 1: Emerging technologies in cardiac rhythm management: modular, extravascular and biological approaches. The figure illustrates three main directions in modern cardiac rhythm management: (A) modular CRM, where a subcutaneous ICD communicates with a leadless pacemaker for coordinated ATP and defibrillation; (B) extravascular ICD systems using substernal leads to avoid transvenous hardware; and (C) biological pacemaker strategies based on gene and cell therapy (e.g., TBX18-mediated reprogramming) to restore intrinsic cardiac automaticity. Collectively, these approaches reflect a shift toward less invasive and more physiological rhythm management.

This schematic illustrates the evolving landscape of CRM technologies across three complementary paradigms. System A depicts a modular cardiac rhythm management (mCRM) configuration, consisting of a subcutaneous implantable cardioverter

defibrillator (S-ICD) and a leadless pacemaker (LP) that communicate via wireless inductive signaling. In this system, detection of ventricular tachyarrhythmias by the S-ICD triggers coordinated antitachycardia pacing (ATP) delivery from the leadless pacemaker, enabling painless arrhythmia termination and reducing reliance on high-energy shocks.

System B in figure 1 demonstrates the extravascular implantable cardioverter-defibrillator (EV-ICD), in which a single device with a substernal lead provides defibrillation and ATP capabilities without the need for intravascular or intracardiac leads. This configuration offers improved electrical coupling compared with subcutaneous systems while minimizing vascular complications associated with transvenous leads.

The lower panel summarizes key clinical performance metrics and safety benchmarks, highlighting high defibrillation efficacy, substantial freedom from device-related complications, and successful ATP-mediated arrhythmia termination. The right lower section introduces the future horizon of CRM, emphasizing biological pacemaker strategies based on gene and cell therapy, including transcription factor-mediated reprogramming (e.g., TBX18), aimed at restoring intrinsic cardiac automaticity without implanted hardware.

The Substernal Revolution: Redefining ICD Therapy Beyond the Vasculature

The extravascular implantable cardioverter-defibrillator (EV-ICD) represents a novel generation of cardiac rhythm management technology developed as an alternative to conventional transvenous ICD systems (Figure1).

Its defining characteristic is the absence of intracardiac or intravascular leads. Instead, the defibrillation lead is positioned

within the substernal space, posterior to the sternum. Owing to its close anatomical proximity to the heart, this location enables more effective electrical coupling than fully subcutaneous ICD systems, thereby facilitating not only defibrillation but also antitachycardia pacing (ATP) and limited pacing support (Friedman, et al., 2022: 1292–1302; Thompson, et al., 2022: 1085–1095).

The primary rationale behind EV-ICD development has been the reduction of complications associated with transvenous leads. Conventional TV-ICD systems are associated with venous obstruction, lead dysfunction, mechanical failure, systemic infection, and infective endocarditis, all of which represent major clinical concerns, particularly in younger patients with prolonged life expectancy (Bardy, et al., 2010: 36–44; Weiss, et al., 2013: 944–953). Although subcutaneous ICD (S-ICD) systems have substantially reduced vascular complications by eliminating intracardiac leads, their inability to provide pacing therapy and ATP limits their applicability in certain patient populations. EV-ICD technology has therefore emerged as a hybrid solution designed to bridge this therapeutic gap.

One of the principal advantages of EV-ICD systems is the complete avoidance of intravascular hardware, thereby reducing the risk of vascular complications and cardiac structural injury (Friedman, et al., 2022: 1292–1302). Furthermore, substernal lead positioning enables lower defibrillation energy requirements compared with S-ICD systems and permits painless termination of ventricular tachyarrhythmias through ATP delivery. These features represent significant clinical advantages over conventional S-ICD therapy. Additional benefits include a more compact pulse generator design and the potential for extended battery longevity (Nso, et al., 2022: 62–78; Thompson, et al., 2022: 1085–1095).

Despite these advantages, several limitations remain. As a relatively new technology, long-term safety and efficacy data are not yet comparable to the extensive evidence base available for transvenous systems. Moreover, substernal implantation requires specialized anatomical knowledge and procedural expertise distinct from traditional transvenous implantation techniques, resulting in a measurable learning curve for operators.

Among the most important clinical investigations in this field is the EV-ICD Pivotal Trial. This study demonstrated a high success rate for termination of induced ventricular arrhythmias and showed that a substantial proportion of spontaneous ventricular tachyarrhythmias could be managed painlessly through ATP therapy. These findings suggest that EV-ICD technology may evolve beyond a purely defibrillation-based platform and serve as a comprehensive rhythm management system capable of delivering both pacing and defibrillation therapies (Friedman, et al., 2025: 322–332).

From Devices to Networks: The Evolution of Modular Rhythm Management

The introduction of the subcutaneous implantable cardioverter defibrillator (S-ICD) represented a major advancement in cardiac rhythm management by eliminating transvenous leads and thereby reducing the risks of vascular complications and device-related infections. Despite these advantages, the inability of S-ICD systems to provide bradycardia pacing, cardiac resynchronization therapy, or antitachycardia pacing (ATP) remains a significant limitation. In particular, patients experiencing monomorphic ventricular tachycardia are deprived of the opportunity for painless arrhythmia termination and often require high-energy defibrillation shocks, which may adversely affect quality of life and psychological well-being (Al-Khatib, et al., 2018: e91–e220).

To address these limitations, modular cardiac rhythm management (mCRM) systems have emerged as an innovative therapeutic concept. This approach integrates multiple independently functioning cardiac implantable electronic devices into a coordinated network capable of delivering comprehensive rhythm management. In its current configuration, mCRM typically combines a subcutaneous ICD with an intracardiac leadless pacemaker, allowing the devices to communicate wirelessly and operate as a unified therapeutic platform.

The cornerstone of mCRM technology is reliable device-to-device communication. When the S-ICD detects a potentially malignant ventricular arrhythmia, wireless communication signals are transmitted to the leadless pacemaker, which can deliver ATP before initiation of shock therapy. This strategy enables painless termination of selected ventricular tachyarrhythmias while potentially reducing the frequency of unnecessary high-energy shocks. Early clinical studies have demonstrated high communication success rates between devices and encouraging ATP efficacy in appropriately selected ventricular arrhythmias (Lloyd, et al., 2026: e014395).

Beyond ATP delivery, modular systems offer a flexible and patient-centered treatment paradigm. Unlike traditional transvenous systems, which require implantation of multiple intracardiac leads at the outset, mCRM platforms allow therapeutic components to be added according to evolving clinical requirements. Consequently, treatment can be individualized and expanded over time without exposing patients to the cumulative risks associated with transvenous lead implantation.

Several patient populations may derive particular benefit from this approach. Young individuals with inherited arrhythmia syndromes or nonischemic cardiomyopathies often face decades of

device dependency and therefore represent ideal candidates for strategies that minimize lead-related complications. Similarly, patients with a history of infective endocarditis, recurrent bloodstream infections, or limited venous access may benefit from avoiding permanent transvenous hardware. Individuals receiving chronic hemodialysis constitute another important population in whom preservation of venous anatomy is of considerable clinical importance (Knops, et al., 2024: 1402–1412).

The principal advantage of mCRM systems lies in their ability to preserve the benefits of completely extravascular therapy while restoring pacing functionality. By eliminating transvenous leads, these systems may reduce the incidence of lead fracture, venous obstruction, tricuspid valve dysfunction, and systemic infections. Furthermore, the modular architecture provides unprecedented flexibility for future technological integration and device upgrades.

Nevertheless, important challenges remain. Current systems require implantation of multiple devices, increasing procedural complexity and overall healthcare costs. Long-term data regarding durability, communication reliability, battery longevity, and clinical outcomes remain limited. In addition, optimization of wireless communication protocols and cybersecurity considerations represent important areas for future development (Burke, et al., 2015: 1605–1615).

As technology continues to evolve, modular CRM platforms may ultimately form the foundation of fully wireless and highly personalized rhythm management systems. Future iterations could incorporate multisite pacing, physiologic pacing modalities, advanced hemodynamic monitoring, and artificial intelligence–guided arrhythmia management, thereby transforming the landscape of cardiac electrophysiology.

Reprogramming the Heart: The Quest for a Living Pacemaker

The sinoatrial node (SAN), located at the junction of the superior vena cava and the right atrium, serves as the heart's primary pacemaker by generating spontaneous electrical impulses that initiate each cardiac cycle. Dysfunction of the SAN or disturbances within the cardiac conduction system may impair impulse generation or propagation, resulting in symptomatic bradycardia, chronotropic incompetence, and hemodynamic compromise. Although electronic pacemakers remain the standard of care for these conditions, device-related complications including infection, lead failure, mechanical malfunction, and finite battery longevity have stimulated interest in the development of biological alternatives (Cingolani, Goldhaber, & Marban, 2018: 139–150).

The concept of a biological pacemaker seeks to recreate physiological cardiac automaticity through cellular or molecular engineering approaches. Unlike conventional electronic devices, biological pacemakers possess the theoretical potential to respond dynamically to autonomic stimulation, metabolic demand, and neurohumoral regulation, thereby more closely mimicking native sinoatrial node function.

The electrophysiological basis of spontaneous pacemaker activity resides in a complex interplay between membrane ion channels and intracellular calcium cycling. Hyperpolarization-activated cyclic nucleotide-gated (HCN) channels generate the *I_f* (“funny”) current, which contributes significantly to diastolic depolarization and spontaneous impulse initiation. Intracellular calcium oscillations further support automaticity through the calcium clock mechanism. Together, these membrane and intracellular processes constitute the coupled-clock system responsible for SAN automaticity. Current biological pacemaker strategies are based on modifying these mechanisms through ion

channel engineering, somatic reprogramming, or stem cell–based approaches (Figure 2) (Mangoni & Nargeot, 2008: 919–982). Advances in the understanding of these electrophysiological mechanisms have provided the scientific foundation for the development of biological pacemakers and accelerated the emergence of novel therapeutic strategies.

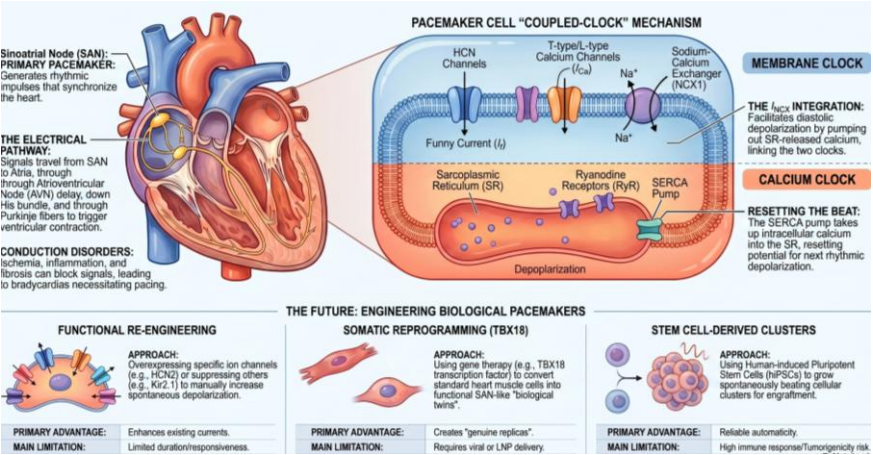


Figure 2: Physiological basis and emerging strategies for biological pacemaker development

Normal sinoatrial node (SAN) automaticity is regulated by the coupled-clock mechanism involving membrane ion channels, including HCN-mediated If current, and intracellular calcium cycling. The figure also illustrates the three principal biological pacing approaches: ion channel engineering, somatic reprogramming using transcription factors such as TBX18, and stem cell–based pacemaker therapies derived from human induced pluripotent stem cells (hiPSCs).

Three principal strategies have emerged in the pursuit of biological pacing.

Ion Channel Engineering

The earliest approach involved modification of ion channel expression within non-pacemaker cardiomyocytes. By enhancing depolarizing currents or suppressing stabilizing potassium currents, investigators sought to induce spontaneous electrical activity in otherwise quiescent ventricular myocardium. Experimental studies demonstrated proof-of-concept feasibility; however, limitations in long-term stability and physiological responsiveness restricted clinical translation (Bucchi, et al., 2006: 992–999).

Somatic Reprogramming

Among contemporary approaches, somatic reprogramming has attracted the greatest scientific interest. This strategy aims to directly convert mature cardiomyocytes into pacemaker-like cells through targeted genetic manipulation. Particular attention has focused on the transcription factor TBX18, a key regulator of sinoatrial node development during embryogenesis.

Experimental studies have demonstrated that TBX18 expression can induce profound structural and electrophysiological remodeling of ventricular myocytes, resulting in the acquisition of pacemaker-like characteristics. Reprogrammed cells exhibit spontaneous automaticity, altered ion channel expression profiles, and morphological features resembling native SAN cells. Importantly, large-animal studies have shown that TBX18-mediated biological pacing can generate stable heart rhythms and improve chronotropic responsiveness, supporting the translational potential of this strategy (Hu, et al., 2014: 245ra294; Kapoor, et al., 2013: 54–62).

Stem Cell–Based Therapies

A third approach involves the transplantation of pacemaker-like cells derived from stem cell sources. Human induced pluripotent

stem cells (hiPSCs) can be differentiated into specialized pacemaker cells and subsequently implanted into the myocardium. Theoretically, this strategy offers the closest approximation to a native biological sinoatrial node.

Despite its promise, several challenges remain unresolved. Long-term cell survival, electrical integration with host myocardium, immunological compatibility, and prevention of arrhythmogenesis continue to represent major barriers to clinical implementation. Furthermore, ensuring controlled maturation and functional stability of transplanted cells remains an active area of investigation (Chauveau, et al., 2017: e004508; Komosa, et al., 2021: e009957).

Toward a Living Rhythm: Emerging Frontiers and Translational Challenges in Biological Pacing

Recent advances in biological pacing have extended beyond gene transfer and cell therapy. Tissue engineering approaches utilizing biomimetic cardiac scaffolds, bioengineered conduction tissues, and three-dimensional cardiac constructs are being explored to enhance electrical integration and long-term functionality. Simultaneously, nonviral gene delivery platforms have been developed to improve safety while reducing concerns associated with viral vectors.

Despite these advances, several fundamental challenges continue to impede clinical translation. Among the most significant is the phenomenon known as sink–source mismatch, whereby a relatively small population of pacemaker cells is unable to generate sufficient current to depolarize the surrounding ventricular myocardium effectively. Additional concerns include maintenance of long-term gene expression, prevention of proarrhythmic effects, durability of biological pacing, and regulation of host immune

responses (Mesquita, Miguel-Dos-Santos, & Cingolani, 2024: 837–841).

Although biological pacemakers remain largely within the preclinical and early translational research stages, they represent one of the most ambitious and potentially transformative innovations in cardiovascular medicine. Successful development of this technology could ultimately eliminate dependence on permanent implantable hardware and establish a new paradigm for physiological rhythm restoration.

Conclusion

Cardiac rhythm management is undergoing a profound technological transformation. Although conventional transvenous systems remain highly effective and continue to represent the standard of care for many patients, their long-term limitations have driven the development of alternative therapeutic strategies.

Extravascular implantable cardioverter-defibrillator (ICD) systems address several challenges associated with transvenous leads while preserving essential therapeutic capabilities, including antitachycardia pacing and defibrillation therapy. Building upon this concept, modular cardiac rhythm management (CRM) platforms enable wireless communication among multiple implantable devices, offering unprecedented flexibility and a more personalized approach to treatment. Simultaneously, advances in biological pacemaker research aim to eliminate dependence on hardware-based therapies by restoring intrinsic cardiac automaticity through molecular and cellular engineering.

Although many of these innovations remain at different stages of clinical development, current evidence suggests a clear transition toward rhythm management systems that are less invasive, more physiological, and increasingly tailored to individual patient

needs. Continued progress in biomedical engineering, molecular biology, and computational medicine is expected to further expand therapeutic opportunities and redefine the future landscape of cardiac electrophysiology.

Ultimately, the evolution from transvenous devices to extravascular, modular, and biological solutions represents more than a technological advancement; it signifies a fundamental paradigm shift in the management of cardiac rhythm disorders and has the potential to transform patient care in the decades ahead.

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COMPLICATIONS AND MANAGEMENT OF PERMANENT PACEMAKERS

GÖKHAN GÜNGÖR¹

Introduction

Since the first successful implantation in 1958, cardiac pacing technology has emerged as one of the greatest success stories of modern medicine. Initially utilized solely for the management of life-threatening bradyarrhythmias, these devices currently serve a broad clinical spectrum ranging from heart failure to the prevention of sudden cardiac death, thereby extending life expectancy and enhancing the quality of life for millions of individuals.

This tremendous advancement in pacemaker technology, along with the miniaturization and increasing complexity of these devices, does not guarantee an uncomplicated clinical course. Although permanent pacemaker implantations are generally regarded as routine and safe procedures, they inherently carry specific risks due to their invasive nature. Every step of the process—ranging from vascular access and lead placement to pocket

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creation and long-term programming follow-up—represents a potential source of complications.

Clinical success is measured not only by the uncomplicated implantation of the device, but also by the anticipation, early recognition, and appropriate management of potential complications.

Large-scale cohort studies in the literature demonstrate that the incidence of complications within the first year following pacemaker implantation ranges from 10% to 12.4% (Kirkfeldt, et al., 2014: 1186–1194). These rates vary depending on institutional volume, operator experience, and device complexity (single-chamber, dual-chamber, or biventricular).

Acute and Subacute Complications (0-90 Days): Approximately 60% of complications occur within the first 30 days. The most common acute complications include pocket hematoma (2-5%), lead dislodgement (1-3%), and pneumothorax (1%).

Late Complications: In the long term, device infections and lead failures become prominent. Notably, the risk of complications in patients undergoing device replacement is approximately twofold higher compared to those undergoing initial implantation (Poole, et al., 2010: 1553–1561).

Acute procedural mortality associated with pacemaker implantation is exceedingly low (<0.5%). However, certain complications that develop in the long term dramatically increase mortality risk.

The Fatal Impact of Infection: Among pacemaker complications, device infections and lead endocarditis represent the entities most strongly correlated with mortality. A study conducted in 2011 demonstrated that while in-hospital mortality ranged between 5% and 8% in patients who developed cardiac implantable

electronic device (CIED) infections, the 1-year mortality rate reached 15% to 20%. Furthermore, in cases where complete system extraction cannot be achieved due to infection, mortality rates can exceed 50%.

Lead Extraction Risks: Transvenous lead extraction (removal of leads from the vein) procedures, performed due to device infection or lead fracture, inherently carry a risk of major intraprocedural mortality (e.g., myocardial rupture, cardiac tamponade) ranging from 0.5% to 1% (Bongiorni, et al., 2018: 1217).

Acute Complications (Implantation and Early Phase)

The first 30 days following the implantation of permanent pacemakers (PPMs) and implantable cardioverter-defibrillators (ICDs) constitute a critical period during which procedural complications are most frequently observed. These early-phase complications typically arise secondary to surgical technique, anatomical variations, or patient comorbidities (e.g., anticoagulant therapy). Early recognition and protocol-driven intervention are fundamental prerequisites for preventing permanent morbidity and potential mortality.

Vascular Access Injuries

Pneumothorax and Hemothorax: These conditions develop as a consequence of inadvertent entry into the pleural cavity during conventional "blind" subclavian vein puncture, with an incidence ranging from 0.4% to 2.8%. Advanced age (>80 years), female sex, low body mass index (BMI), and chronic obstructive pulmonary disease (COPD) constitute significant risk factors. These complications must be highly suspected in the presence of acute-onset dyspnea and oxygen desaturation. The majority of cases are detected via intraprocedural fluoroscopy or routine post-procedural chest radiography (Sriramoju, Iyengar, & Srivathsan, 2024: 299).

Asymptomatic apical pneumothoraces measuring less than 15% can be managed conservatively with supplemental oxygen and serial radiographs. However, in symptomatic or expanding pneumothoraces, the insertion of a chest tube (tube thoracostomy) is indicated (Kirkfeldt, et al., 2014: 1186–1194).

Hemothorax is a rare but severe complication resulting from major vascular injury, necessitating urgent surgical drainage and hemorrhage control in the majority of patients.

Arterial Puncture and Air Embolism: Inadvertent puncture of the subclavian artery can generally be managed successfully with local compression. In contrast, air embolism resulting from the entry of air into the vascular system through the sheath, although uncommon (0.5%), represents a serious complication that may lead to significant hemodynamic instability and even circulatory collapse. Upon recognition of this condition, the patient should be immediately placed in the left lateral decubitus and Trendelenburg positions, and 100% oxygen therapy should be initiated without delay to reduce the volume of intravascular air and optimize tissue oxygenation (Ganesan, et al., 2022).

Local Pocket Complications

Pocket Hematoma: With an incidence ranging from 2% to 5%, pocket hematoma is among the most common early complications following device implantation. It is typically associated with inadequate intraoperative hemostasis or the use of antithrombotic medications, including antiplatelet and anticoagulant agents. Clinical studies have demonstrated that, in high-risk patients, interruption of warfarin therapy with subsequent heparin bridging significantly increases the risk of pocket hematoma formation. In contrast, continuation of the procedure under uninterrupted warfarin therapy while maintaining a therapeutic international normalized

ratio (INR) has been shown to be a substantially safer strategy (Birnie, et al., 2013: 2084–2093).

In cases of pocket hematoma, needle aspiration should be strictly avoided, as it may increase the risk of subsequent infection. Management is generally conservative and consists of the application of a pressure dressing, local ice therapy, and close clinical observation. Surgical revision and evacuation are reserved for selected cases, particularly when there is a risk of skin flap necrosis or wound dehiscence.

Acute Pocket Infections: Infections occurring within the first 30 days are most commonly attributed to intraoperative contamination, typically involving pathogens such as *Staphylococcus aureus* or coagulase-negative staphylococci. While superficial incisional infections may be managed with empirical oral or intravenous antibiotic therapy, the presence of a true pocket infection or evidence of systemic involvement constitutes a Class I indication for complete system extraction (generator and leads), followed by targeted intravenous antimicrobial therapy (Baddour, et al., 2010: 458–477).

Lead-Related Mechanical Complications

Acute Lead Dislocation (Displacement): This complication typically occurs within the first 24–48 hours and is often associated with sudden patient movements or inadequate myocardial fixation of the lead. Macro-dislocation refers to a clearly visible displacement on fluoroscopy, whereas micro-dislocation is characterized by electrical parameter abnormalities alone, such as a sudden increase in pacing threshold and impedance changes. The use of active-fixation (screw-in) leads has significantly reduced the incidence of this complication. When dislocation is detected, early surgical repositioning of the lead is the standard management approach (van Rees, et al., 2011: 995–1000).

Myocardial Perforation and Cardiac Tamponade: The right ventricular apex is the most susceptible site for perforation due to its relatively thin myocardial wall. The risk is increased in cases of excessive torque applied to active-fixation leads or in patients with fragile myocardial tissue, such as elderly individuals or those receiving corticosteroid therapy (0.1–0.8%). Intra-procedural onset of sudden chest pain, hypotension, or loss of electrical parameters should raise immediate suspicion. In cases of acute cardiac tamponade, emergent echocardiography-guided pericardiocentesis is life-saving. Most perforations can be managed without surgical intervention through pericardiocentesis and lead withdrawal (Cano, et al., 2017: 96–102).

Other Early Complications

Diaphragmatic or Phrenic Nerve Stimulation: This refers to inadvertent stimulation of the diaphragm due to the anatomical proximity of the leads. Initial management involves reprogramming of device electrical parameters, including reduction of output or alteration of polarity. If these measures fail to resolve the problem, surgical lead repositioning is indicated.

Late (Chronic) Complications

Following the first 30 days after pacemaker implantation, complications that may develop over months or even years are classified as late (chronic) complications. While early complications are generally related to surgical technique, late complications are more commonly associated with material fatigue (mechanical stress), chronic tissue reactions, device longevity, and the risk of systemic infection.

Late Device Infections and CIED Endocarditis

Infections related to cardiac implantable electronic devices (CIEDs) represent the complication with the highest morbidity and

mortality. Late infections typically develop through two main mechanisms: either due to low-virulence bacteria introduced during the procedure (e.g., *Staphylococcus epidermidis*) that manifest clinically months later, or secondary seeding of the leads as a result of bacteremia originating from a distant infectious focus.

Local Pocket Infection: This is characterized by erythema, increased local temperature, and pain over the device pocket, and in advanced stages, by skin thinning with subsequent device exposure (erosion).

CIED Endocarditis: This refers to the extension of infection along the intravascular leads to involve the right-sided cardiac structures, particularly the tricuspid valve. Diagnosis is established by the presence of positive blood cultures, fever, and the detection of vegetations on echocardiography.

Whether presenting as a localized erosion or systemic endocarditis, current guidelines emphasize that antibiotic therapy alone is both insufficient and contraindicated in the management of infected CIED systems. The cornerstone of treatment is complete system extraction, including both the generator and all leads, which constitutes a Class I (absolute) indication. Management with antibiotics alone is associated with a markedly increased risk of infection recurrence, ranging from 50% to 100%, whereas complete device removal provides definitive and durable treatment (Kusumoto, et al., 2017: e503–e551).

Mechanical and Hardware-Related Problems

Lead Fracture and Insulation Defect: Lead fracture refers to the disruption of the internal conductor wire, whereas insulation defect denotes the compromise of the external silicone or polyurethane insulation. A well-recognized etiological mechanism is “subclavian crush syndrome,” in which the lead is subjected to

mechanical compression between the clavicle and the first rib. Diagnosis is primarily established through device interrogation and serial monitoring of electrical parameters. In cases of conductor fracture, impedance is typically markedly elevated ($>1000\ \Omega$), whereas insulation defects are characterized by abnormally low impedance values ($<200\ \Omega$) due to current leakage. Management involves implantation of a new lead and/or removal of the malfunctioning lead, most commonly via transvenous lead extraction (TLE).

Battery Depletion: Although this is not a true complication but rather a physiological and expected device lifecycle process, inadequate follow-up may result in serious clinical consequences, including syncope or asystole. Generator replacement should be planned upon detection of the Elective Replacement Indicator (ERI), which signals impending battery depletion and the need for timely device exchange.

Physical Complications

Pocket Erosion: This refers to the progressive thinning of the subcutaneous tissue over time, particularly in elderly or cachectic patients, or in cases where the device pocket is created too superficially, ultimately leading to exposure of the generator and/or leads through the overlying skin. As pocket erosion represents an open source of infection, it requires urgent surgical intervention and revision (Baddour, et al., 2010: 458–477).

Twiddler Syndrome: This syndrome occurs when the patient, often due to an unconscious habit or repetitive manipulation, rotates the generator within the pectoral pocket around its own axis. As the device rotates, the leads become coiled around the generator, leading to traction on the leads and subsequent dislodgement (dislocation) with loss of proper myocardial fixation. Management requires urgent surgical revision, including lead repositioning, and

secure fixation of the device—typically by reducing pocket size and/or anchoring the generator to the pectoral fascia to prevent further rotation (Young & Bailey, 2002: 152–153).

Electrophysiological and Algorithmic Complications

Pacemaker Syndrome: This condition typically occurs in patients with ventricular-only pacing systems (VVI), in which physiological atrioventricular synchrony is lost. Atrial contraction against closed atrioventricular valves may lead to increased jugular venous distension, fatigue, hypotension, and palpitations. The definitive management consists of upgrading the device to a dual chamber pacing system (DDD) or optimizing device programming algorithms to restore atrioventricular synchrony.

Pacemaker-Mediated Tachycardia (PMT): This is a re-entrant tachycardia that occurs predominantly in dual-chamber pacing systems when retrograde atrial conduction is sensed by the device as intrinsic atrial activity, resulting in continuous ventricular pacing and the establishment of a “endless loop” circuit. In most cases, it can be managed non-invasively through device reprogramming. Extension of the post-ventricular atrial refractory period (PVARP) allows the device to ignore retrograde atrial signals. In addition, activation of dedicated PMT termination algorithms within the device is recommended.

Undersensing: Undersensing refers to the failure of the device to appropriately detect intrinsic cardiac activity, resulting in inappropriate and unnecessary pacing output (asynchronous pacing). This may lead to competition between intrinsic and paced rhythms. If a pacing stimulus coincides with ventricular repolarization, particularly the vulnerable phase corresponding to the peak of the T wave on the electrocardiogram, the so-called “R-on-T” phenomenon may be precipitated, potentially triggering ventricular tachycardia or

ventricular fibrillation and thereby increasing the risk of sudden cardiac death.

Initial management consists of device reprogramming by increasing sensing sensitivity (i.e., lowering the sensing threshold in millivolts, for example from 2.5 mV to 1.0 mV). Electrocardiographic evaluation and device interrogation should be performed to assess system function. In cases where the problem is not algorithmic but rather secondary to lead dislodgement or significant insulation defect, surgical lead revision or replacement is indicated.

Oversensing: Oversensing occurs when the device inappropriately interprets external electrical signals or non-physiological noise as intrinsic cardiac activity, resulting in inhibition of pacing output. Clinically, this may manifest as bradycardia, dizziness, visual disturbance, or syncope due to inappropriate suppression of necessary pacing stimuli. In some cases, misinterpretation of T waves or electrical interference as ventricular fibrillation signals may trigger inappropriate high-energy therapies, which can be both clinically harmful and psychologically distressing for the patient.

Initial management involves non-invasive device reprogramming. This is achieved by reducing sensing sensitivity, i.e., increasing the sensing threshold (in millivolts), for example from 1.0 mV to 2.5 mV. If the issue is related to T-wave oversensing, device-specific filtering algorithms may be activated. When oversensing is secondary to mechanical lead failure, such as lead fracture, surgical lead revision or replacement is mandatory.

Inappropriate Shocks (ICDs): Inappropriate implantable cardioverter-defibrillator (ICD) shocks occur when atrial fibrillation, T-wave oversensing, or external electrical noise is erroneously interpreted by the device as ventricular fibrillation, resulting in

unnecessary shock delivery to the patient. Management involves activation and optimization of supraventricular tachycardia (SVT) and ventricular tachycardia (VT) discrimination algorithms. In cases of T-wave oversensing, device sensitivity settings should be adjusted accordingly. If concomitant supraventricular arrhythmias are present, pharmacological therapy (e.g., beta-blockers and/or amiodarone) or catheter ablation should be incorporated into the treatment strategy in accordance with established protocols.

Venous Thrombosis and Tricuspid Valve Regurgitation

Intravenous foreign bodies (leads) increase the risk of thrombosis and fibrosis by inducing endothelial injury of the vessel wall and causing venous flow stasis.

Upper Extremity Deep Vein Thrombosis and Venous Stenosis: Venous stenosis or occlusion of the subclavian vein or superior vena cava develops in approximately 10–20% of patients following pacemaker implantation. Due to the development of a robust collateral venous network, patients are often asymptomatic. However, these venous obstructions may pose significant technical challenges in cases requiring device upgrade or the addition of new leads. In symptomatic patients, or when additional lead implantation is necessary, percutaneous venoplasty (balloon dilation) may be performed as a therapeutic option.

Tricuspid Regurgitation: Pacemaker leads traverse the tricuspid valve to reach the right ventricle. Over time, lead adherence to valvular structures, mechanical injury to the chordae tendineae, or impairment of leaflet coaptation (impingement) may result in the development of significant tricuspid regurgitation over months or years. This condition can lead to progressive right-sided heart failure, manifesting as peripheral edema, ascites, and hepatomegaly. In advanced symptomatic cases unresponsive to medical therapy,

surgical intervention, including tricuspid valve repair or replacement, may be required (Dehmer & Holper, 2017: 928–930).

Transvenous Lead Extraction (Tle): Indications and Advanced Techniques

Transvenous Lead Extraction (TLE): Transvenous lead extraction (TLE) is defined as the removal of cardiac implantable electronic device (CIED) leads that have been implanted for more than one year or that cannot be retrieved by simple traction, utilizing dedicated extraction systems through the venous circulation. With increasing lead dwell time, progressive fibrotic encapsulation and endothelialization lead to firm adherence of the lead to the subclavian vein, superior vena cava (SVC), and myocardial endocardium. Accordingly, TLE constitutes a complex, highly specialized procedure rather than a routine device replacement, characterized by well-defined indications and an inherent risk of major procedural complications.

Indications for Lead Extraction

TLE Indications: Indications for transvenous lead extraction (TLE) are primarily classified into two main categories: infectious and non-infectious (mechanical/functional).

Infectious Indications

Class I Indications (Definite Indications):

CIED Endocarditis (with or without valvular involvement): This includes cardiac implantable electronic device (CIED)-associated endocarditis irrespective of valvular involvement, defined by positive blood cultures and/or the detection of vegetations on echocardiography.

Local Device Pocket Infection, Pocket Erosion, or Purulent Discharge: This includes localized infection of the device pocket,

pocket erosion with or without device exposure, and the presence of purulent discharge from the generator site.

Recurrent Bacteremia of Unexplained Origin: This refers to persistent or recurrent bacteremia in patients with a cardiac implantable electronic device (CIED), in the absence of an identifiable alternative infectious source, and showing poor response or non-responsiveness to appropriate antibiotic therapy.

Non-Infectious Indications

Class I and Class IIa Indications:

Life-Threatening Arrhythmias: This includes situations in which abandoned or fractured leads result in inappropriate shocks or the induction of malignant arrhythmias, thereby posing a direct threat to patient survival.

Venous Occlusion: This refers to subclavian vein occlusion in patients requiring device upgrade, in which the obstruction precludes the implantation of additional leads and necessitates the creation of new venous access for system revision.

Prevention of Lead Burden: This refers to the extraction of malfunctioning or non-functional leads, particularly in younger patients, in order to prevent excessive intravascular lead burden. Increased lead burden is associated with a higher risk of tricuspid regurgitation and venous stasis, as well as potential long-term vascular complications (Kusumoto, et al., 2017: e503–e551).

Extraction Techniques and Equipment

Modern TLE Procedure: The modern transvenous lead extraction (TLE) procedure extends far beyond simple traction and is best characterized as a staged, technology-intensive process. The procedural steps are as follows:

Preparation and Safety Net: The procedure is performed under general anesthesia with invasive arterial monitoring and transesophageal echocardiography (TEE) guidance. In anticipation of potential vascular injury and cardiac tamponade, a cardiothoracic surgical team must be immediately available, and both pericardiocentesis and median sternotomy sets should be prepared in the operating room (surgical standby).

Locking Stylets: Standard leads are prone to fracture during traction-based extraction. To prevent this, specialized stainless-steel wires are advanced into the inner lumen of the lead and locked at the distal tip, thereby providing internal reinforcement along the entire lead body. This configuration ensures that the applied traction force is evenly distributed throughout the lead, reducing the risk of fragmentation during extraction.

Fibrotic Tissue–Dissecting Sheaths (Sheaths): In order to free the lead from surrounding adhesions, outer sheaths are advanced over the electrode into the venous system:

Mechanical Dilator Sheaths: These consist of telescoping Teflon or polypropylene sheaths. They mechanically disrupt fibrotic adhesions through operator-applied manual rotational (twisting) force, facilitating progressive dissection and release of the lead from surrounding tissue.

Energy-Based Sheaths (Laser and Radiofrequency): In regions characterized by dense fibrosis and calcification, such as the subclavian vein and superior vena cava (SVC), mechanical force may be insufficient and may carry an increased risk of vascular injury or rupture.

Excimer Laser Sheaths: These devices utilize photochemical and photomechanical energy to ablate fibrotic tissue surrounding the lead through vaporization. Operating on the principle of “cold laser” technology, they minimize thermal injury to

the adjacent vascular wall while enabling controlled dissection of adherent scar tissue.

Radiofrequency (RF) Sheaths: These sheaths utilize bipolar electrodes at the distal tip to deliver radiofrequency energy, enabling controlled tissue cutting and dissection of fibrotic adhesions surrounding the lead.

Alternative Approaches (Femoral Snare Techniques): In cases where leads cannot be extracted via the pectoral (infraclavicular) approach such as fractured leads, leads with free-floating fragments, or those with extensive myocardial adhesions the right femoral venous access (groin) is utilized. Through this route, dedicated snaring devices (e.g., goose-neck snares) are advanced via a catheter system to capture the lead body, which is subsequently retrieved and extracted from the body under controlled traction.

Transvenous Lead Extraction (TLE): Complications and Risk Management

The overall rate of major complications associated with transvenous lead extraction (TLE) is approximately 1–2%, while procedure-related mortality ranges between 0.1% and 0.8%. The most catastrophic complication is superior vena cava (SVC) tear, typically occurring at the SVC–right atrial junction. This event can rapidly lead to massive hemorrhage and cardiac tamponade within seconds.

In recent years, endovascular occlusion balloons (e.g., the Bridge Balloon) have been increasingly utilized as a preventive safety strategy. These balloons can be positioned via the femoral venous route into the SVC and rapidly inflated in the event of vascular injury, temporarily controlling intrathoracic bleeding from within the vessel lumen. This maneuver provides critical time for emergent surgical intervention, including sternotomy and

definitive vascular repair (Bongiorni, et al., 2017: 2995–3005; Brunner, et al., 2015: 2381–2386).

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SPECIAL SITUATIONS AND PATIENT MANAGEMENT IN CARDIOVASCULAR IMPLANTABLE ELECTRONIC DEVICES

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Introduction

The management of cardiovascular implantable electronic devices (CIEDs) in the female patient population necessitates specific strategies tailored to both anatomical and physiological considerations. Notably, implantable cardioverter-defibrillators (ICDs) and cardiac resynchronization therapy (CRT) devices possess significantly larger volumes and greater mass compared to standard bradycardia pacemakers, frequently precipitating substantial aesthetic and psychosocial concerns in this demographic (Asirvatham, et al., 2021; Chow & Buxton, 2006). To mitigate cosmetic disfigurement, the placement of the device generator in a retromammary (subglandular) position is often considered; however, this approach introduces a significant clinical dilemma. Retromammary positioning can generate artifacts in routine screening mammograms, thereby obscuring the optimal

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visualization of breast parenchyma and potentially delaying the early detection of malignancies (Ellenbogen & Kaszala, 2020). Consequently, prior to elective implantation procedures, it is imperative to verify that the patient has undergone a recent mammogram. Furthermore, surgical planning must meticulously calculate anatomical projections to minimize the obscuration of breast tissue (Asirvatham, et al., 2021).

Pacemakers in Pregnancy and Female-Specific Conditions

When implantation is mandated for women of childbearing age or during pregnancy, management protocols must be unequivocally focused on fetal protection. It is a clinical imperative to minimize the teratogenic and mutagenic effects of ionizing radiation during invasive procedures performed in the gestational period. Therefore, strict adherence to the ALARA (As Low As Reasonably Achievable) principle is mandatory (Asirvatham, et al., 2021; Ellenbogen & Kaszala, 2020). Fluoroscopy time must be restricted to an absolute minimum, "pulsed fluoroscopy" modes should strictly replace conventional continuous fluoroscopy, and the maternal abdomen and pelvis must be adequately shielded with lead aprons. To maximize both maternal and fetal safety, non-fluoroscopic implantation techniques utilizing electroanatomical mapping systems should be strongly considered in selected cases.

Pediatric and Congenital Patient Management

Permanent pacing therapy in pediatric patients and individuals with congenital heart disease (CHD) demands a multidisciplinary approach owing to the patient's anthropometric dimensions, dynamic somatic growth, the necessity for lifelong pacing, and the presence of complex vascular or cardiac anomalies (Asirvatham, et al., 2021; Chow & Buxton, 2006). The diagnosis of bradycardia and the establishment of treatment indications in children are entirely contingent upon age-specific physiological

parameters. While a resting heart rate of 45 bpm might be clinically tolerated by an adult, it constitutes a critical condition in a neonate or infant—whose cardiac output is entirely heart-rate dependent due to a fixed stroke volume—potentially precipitating profound hypoperfusion, hemodynamic collapse, and sudden cardiac arrest (Kusumoto, et al., 2019: e333–e381; Tracy, et al., 2012: 1297–1313).

Although transvenous access is widely utilized in the pediatric population, surgically implanted epicardial pacing systems retain primary importance, particularly in neonates and infants presenting with extremely diminutive vascular structures (Asirvatham, et al., 2021; Ellenbogen & Kaszala, 2020). When a transvenous approach is indicated for children with adequate body weight and vessel caliber, it is technically requisite to leave a specific "lead loop" (redundant lead sweep) within the right atrium or right ventricle to accommodate the child's longitudinal skeletal growth. This anatomical reserve gradually straightens as somatic elongation occurs. If this reserve is exhausted during growth, the resultant mechanical tension at the electrode-tissue interface (myocardial fixation point) can lead to lead dislocation, sensing/pacing threshold aberrations, or tricuspid valve dysfunction, rendering surgical placement of a new lead or system revision inevitable (Chow & Buxton, 2006; Ellenbogen & Kaszala, 2020). Moreover, considering the inherently high physical activity levels of pediatric patients and the elevated probability of future lead extraction during somatic growth or device upgrades, active fixation (screw-in) leads are generally favored over passive (tined) leads. Active fixation provides more secure anchoring and facilitates future lead extraction by mitigating the extensive fibrosis typically associated with passive leads (Asirvatham, et al., 2021).

Congenital anatomical variations and prior surgical shunt or corrective operations directly dictate the optimal implantation trajectory. For instance, in the presence of a persistent left superior

vena cava (SVC), the venous system drains into the right atrium via the coronary sinus, rendering transvenous access to the right ventricle and subsequent lead manipulation technically arduous. Should this anatomical variant be suspected, a right subclavian venous approach is preferred (Asirvatham, et al., 2021; Chow & Buxton, 2006). In more complex scenarios, such as in patients who have undergone a Mustard, Senning, or Fontan procedure (total right-to-left shunt correction or cavopulmonary anastomosis), systemic venous return is either redirected to the pulmonary artery or obstructed by anatomical barriers, rendering transvenous access to the right ventricle entirely unfeasible. In such complex anatomical anomalies, a hybrid synchronized approach comprising a ventricular epicardial lead combined, if necessary, with a transvenous atrial lead is mandated (Asirvatham, et al., 2021; Ellenbogen & Kaszala, 2020).

End-Of-Life Decisions and Device Deactivation

The management of CIEDs during the end-of-life stages in patients with terminal or fatal illnesses constitutes one of the most profound and sensitive domains of medical ethics (Lampert, et al., 2010: 1008–1026). The paramount objective of end-of-life (palliative) care is the alleviation of suffering and the preservation of the patient's quality of life. Within this context, deactivating tachycardia detection algorithms and shock therapies in a terminally ill oncology or end-stage heart failure patient is universally endorsed by medical and ethical committees as a rational and compassionate intervention, designed to preclude the delivery of recurrent, painful ICD shocks during ventricular tachyarrhythmias that frequently manifest during the dying process (Lampert, et al., 2010: 1008–1026). In strict accordance with the foundational bioethical principle of "patient autonomy," the conscious patient—or their designated legal surrogate in cases of incapacitation—retains the ultimate legal authority regarding the withdrawal of these therapies (Lampert, et al., 2010: 1008–1026).

Conversely, the decision to deactivate pacemaker functions intended for bradycardia support provokes considerably deeper contention among physicians and ethics committees. Deactivating the device in a pacemaker-dependent patient may precipitate immediate bradycardic asystole and subsequent death, a scenario often clinically perceived as a more aggressive intervention. Nevertheless, contemporary international expert consensus and medico-legal guidelines delineate a definitive boundary: provided the request aligns with the patient's clinical trajectory, personal values, and established goals of care, the cessation of pacemaker support is recognized as a fundamental legal right and is not legally or ethically synonymous with "physician-assisted suicide" or "euthanasia" (Lampert, et al., 2010: 1008–1026). Clinically, this is defined as the withdrawal of a disproportionate, artificial life-sustaining therapy that ceases to confer benefit, thereby permitting the underlying terminal pathology to follow its natural course. Should fulfilling a deactivation request contravene a physician's personal, religious, or moral convictions (conscientious objection), the physician cannot be compelled to execute the procedure. However, the physician maintains a non-negotiable obligation to safely transfer the patient's care to a qualified colleague or an ethics committee capable of objectively fulfilling the request without compromising the continuity of palliative care (Lampert, et al., 2010: 1008–1026).

Magnetic Resonance Imaging (MRI) Protocols

The magnetic resonance imaging (MRI) environment engenders significant, life-threatening risks for patients with CIEDs due to the high-intensity static magnetic field, time-varying gradient magnetic fields, and pulsed radiofrequency (RF) fields (Indik, et al., 2017: e97–e153). These physical forces can precipitate major device malfunctions, including mechanical torque on the generator and leads, electrical parameter resetting (power-on reset), inappropriate

pacing inhibition subsequent to the misinterpretation of external electromagnetic waves as intrinsic myocardial signals (oversensing), or the delivery of inappropriate shocks by ICD units. Among the most critical biophysical hazards is the "antenna effect," wherein RF energy is channeled along the lead conductor and concentrated at the distal tip, inducing thermal injury to the adjacent myocardial tissue and precipitating acute or chronic pacing threshold elevations (Indik, et al., 2017: e97–e153).

Contemporary "MRI-conditional" device systems are specifically engineered to obviate these biophysical risks. In such systems, ferromagnetic components are strictly minimized, conventional magnetic reed switches are substituted with solid-state Hall sensors, and specialized internal filters are incorporated to prevent RF energy absorption by the leads. However, in clinical practice, a system is deemed fully MRI-conditional only if all implanted components are mutually compatible and certified. The presence of an abandoned or fractured lead from a prior procedure, or a mismatch between the generator and lead models (e.g., components from differing manufacturers), unequivocally renders the entire system non-MRI-conditional, thereby contraindicating routine MRI scanning (Indik, et al., 2017: e97–e153).

A rigorous protocol must be instituted prior to and during the scanning procedure. Scans should generally be restricted to 1.5 Tesla closed-bore MRI scanners, and whole-body specific absorption rate (SAR) limits must be meticulously regulated in accordance with the manufacturer's specifications, typically constrained to <1.5 W/kg or <2.0 W/kg. Prior to entering the MRI suite, the device must be reprogrammed to a dedicated "MRI mode" via a programmer. Pacemaker-dependent patients require programming to an asynchronous mode (DOO or VOO) to preclude pacing inhibition induced by electromagnetic interference. In ICD patients, all tachyarrhythmia detection and therapy parameters must be entirely

disabled to prevent the misinterpretation of MRI gradient noise as ventricular fibrillation and the subsequent delivery of inappropriate shocks. Throughout the duration of the scan, the patient's hemodynamic status must be continuously monitored using MRI-compatible pulse oximetry and plethysmography, which remain impervious to magnetohydrodynamic artifacts (Indik, et al., 2017: e97–e153).

Electrocautery Management in Surgical Interventions

Electrocautery (electrosurgical) units utilized during surgical procedures represent the most prevalent and potent sources of external electromagnetic interference (EMI) for cardiac devices within the hospital setting. The high-frequency (300-500 kHz) electrical currents emitted by cautery devices intended for tissue dissection or coagulation can be erroneously interpreted by CIED leads as intrinsic cardiac electrical activity (P or R waves). This oversensing can yield fatal clinical consequences: in pacemaker-dependent patients, it may induce pacing inhibition resulting in asystole and prolonged pauses; it may precipitate a power-on reset (POR) returning the device to rudimentary factory settings; or in ICD patients, the high-frequency noise may be classified as ventricular tachycardia/fibrillation, culminating in the delivery of high-energy, inappropriate shocks intraoperatively (Crossley, et al., 2011: 1114–1154).

Risk stratification for EMI during electrosurgical interventions is fundamentally predicated on the anatomical locus of the surgical field. Surgeries performed inferior to the umbilicus (e.g., lower extremity or pelvic procedures) pose a relatively nominal EMI risk. Conversely, operations superior to the umbilicus—particularly thoracic, upper abdominal, breast, head-neck, and spinal surgeries—carry an elevated EMI risk, as the electrocautery current vector may traverse directly across the CIED system. Prior to high-risk surgical

interventions, prospective device reprogramming is imperative. Pacemaker-dependent patients must be programmed to an asynchronous mode (VOO/DOO) to avert cautery-induced asystole, while tachyarrhythmia detection must be suspended in ICD patients to preclude inappropriate shocks. In emergent scenarios precluding formal reprogramming, the application of a sterile clinical magnet over the generator can temporarily revert pacemakers to an asynchronous mode and suspend anti-tachycardia therapies in ICDs. The surgical team should preferentially utilize bipolar cautery, which localizes the current between the forceps tips. Should monopolar cautery be unavoidable, the dispersive electrode (grounding pad) must be positioned to ensure the current vector does not intersect the generator-lead axis, and cautery application should be restricted to brief, intermittent bursts lasting less than 5 seconds (Crossley, et al., 2011: 1114–1154).

Radiotherapy And Device Interactions

Therapeutic ionizing radiation (radiotherapy) administered to oncological patients can inflict permanent, irreversible microstructural damage upon the complementary metal-oxide-semiconductor (CMOS) integrated circuits that comprise the electronic core of modern CIEDs (Crossley, et al., 2011: 1114–1154; Indik, et al., 2017: e97–e153). High-energy radiation particles induce electrical charge accumulation within the CMOS silicon oxide insulating layers, potentially precipitating software latch-up, spontaneous RAM corruption, catastrophic hardware failure, or the induction of a fatal "runaway pacemaker" phenomenon—characterized by the uncontrolled delivery of pacing stimuli at a dangerously elevated rate. The severity of this electronic degradation correlates directly with the cumulative radiation dose. Extant literature indicates that cumulative doses exceeding the 10 Gy threshold exponentially augment the risk of major hardware failure (Indik, et al., 2017: e97–e153).

A formalized, multidisciplinary onco-cardiology protocol is mandatory for any CIED patient scheduled for radiotherapy. If dosimetric calculations project a cumulative device exposure >20 Gy due to tumor proximity, or if a pacemaker-dependent patient is anticipated to receive a moderate-to-high dose of 2-20 Gy with the device situated directly within the primary radiation field, surgical relocation of the generator to the contralateral pectoral region—completely outside the radiation field—must be strongly considered (Crossley, et al., 2011: 1114–1154; Indik, et al., 2017: e97–e153). Conversely, if the anticipated cumulative dose is maintained at <5 Gy, surgical explantation is generally unwarranted, and stringent clinical monitoring suffices (Indik, et al., 2017: e97–e153). Furthermore, close collaboration with the radiation oncology department is essential to ensure the selection of low-energy photon beams (<10 MV) during treatment. This specific parameter mitigates the generation of secondary neutron scattering, which possesses a markedly higher propensity to induce permanent device memory corruption compared to standard photon irradiation (Crossley, et al., 2011: 1114–1154).

Electromagnetic Interference and Daily Life

Technological advancements have equipped modern implantable devices with highly sophisticated internal protection circuitry, encompassing band-pass filters and bipolar sensing algorithms engineered to reject ambient electromagnetic noise (Carlson, et al., 2006: 1250–1273). Consequently, the preservation of the patient's daily social and occupational quality of life is maximized. Patients may safely operate ubiquitous household appliances—including microwave ovens, properly grounded toasters, hair dryers, televisions, and personal computers—without necessitating special precautions or incurring operational restrictions (Asirvatham, et al., 2021; Chow & Buxton, 2006). The utilization of cellular mobile phones is similarly safe; however, to circumvent

near-field interaction between emitted radiofrequency waves and the device generator, patients must be explicitly instructed never to carry the handset in a shirt or jacket pocket ipsilateral to the implant. During active use, the phone should be held to the contralateral ear, continuously maintaining a minimum safety margin of 15 cm between the device and the generator (Carlson, et al., 2006: 1250–1273; Chow & Buxton, 2006).

In public and transit environments, Electronic Article Surveillance (EAS) anti-theft portals in retail settings and high-sensitivity walk-through metal detectors at transportation hubs often elicit transient anxiety among patients. As the magnetic fields generated by these security apparatuses can temporarily perturb device functionality, patients must be advised against pausing, leaning on, or lingering within the portal footprint; rather, they should proceed straight through at a normal, unimpeded walking pace (Asirvatham, et al., 2021; Carlson, et al., 2006: 1250–1273). For patients engaged in heavy industrial occupations or utilizing electric arc welding equipment recreationally, hazard profiles are distinctly elevated. During arc welding operations, the current output must be strictly capped at 130 Amperes; the deployment of industrial-grade machinery exceeding 400 Amperes is absolutely contraindicated. Moreover, welding cables must never be draped across the torso, they should be routed as distantly from the generator axis as feasible, and a strict minimum spatial separation of 60 cm must be maintained between the welding arc and the patient's pectoral region (Asirvatham, et al., 2021; Ellenbogen & Kaszala, 2020).

Travel, Sports and Occupational Restrictions

The immediate postoperative period following device implantation constitutes the most critical window for securing long-term lead stability. The biological adhesion of intracardiac electrodes

to the myocardial substrate and the subsequent formation of a stabilizing fibrotic capsule (lead maturation) typically requires an interval of 4 to 6 weeks. Throughout this convalescent phase, to preclude the micro- or macro-dislocation of leads traversing the venous anatomy, patients must be strictly enjoined from elevating their ipsilateral arm above the shoulder plane (>90 degrees), executing sudden or forceful arm-swinging motions, and lifting objects exceeding 4.5 kg in weight (Asirvatham, et al., 2021; Chow & Buxton, 2006; Ellenbogen & Kaszala, 2020).

Statutory and medical restrictions pertaining to the operation of motor vehicles post-implantation are predominantly predicated upon the patient's underlying cardiovascular pathology rather than the surgical intervention per se. From a purely surgical perspective, a patient may resume driving once acute postoperative pain has resolved and the administration of reflex-impairing narcotic or sedative analgesics has ceased. However, regulatory frameworks are markedly more stringent for patients implanted with ICDs. The persistent risk of sudden syncope during arrhythmic episodes constitutes a severe hazard to both personal and public traffic safety. Consequently, absolute compliance with the legal driving restriction intervals mandated by international regulatory bodies, such as the European Heart Rhythm Association (EHRA), is obligatory (Task force, et al., 2009: 1097–1107). The duration of driving prohibitions fluctuates based on whether the device indication was for primary prevention or secondary prevention (following a documented ventricular tachyarrhythmia), and whether the patient has experienced appropriate or inappropriate shock therapies during longitudinal follow-up. These stipulations are significantly more rigorous, and frequently unequivocally prohibitive, for individuals holding commercial driving licenses.

Patient Education and Id Card Information

The enduring efficacy of CIED therapies, the mitigation of longitudinal complications, and the optimization of patient compliance are inextricably linked to the delivery of comprehensive, high-quality patient education prior to hospital discharge (Burri, Deharo, & Israel, 2015; Burri, et al., 2022). Before exiting the clinical setting, patients must receive exhaustive instruction delineating surgical incision care, appropriate dressing protocols, the identification of localized infection indices (erythema, localized warmth, edema, or purulent exudate), shoulder mobility restrictions, and the operational mechanics of home-based remote monitoring (telemetry) consoles (Burri, Deharo, & Israel, 2015; Slotwiner, et al., 2015: e69–100). It is imperative that patients are furnished with a formalized "Device Identification Card" cataloging the manufacturer's credentials alongside the precise serial numbers of the generator and leads. Patients must be emphatically instructed to carry this documentation on their person continuously, ensuring that emergency medical personnel or clinicians at disparate centers can rapidly identify and deploy the correct programmer unit during acute interventions (Asirvatham, et al., 2021).

Particularly among the ICD recipient cohort, the pervasive apprehension that the device may spontaneously discharge a high-energy, painful shock constitutes a profound psychosocial burden, frequently precipitating significant anxiety and detrimentally impacting the quality of life. During subsequent clinical surveillance, a notable proportion of patients manifest Post-Traumatic Stress Disorder (PTSD), panic attacks, and the phenomenon of "phantom shocks"—a psychological paradigm wherein the patient vividly perceives a shock discharge despite device telemetry confirming no such therapy was delivered (Burri, et al., 2022). To preempt these psychosocial sequelae, the characteristic sensation of a shock discharge (commonly articulated

as a sudden, forceful precordial blow) must be explicitly described to the patient pre-discharge. Patients should be counseled to eschew panic and immediately assume a seated, safe position should a shock occur. A definitive "Shock Action Plan" must be formulated and imparted: If the patient remains hemodynamically stable and experiences a solitary, isolated shock, they should remain calm and notify their managing clinic in a non-emergent manner. Conversely, if multiple shocks are delivered in rapid succession (suggestive of an electrical storm), or if a shock is accompanied by severe symptomatology such as angina, dyspnea, or profound presyncope, this constitutes an acute medical emergency. Under these circumstances, the patient must immediately mobilize emergency medical services (e.g., 112) for rapid transport to an advanced, fully equipped cardiology center (Burri, Deharo, & Israel, 2015; Burri, et al., 2022).

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PROBLEM SOLVING AND CASE-BASED APPROACH

ELİF MİRAY ALPAY¹

Introduction

The ECG is the most important tool to determine pacemaker function and malfunction. In a patient with a pacemaker, the ECG trace depends on the pacing mode used, the placement of the pacing electrodes, the pacing threshold, and the presence of spontaneous electrical activity.

The systematic approach used in the analysis of a pacemaker ECG aims to determine whether both the pacing and sensing functions of the pacemaker are working correctly. The following steps should be followed in this analysis:

Detection of Pacing Spikes

When beginning the analysis, one should look for pacing spikes in each lead. These are short vertical lines lasting approximately 2 ms(*Kalp Aritmilerinin Takibi: Kardiyologlar İçin Pratik Kılavuz*, n.d.).

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- Spikes from bipolar electrodes are smaller than those from unipolar electrodes and may be difficult to detect.
- If no spikes are observed, this may be due to the pacemaker being inhibited because the patient's natural rhythm is higher than the pacemaker's lower rate limit. If the patient's natural heart rate is above the pacemaker threshold, pacemaker activity is not expected, and therefore output failure and capture failure cannot be identified on the ECG(L.M. Gelder, 1995).

Pacing and Capture Analysis

When a pacing spike is observed, it is determined whether this stimulus induces depolarisation in the myocardium:

- Atrial Pacing: The pacing spike must precede the P wave. If every atrial spike is followed by a small P wave, 100% atrial capture is present.
- Ventricular Pacing: The pacing spike must precede the QRS complex. Right ventricular pacing typically produces a wide QRS complex with a left bundle branch block morphology. A left epicardial pacing electrode placement results in a QRS morphology similar to that of a right bundle branch block. The ST segments and T waves should be in the opposite direction (dissonant) to the QRS complex(BERNSTEIN et al., 1987).
- Capture Loss: This is the situation where a P wave or QRS complex does not follow the pacing pulse.

Rate and Interval Assessment

The distance between pacing spikes is checked to ensure it is consistent with the device's programmed lower rate limit(Lazar et al., 2017).

- If there is no natural rhythm, the pacemaker should deliver pulses at a constant and regular rate(L.M. Gelder, 1995).
- In dual-chamber pacemakers, the interval between the atrial spike and the ventricular spike (AV interval) should be assessed.

Analysis of the Sensing Function

The pacemaker's ability to recognise the heart's natural electrical activity is examined:

- Normal Sensing: When a natural heartbeat (P wave or QRS) occurs, the pacemaker must delay (inhibit) its next impulse.
- Undersensing: This occurs when the pacemaker fails to detect natural activity and delivers a spike asynchronously. Spikes are typically observed within QRS complexes [18]. Causes include an increased stimulation threshold at the electrode site (output block), poor electrode contact, a new bundle branch block, or programming issues.
- Oversensing: This occurs when the pacemaker mistakenly interprets signals such as muscle activity or noise as natural heartbeats, causing it to remain inactive(Harrigan et al., 2006).

Morphological Details and Discordance

- In ventricular pacing, the ST segment and T wave should be in the opposite direction (discordant) to the main axis of the QRS complex(*Kalp Aritmilerinin Takibi: Kardiyologlar İçin Pratik Kılavuz*, n.d.).
- Fusion beats: These are beats with an intermediate morphology that resemble both paced and normal beats, arising when a natural impulse and a pacemaker impulse

activate the ventricle simultaneously(Salgılayan & Endokardiyal, n.d.).

Magnet Test

If the pacemaker's function cannot be clearly determined on the ECG or if no spike is observed, an ECG is recorded with a magnet placed on the generator.

- The magnet disables the battery's sensing function, putting the device into asynchronous mode (VOO/DOO).
- This provides information on the battery's output capacity and battery status (Salgılayan & Endokardiyal, n.d.).

Sensing Errors

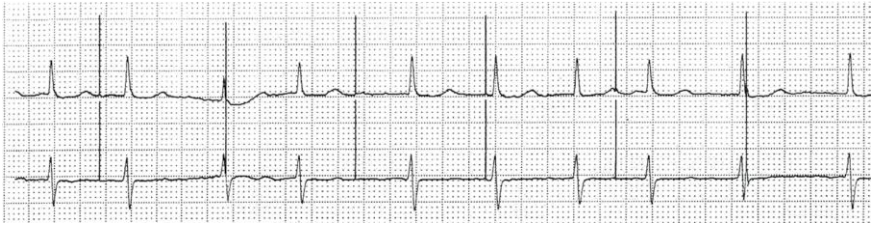
Sensing errors, which are among the types of pacemaker malfunction, refer to a disruption in the device's ability to correctly recognise the heart's natural electrical signals (P wave or QRS complex). This condition is broadly categorised into two types: undersensing and oversensing(*Pacemaker Intervals, Sensing, and Pacing - ECG*, n.d.).

Undersensing

Undersensing is a condition in which the pacemaker fails to detect the heart's natural activity. In this situation, as the device does not 'detect' the heart's own beats, it behaves as if the heart were not beating at all and continues to deliver asynchronous pacing pulses(Haghjoo & Haghjoo, 2011).

- ECG Findings: Inappropriate pacing spikes are observed either within the natural P waves or QRS complexes, or following them very shortly afterwards. This condition may also be referred to as "overpacing" because the pacemaker is generating unnecessary pulses(Lazar et al., 2017).

Picture 1: Ventricular Undersensing



(“The EHRA Book of Pacemaker, ICD, and CRT Troubleshooting: Case-Based Learning with Multiple Choice Questions,” 2015)

- Causes: These include incorrect setting of the detection threshold (resulting in the device becoming less sensitive due to the mV value being set too high), lead dislodgement, lead fracture, myocardial infarction or fibrosis, electrolyte disturbances such as hyperkalemia, and the effects of antiarrhythmic drugs (*Pacemaker Malfunction • LITFL • ECG Library Diagnosis*, n.d.).
- Solution: The pacemaker’s sensitivity should be increased, i.e. the millivolt (mV) threshold required for detection should be lowered. If the problem is mechanical, lead revision may be necessary (L.M. Gelder, 1995).

Oversensing

Oversensing occurs when the pacemaker detects signals that are not part of the heart’s natural activity (T waves, muscle activity or external interference) as if they were genuine heartbeats. This situation leads to the device being inadvertently inhibited and failing to deliver a pulse when required (Safavi-Naeini et al., 2016).

- ECG Findings: Unexpected pauses in heart rate, absence of pacemaker spikes, and episodes of bradycardia or asystole may occur. It is particularly common for the pacemaker to stop firing when the patient contracts their chest (pectoral) muscles.

- Causes: Sensitivity set too high (mV value set too low), myopotentials, misinterpretation of T-waves or large P-waves, electromagnetic interference, lead insulation defects, and crosstalk in dual-chamber pacemakers (where the signal from one chamber is detected by the other)(*Pacemaker Malfunction • LITFL • ECG Library Diagnosis*, n.d.). Myopotentials are a common cause of oversensing, which is seen predominately in unipolar pacemakers and usually results from sensing noncardiac muscle activity (e.g. pectoralis muscle or abdominal rectus muscles). Myopotentials are triggered by arm movements such as arm lifting in patients with prepectoral implants, or moving from a lying to sitting position in patients with abdominal implants. Oversensing may also occur if the ventricular lead falsely senses the T-wave.
- Solution: The device's sensitivity should be reduced; that is, the mV threshold should be raised to make the device 'less sensitive'(Lazar et al., 2017).

The Relationship Between Sensing and Sensitivity

Sensing settings in pacemaker programming can often be confusing because there is an inverse relationship between sensitivity and sensing values.

- A low mV value (e.g. 1.5 mV): Indicates that the device is highly sensitive and detects even small signals; this increases the risk of oversensing(*Kalıcı Pil Hastasının Takibi Follow-up of a Patient with Permanent Pacemaker*, 2011).
- A high mV value (e.g. 5.0 mV): This indicates that the device is not very sensitive and only detects very large signals; this increases the risk of undersensing(*Pacemaker Intervals, Sensing, and Pacing - ECG*, n.d.).

Failure to Capture and Pacing Threshold

In pacemaker analysis, ‘capture’ refers to the successful depolarisation of the heart muscle (myocardium) by the electrical impulse sent by the device, thereby generating a heartbeat. A disruption in this process is termed a ‘capture failure’ and is generally associated with an increase in the stimulation threshold(Safavi-Naeini & Saeed, 2016a).

Failure to Capture and ECG Appearance

This refers to a situation where a pacing spike is visible on the ECG but is not followed by a P wave (for atrial pacing) or a QRS complex (for ventricular pacing). A capture failure may be continuous or, in cases where the pacemaker’s output power is very close to the threshold value, it may occur intermittently(L.M. Gelder, 1995)(Safavi-Naeini & Saeed, 2016a).

What is the Pacing Threshold?

The pacing threshold is the minimum amount of electrical energy (in terms of amplitude and pulse width) required to induce consistent depolarisation in the chamber of the heart to be paced. To ensure safe operation, the device is typically programmed to deliver a voltage output of 2–3 times the measured threshold value (safety margin)(*Kalıcı Pil Hastasının Takibi Follow-up of a Patient with Permanent Pacemaker*, 2011).

Factors Causing Threshold Elevation and Capture Failure

An ‘exit block’ may develop if the pacing threshold rises above the battery’s maximum output power(*Pacemaker Malfunction • LITFL • ECG Library Diagnosis*, n.d.). The causes of threshold elevation are as follows:

- **Lead Dislodgement:** This is the most common cause of capture failure, particularly in the early post-implantation

period(*Kalp Pillerinde Sorun Tespiti - Troubleshooting in Cardiac Pacemakers - Ekg - Ecg - Ankara Kardiyoloji - Mete Alpaslan - Kalp Hastalıkları - Doktorekg.Com, n.d.*).

- Lead Fracture or Insulation Defect: Compromised lead integrity prevents energy from reaching the heart(Lazar et al., 2017).
- Lead Maturation and Fibrosis: The formation of excessive fibrous tissue around the electrode tip (foreign body reaction) impedes energy conduction and raises the threshold(L.M. Gelder, 1995).
- Myocardial Infarction: Development of tissue death (necrosis) or ischaemia in the region where the electrode tip is located(Lazar et al., 2017).
- Electrolyte Imbalances: Hyperkalaemia in particular (serum potassium exceeding 7.0 mEq/L) significantly increases the threshold value(*Pacemaker Malfunction • LITFL • ECG Library Diagnosis, n.d.*).
- Metabolic Disorders: Severe acidosis or alkalosis.
- Drug Effects: Class Ic antiarrhythmic drugs (flecainide, etc.) and sotalol may raise the threshold for depolarisation(*Kalp Pillerinde Sorun Tespiti - Troubleshooting in Cardiac Pacemakers - Ekg - Ecg - Ankara Kardiyoloji - Mete Alpaslan - Kalp Hastalıkları - Doktorekg.Com, n.d.*)(L.M. Gelder, 1995).
- Battery Depletion: A drop in battery voltage prevents sufficient output energy from being provided.
- DC Shock (Defibrillation/Cardioversion): Shocks delivered in the vicinity of the device may acutely increase the

threshold by causing temporary trauma or ischaemia at the electrode-tissue interface(L.M. Gelder, 1995).

- Air Lock: In unipolar systems, the presence of air in the battery compartment may prevent the energy from completing the circuit(L.M. Gelder, 1995).

Diagnostic Approach and Differential Diagnosis

If no spike is observed on the ECG, this is termed ‘failure to output’; if a spike is present but there is no capture, this is termed ‘capture defect’(Lazar et al., 2017).

- Magnet Test: When a magnet is placed on the battery, the device switches to asynchronous mode (VOO/DOO). If spikes are visible in this mode but capture does not occur, the problem is definitely a capture defect or increased threshold.
- Impedance Measurement: In telemetry measurements, an increase in resistance suggests a lead fracture, a decrease in resistance suggests insulation failure.
- Radiological Examination: Displacement or breakage of the lead can be confirmed by chest X-ray or fluoroscopy(*Pacemaker Malfunction • LITFL • ECG Library Diagnosis*, n.d.).

In a patient with a capture defect, emergency management may require increasing the pacemaker output (amplitude and pulse width) or providing temporary pacing support(Safavi-Naeini et al., 2016).

Crosstalk and Far-field Sensing

Crosstalk and far-field sensing are specific scenarios that fall under the category of ‘oversensing’ in relation to the pacemaker’s sensing function, but which arise from interactions between different chambers. Although these two terms are sometimes used

interchangeably in the medical literature, they technically refer to different phenomena.

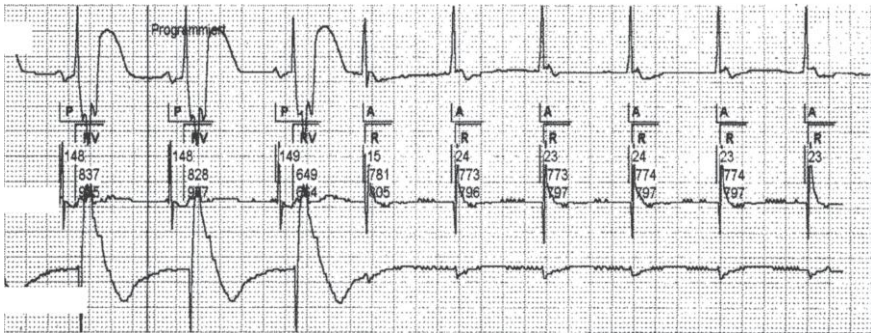
Crosstalk

Crosstalk occurs when a pacemaker impulse (pace spike) in one heart chamber is mistakenly detected by an electrode in the other chamber as natural cardiac activity, resulting in the inappropriate suppression of the impulse in the second chamber.

This condition is most commonly observed in dual-chamber or biventricular pacemakers(*Pacemaker Intervals, Sensing, and Pacing - ECG*, n.d.).

- Mechanism: The most common form involves the ventricular electrode detecting an atrial pacing impulse. The ventricular channel misinterprets this impulse as a genuine R wave (a natural ventricular beat) and ceases to generate a ventricular impulse (inhibits it)(*Pacemaker Malfunction: Background, Pathophysiology, Etiology*, n.d.).
- Clinical Risk: If the patient has no intrinsic ventricular rhythm (is pacemaker-dependent), this poses a life-threatening risk that can lead to ventricular asystole(Dauw et al., 2021).
- Causes: High atrial output voltage, high ventricular sensitivity (low mV value), a short ventricular blanking period, and the use of unipolar systems increase the risk of crosstalk(L.M. Gelder, 1995).

Picture 2:AV Crosstalk



(“The EHRA Book of Pacemaker, ICD, and CRT Troubleshooting: Case-Based Learning with Multiple Choice Questions,” 2015)

The first 3 cycles prior to the start of the ventricular threshold test are in sinus rhythm with ventricular pacing and ventricular capture. The ventricular threshold test is performed in DDD mode at a rate of 75 bpm with atrial pacing and atrial capture. A VS(ventricular sensing) event occurs 15–24 ms after atrial pacing and blocks ventricular pacing; this corresponds to AV cross-talk in the presence of ventricular asystole.

Protection Mechanisms

- **Ventricular Blanking Period:** The ventricular sensor is rendered completely ‘blind’ for a very short period at the moment an atrial pace is delivered.
- **Ventricular Safety Pacing (VSP):** If a signal is detected immediately after the blanking period ends (within the crosstalk window), the device assumes this may be crosstalk and sends a ventricular pacing signal within a short AV interval to prevent asystole(Safavi-Naeini & Saeed, 2016b). On the ECG, this appears as two very close (double) pacing spikes(Srivastava & Prasad, 2019).

- **Programming Changes:** Reducing atrial output or ventricular sensitivity, extending the blanking period, or switching to a bipolar lead system reduces the risk of crosstalk.

Far-field Sensing

Far-field sensing refers to the detection of electrical signals originating outside the chamber in which the electrode is located (for example, an atrial lead detecting depolarisation in the ventricle)(*Progress in Biomedical Research*, 2000).

The most common scenario is when the atrial electrode detects the depolarisation of the ventricle (the R-wave). As R-waves are much larger in voltage than P-waves, they can be easily ‘detected’ by the atrial lead(*Progress in Biomedical Research*, 2000).

Clinical Outcomes

- **Pacemaker-mediated Tachycardia (PMT):** The device may mistake the R-wave for atrial activity and trigger the ventricle, potentially initiating an "endless loop tachycardia"(Safavi-Naeini & Saeed, 2016b).
- **False Mode Switch:** The device may mistakenly interpret detected far-field ventricular signals as rapid atrial fibrillation or flutter and inadvertently cease atrial pacing(*Progress in Biomedical Research*, 2000).

Solutions

- **Bipolar Detection:** As bipolar electrodes detect signals only from a very narrow area at their tips, they are far more resistant to detecting far-field signals than unipolar systems.
- **PVARP (Post-Ventricular Atrial Refractory Period):** Keeping the atrial channel ‘deaf’ for a specific period (refractory period) following a ventricular beat prevents the

misinterpretation of these distant-field signals(Mukherjee et al., 2021).

In summary, whilst crosstalk is generally associated with the detection of pacing spikes and the suppression of stimulation, far-field sensing involves the misinterpretation of the heart's own electrical waves (P/R waves) as originating from the wrong chamber. Both conditions can be managed by analysing the device's intracardiac electrograms (EGMs) and programming appropriate refractory/blocking periods.

Picture 3:Far-field R-wave (FFRW) oversensing



Abbreviations: AS=atrial sensing, ,VP=ventricular pacing

(“The EHRA Book of Pacemaker, ICD, and CRT Troubleshooting: Case-Based Learning with Multiple Choice Questions,” 2015)

The sharp signals are near-field atrial EGMs. The smaller signals are FFRWs that appear just after the VP, slightly below 160

ms, and fall within the PVARP (post-ventricular atrial refractory period) interval (but occur after the 150-ms atrial blanking period).

Endless Loop Tachycardia

Endless loop tachycardia (ELT), more commonly known as pacemaker-mediated tachycardia (PMT) or pacemaker circus movement tachycardia, is a form of re-entrant tachycardia occurring in patients with dual-chamber (DDD or VDD) pacemakers(*Prague ICU*, n.d.)(Couturier & Anne, n.d.). It occurs when the pacemaker becomes part of a re-entry circuit, serving as the antegrade limb (atrium to ventricle), while the patient's own conduction system (AV node or accessory pathway) serves as the retrograde limb (ventricle to atrium)(Abu-haniyeh & Hajouli, 2023).

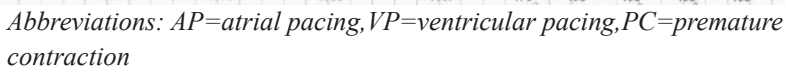
Mechanism and Initiation

The tachycardia begins when a ventricular event results in a retrograde impulse that travels back to the atria. If this retrograde P-wave occurs after the pacemaker's post-ventricular atrial refractory period (PVARP) has ended, the pacemaker senses it as a native atrial beat(Abu-haniyeh & Hajouli, 2023).The sequence typically follows these steps:

- **Triggering Event:** A premature ventricular contraction (PVC) is the most common trigger, but it can also be initiated by an atrial premature contraction (PAC), loss of atrial capture, or atrial sensing of external interference (oversensing)(Dauw et al., n.d.).
- **Sensing and Tracking:** The pacemaker senses the retrograde P-wave and, after a programmed AV delay, delivers a ventricular pacing stimulus(Abu-haniyeh & Hajouli, 2023).
- **Completion of the Loop:** This paced ventricular event again conducts retrogradely to the atrium, restarting the cycle and creating an "endless loop"(Couturier & Anne, n.d.).

ECG Characteristics

- Picture 4: Endless Loop Tachycardia*



The first event is marked as “PC” (premature contraction) in the marker channel, while subsequent events are marked as “TS”

(tachycardia sensing). These AS(atrial sensing) events trigger a 210-ms atrioventricular interval (corresponding to the detected atrioventricular interval); this results in ventricular pacing, which in turn leads to retrograde ventriculoatrial conduction and sustains the infinite-loop tachycardia.

Management and Termination

PMT is considered an emergency, especially in patients with ischemic heart disease where rapid rates can lead to ischemia or heart failure(Srivastava & Prasad, 2019).

Acute Termination

- **Magnet Application:** Placing a magnet over the pulse generator is the fastest bedside intervention(Safavi-Naeini & Saeed, 2016b). It switches the pacemaker to an asynchronous mode (VOO or DOO), disabling sensing and immediately breaking the re-entrant circuit(Raj Subramanian et al., 2008).
- **Pharmacologic Intervention:** IV adenosine (typically 6 mg) can terminate the loop by causing a transient ventriculo-atrial (VA) block, interrupting the retrograde limb of the circuit(*What Is the Appropriate Management for Pacemaker-mediated Tachycardia?*, n.d.)(*Pacemaker Malfunction • LITFL • ECG Library Diagnosis*, n.d.).
- **Vagal Maneuvers:** Standard maneuvers can also be used to induce transient AV block and terminate the tachycardia.

Prevention and Long-term Programming

- **PVARP Extension:** The cornerstone of prevention is programming a PVARP that is longer than the patient's retrograde conduction time so that retrograde P-waves fall into the refractory period and are ignored(Lazar et al.,

2017)(*What Is the Appropriate Management for Pacemaker-mediated Tachycardia?*, n.d.).

- Automatic Algorithms: Modern pacemakers have specific PMT termination algorithms(*Prague ICU*, n.d.). These devices detect a sequence of fast beats at the MTR with stable VA intervals and automatically extend the PVARP for one cycle to break the loop.
- Reducing AV Delay: Shortening the AV delay can sometimes stress the retrograde conduction system enough to induce a block and stop the loop(Couturier & Anne, n.d.)(*What Is the Appropriate Management for Pacemaker-mediated Tachycardia?*, n.d.).

Pacemaker Interrogation

Pacemaker or ICD (Implantable Cardioverter Defibrillator) interrogation is the process of wirelessly scanning the device using an external programmer and reading the data stored in its memory(Safavi-Naeini & Saeed, 2016b). The reading and analysis of interrogation data should be carried out by following a systematic sequence:

Battery Status and Lifespan Analysis

The first step in the assessment is to check the battery's current voltage and estimated remaining lifespan.

- Voltage: A fully charged battery is typically around 2.8V(*Kalıcı Pil Hastasının Takibi Follow-up of a Patient with Permanent Pacemaker*, 2011).
- Lifespan Indicators: When the battery is nearing the end of its life, the device displays ERI (Elective Replacement Indicator) or EOL (End of Life) warnings. At this stage, the

device should be scheduled for replacement (Electrophysiology & System, 2004).

Assessment of Lead Performance

The integrity of the device's leads (cables connected to the heart) is measured using three main parameters:

- **Impedance (Resistance):** The electrical resistance of the lead is measured (the normal range is generally 300–1000 ohms)(*Kahıcı Pil Hastasının Takibi Follow-up of a Patient with Permanent Pacemaker*, 2011). A sudden increase in impedance may indicate a lead break, whilst a significant decrease may indicate insulation failure(L.M. Gelder, 1995).
- **Sensing Thresholds:** The clarity with which the device 'detects' the heart's natural P and R waves is assessed in millivolts (mV)(*Medtronic Pacemaker Pacing & Sensing Guide | ECG | Cardiacases*, n.d.).
- **Capture Threshold:** This is the minimum voltage required to generate a beat in the myocardium. For safe operation, the device output is typically programmed to 2–3 times this threshold value (safety margin)(*Medtronic Pacemaker Pacing & Sensing Guide | ECG | Cardiacases*, n.d.).

Pacing Statistics and Device Dependency

The duration for which the device has been active since the last check-up is examined:

- **Pacing Percentage:** Indicates the extent to which the patient is dependent on the device. For example, 100% ventricular pacing indicates that the patient's own rhythm is below the device's limit(L.M. Gelder, 1995).
- **Rate Histograms:** Shows the patient's heart rate distribution during daily life. Unexpectedly high rates may indicate

episodes of tachycardia(*Medtronic Pacemaker Pacing & Sensing Guide | ECG | Cardiocases*, n.d.).

Arrhythmia Records and Event Analysis

Modern devices store arrhythmias such as atrial fibrillation (AF) or ventricular tachycardia (VT) in their memory(Mukherjee et al., 2021).

- **Marker Channels:** These are diagrams showing how the device classifies each heartbeat (detection—AS/VS or pacing—AP/VP)(L.M. Gelder, 1995).
- **Intracardiac Electrocardiograms (IEGM):** These are ECG signals recorded from within the heart at the moment of the arrhythmia. These recordings enable the distinction between true arrhythmias and noise caused by ‘oversensing’ (false detection)(*Kalp Aritmilerin Takibi: Kardiyologlar İçin Pratik Kılavuz*, n.d.)(Dauw et al., n.d.).

Review of Programmed Features

The accuracy of the device’s current mode (e.g. DDD, VVI), lower and upper rate limits, and special algorithms (e.g. Autocapture or Mode Switch) is checked(Parkinson & Broadhurst, n.d.).

Interrogation results should always be interpreted in comparison with the patient’s clinical condition and previous control data. If you suspect a physical lead issue or technical fault, radiological investigations such as a chest X-ray or fluoroscopy may be required in addition to the interrogation data (L.M. Gelder, 1995).

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