



# Medical Coverage Policy

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## Cardiac Resynchronization Therapy (CRT)

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### Related Coverage Resources

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## Overview

This Coverage Policy addresses the use of a biventricular pacemaker (alone or combined with an implantable cardioverter defibrillator [ICD]) for cardiac resynchronization therapy (CRT), triple-site or triventricular pacing CRT, and conduction system pacing for CRT.

## Coverage Policy

**The use of a biventricular pacemaker alone or in combination with an implantable cardioverter defibrillator (ICD)\* for cardiac resynchronization therapy (CRT) is considered medically necessary for ANY of the following indications when the individual has been on an optimal pharmacologic regimen for at least 3 months before consideration of implantation:**

- **Ischemic or nonischemic cardiomyopathy, left ventricular ejection fraction (LVEF)  $\leq$  35%, sinus rhythm (SR) for ANY of the following:**
  - QRS 120-149 milliseconds (ms), left bundle branch block (LBBB), New York Heart Association (NYHA) Class II—ambulatory class IV
  - QRS  $\geq$  150 ms, LBBB, NYHA Class I—ambulatory class IV
  - QRS  $\geq$  150 ms, non-LBBB, NYHA Class III—ambulatory class IV
- **Ischemic or nonischemic cardiomyopathy, persistent or permanent atrial fibrillation, and ALL of the following:**
  - LVEF  $\leq$  35%
  - LBBB
  - QRS  $\geq$  150 ms
- **Pre-existing or anticipated right ventricular (RV) pacing with a clinical indication for ICD or pacemaker implantation and ALL of the following:**
  - RV pacing anticipated  $>$  40%
  - intrinsic narrow QRS
  - LVEF  $\leq$  35%
  - NYHA Class I—ambulatory class IV

**\*Note: Please reference Cigna Medical Coverage policy “Cardioverter-Defibrillator Devices” for conditions of coverage of an ICD device.**

**Conduction system pacing (i.e., His bundle pacing [HBP]; left bundle branch area pacing [LBBAP]) is considered medically necessary when BOTH of the following criteria are met:**

- individual meets one of the above indications for biventricular pacing
- **EITHER** of the following:

- coronary sinus (CS) or left ventricular (LV) lead placement was attempted and was unsuccessful
- individual has LBBB and effective CRT cannot be achieved with a CS/LV lead

**Replacement of a biventricular pacemaker generator alone or in combination with an implantable cardioverter defibrillator and/or leads is considered medically necessary.**

**The use of a biventricular pacemaker alone or combined with an implantable cardioverter defibrillator for CRT for any other indication is considered not medically necessary.**

**Triple-site or triventricular pacing CRT is considered experimental, investigational or unproven for any indication.**

## Coding Information

### Notes:

1. This list of codes may not be all-inclusive since the American Medical Association (AMA) and Centers for Medicare and Medicaid Services (CMS) code updates may occur more frequently than policy updates.
2. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

**Considered Medically Necessary when criteria in the applicable policy statements listed above are met and when used to report the insertion or replacement of a biventricular pacemaker alone or when combined with an implantable cardioverter defibrillator (ICD) and/or leads:**

CPT®* Codes	Description
33224	Insertion of pacing electrode, cardiac venous system, for left ventricular pacing, with attachment to previously placed pacemaker or implantable defibrillator pulse generator (including revision of pocket, removal, insertion, and/or replacement of existing generator)
33225	Insertion of pacing electrode, cardiac venous system, for left ventricular pacing, at time of insertion of implantable defibrillator or pacemaker pulse generator (eg, for upgrade to dual chamber system) (List separately in addition to code for primary procedure)
33249	Insertion or replacement of permanent implantable defibrillator system, with transvenous lead(s), single or dual chamber

**Considered Medically Necessary when criteria in the applicable policy statements listed above are met and when used to report conduction system pacing:**

CPT®* Codes	Description
33999 <sup>†</sup>	Unlisted procedure, cardiac surgery

**<sup>†</sup>Note: Considered Experimental/Investigational/Unproven when used to report triple-site or triventricular pacing CRT**

## **General Background**

### **Heart Failure**

Congestive heart failure (CHF), or heart failure (HF), is a serious medical condition in which the heart does not pump blood as efficiently as it should. Approximately one-third of people with heart failure will also develop an arrhythmia (irregular heartbeat) which can cause the contraction of the heart's two lower chambers (ventricles) to become uncoordinated (ventricular dyssynchrony). Dyssynchrony is evidenced by a wide QRS interval seen on electrocardiogram (ECG). Ventricular dyssynchrony can worsen the heart's ability to pump effectively and exacerbate heart failure symptoms. It is also associated with an increased risk of serious illness and death.

The most frequently used measure of heart function is the left ventricular ejection fraction (LVEF). Normal LVEF ranges from 50–75% at rest. Severe heart failure can reduce LVEF to < 35%. Treatment for heart failure includes medications, which may include a combination of diuretics, digoxin, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARB), beta-blockers, and aldosterone antagonists. Some patients may remain symptomatic despite drug therapy. The definitive therapy for end-stage heart failure patients is heart transplantation.

The New York Heart Association (NYHA) classification of heart failure is a four-tier system that categorizes patients based on a subjective impression of the degree of functional compromise. The chart below defines the four NYHA functional classes. Advanced heart failure is categorized as NYHA Class III and Class IV (Colucci, 2025).

Class I	Individuals with cardiac disease but without resulting limitation of physical activity; ordinary physical activity does not cause undue fatigue, palpitation, dyspnea or anginal pain; symptoms only occur on severe exertion
Class II	Individuals with cardiac disease resulting in slight limitation of physical activity; they are comfortable at rest; ordinary physical activity results in fatigue, palpitation, dyspnea or anginal pain
Class III	Individuals with cardiac disease resulting in marked limitation of physical activity; they are comfortable at rest; less than ordinary activity (e.g., mild exertion) causes fatigue, palpitation, dyspnea or anginal pain
Class IV	Individuals with cardiac disease resulting in inability to carry on any physical activity without discomfort; symptoms of cardiac insufficiency or anginal syndrome is present at rest; if any physical activity is undertaken, discomfort is increased  Ambulatory Class IV: Individuals with no active acute coronary syndrome; no inotropes; and on guideline-directed medical therapy

### **Cardiac Resynchronization Therapy (CRT)**

Despite the combination of various therapies for heart failure, some patients remain symptomatic. Of the various non-drug approaches, biventricular pacing or cardiac resynchronization therapy (CRT) has gained interest since its introduction in the early 1990s. CRT is the term applied to reestablishing coordinated contraction between the left ventricular free wall and the ventricular septum in an attempt to improve left ventricular efficiency and, subsequently, to improve NYHA

functional class. Generally, CRT has been used to describe biventricular pacing, but cardiac resynchronization can be achieved by left ventricular pacing only in some individuals. Selected individuals with mild to severe heart failure may benefit from CRT. Combined with stable optimal medical therapy, CRT may help the ventricles beat together and improve the heart's ability to supply blood and oxygen to the body.

An implantable biventricular pacemaker is an advanced version of a standard implantable pacemaker. The biventricular pacemaker is implanted in the muscle tissue of the chest, below the collarbone, or in the abdomen. Three leads or wires, (one atrial lead and two ventricular leads), are transvenously connected from the pacemaker to the heart. The pacing leads are typically placed in the right atrium, the right ventricle, and the coronary sinus, which results in stimulation of the left ventricle. In a small percentage of cases, it may not be possible to place the left ventricular lead transvenously. In such situations, some centers are opting for an epicardial approach if the transvenous approach is unsuccessful. The pacemaker sends out electrical impulses to the heart through the leads. Placement of a biventricular pacemaker can usually be accomplished in an outpatient setting under sedation or general anesthesia. A short inpatient stay may be required for epicardial left ventricular lead placement. Once the pacemaker is implanted, it is programmed so that both ventricles are stimulated to contract after atrial contraction, with the goals of improving left ventricle (LV) function, reducing presystolic mitral regurgitation, and improving LV diastolic filling time.

The benefits of CRT need to be weighed against the risks of the procedure, along with the adverse effects of having a CRT device implanted long term. The reported risks of the procedure are uncommon but some events may be serious, such as pericardial effusion with tamponade or coronary dissection. Minor reported adverse events such as lead dislodgement are more common and may result in repeat procedures.

### **CRT plus Implantable Cardioverter Defibrillator (ICD) System (CRT-D)**

Some individuals with heart failure are also at high risk for life-threatening heart rhythms, including ventricular tachycardia and ventricular fibrillation. Individuals with heart failure who are at high risk for ventricular tachycardia and ventricular fibrillation may require a CRT system that includes implantable cardioverter defibrillator (ICD) therapy. The CRT plus ICD system (CRT-D) is designed to help the right and left ventricles beat at the same time in a normal sequence. Additionally, should an individual experience an episode of ventricular tachycardia or ventricular fibrillation, the CRT-D system will detect the life-threatening arrhythmia and automatically correct the heart's rhythm.

CRT-D may be considered for people who fulfill the criteria for implantation of a CRT-pacing (CRT-P) device and who also separately fulfill the criteria for the use of an ICD device. Clinical indications for ICD devices are discussed in further detail in Cigna Medical Coverage policy "Cardioverter-Defibrillator Devices".

### **Device Replacement**

When an implantable heart rhythm device, including those used for cardiac resynchronization, nears the end of its battery life, it is replaced. The expected lifespan of the device varies among manufacturers. A device may also become damaged or begin to malfunction; and leads may become dislodged or fracture. Such scenarios warrant device replacement. This may occur on an urgent basis (e.g., battery end of life [EOL]), or during an elective replacement interval (ERI).

### **U.S. Food and Drug Administration (FDA)**

Multiple biventricular pacemakers have been approved by the FDA through the Premarket Approval (PMA) process for biventricular pacing alone (CRT-P) or biventricular pacing and defibrillation (CRT-D). CRT-P and CRT-D devices are Class III devices. Although approved

indications vary by device, CRT devices are generally indicated for individuals with heart failure with reduced LVEF and prolonged QRS duration, who remain symptomatic despite optimal drug therapies.

The FDA device approval notifications and manufacturer labels include the following contraindications to CRT-P and CRT-D devices:

- Asynchronous pacing is contraindicated in the presence or likelihood of competitive paced and intrinsic rhythms.
- Unipolar pacing is contraindicated in individuals with an ICD because it may cause unwanted delivery or inhibition of defibrillator or ICD therapy.
- CRT-D devices are contraindicated for patients whose ventricular tachyarrhythmias may have transient or reversible causes and for patients with incessant ventricular tachycardia or ventricular fibrillation.
- CRT-D devices are contraindicated for dual chamber atrial pacing in patients with chronic refractory atrial tachyarrhythmias (FDA, 2014).

Device or Product	Identifier	Manufacturer
Entrant™ CRT-D Gallant™ CRT-D	P030054	Abbott Medical
Edora CRT-P	P070008	Biotronik, Inc.
Ilivia CRT-D	P050023	Biotronik, Inc.
DYNAGEN™ CRT-D INOGEN™ CRT-D MOMENTUM™ CRT-D RESONATE™ HF CRT-D	P010012	Boston Scientific Corp.
INTUA™ CRT-P INVIVE™ CRT-P VALITUDE™ CRT-P VISIONIST™ CRT-P	P030005	Boston Scientific Corp. (Guidant)
Amplia MRI™ CRT-D SureScan™ Cobalt™ MRI SureScan™ CRT-D	P010031	Medtronic
Percepta™ CRT-P MRI SureScan™ Serena™ CRT-P MRI SureScan™ Solara™ CRT-P MRI SureScan™	P010015	Medtronic

\*FDA product codes: NIK, NKE

Note: Coverage decisions are not based solely on FDA approval. Device or product names are provided for example purposes only. Their inclusion does not indicate endorsement or preference for any specific brand or model. This list is not intended to reflect all available products or technologies.

### Literature Review

**CRT in NYHA Class III and IV:** Evidence in the published peer-reviewed literature, including randomized controlled trials, meta-analyses and systematic reviews, indicates that cardiac resynchronization therapy is effective at improving quality of life, patient functional capacity and heart failure symptoms in a subgroup of individuals with heart failure, with or without ICD indications, decreased cardiac function and ventricular dyssynchrony who are on optimal pharmacologic regimen before implantation. The following benchmark large-scale trials included primarily NYHA Class III and IV individuals with a wide QRS complex: MULTIsite STimulation In Cardiomyopathies (MUSTIC); Multicenter InSync Randomized Clinical Evaluation (MIRACLE);

Multicenter InSync ICD Randomized Clinical Evaluation (MIRACLE ICD); Contak CD; Cardiac Resynchronization — Heart Failure (CARE-HF); and Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION). (Deng, et al., 2015; Cleland, et al., 2009; Upadhyay, et al., 2008; Auricchio, et al., 2007; McAlister, et al., 2007; Lindenfeld, et al., 2007; Delnoy, et al., 2007; Sutton, et al., 2006; Gasparini, et al., 2006; Cleland, et al., 2005; Molhoek, et al., 2005; Doshi, et al., 2005; Molhoek, et al., 2004; Bristow, et al., 2004; Garrigue, et al., 2003; Higgins, et al., 2003; Abraham, et al., 2002; Leclercq, et al., 2002; Leon, et al., 2002).

**CRT in NYHA Class I and II:** The majority of newer research in CRT is to evaluate whether the benefits of CRT extend to individuals with mild or less severe heart failure (NYHA Class I/II). While lower morbidity and reduction or alleviation of symptoms are the goals of CRT in advanced heart failure, preventing heart failure progression is the primary objective for CRT in NYHA Classes I and II. The role of CRT in individuals with mild or less severe heart failure is less established. Four key randomized controlled trials have been published in the peer-reviewed literature:

Resynchronization–Defibrillation for Ambulatory Heart Failure Trial (RAFT), Resynchronization Reverses Remodeling in Systolic Left Ventricular Dysfunction (REVERSE), Multicenter InSync ICD Randomized Clinical Evaluation II (MIRACLE ICD II) and Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy (MADIT-CRT). These trials enrolled 4,414 subjects which included individuals with NYHA Class I or II heart failure, at least 25 subjects per treatment group, and reported on at least one relevant health outcome with follow-up ranging from six months to 2.4 years (Tang, et al., 2010; Moss, et al., 2009; Linde, et al., 2008, Abraham, et al., 2004).

Evidence in the published peer-reviewed literature, including randomized controlled trials and a meta-analysis (Al-Majed, et al., 2011), indicates that there is a consistent benefit for CRT in reducing hospitalizations for a subgroup of individuals with mild heart failure (NYHA Class I or II) and in improving echocardiographic parameters. Data indicates that biventricular resynchronization therapy may not demonstrate a benefit on quality of life, functional status, or progression to more advanced stages of heart failure. The evidence on mortality differs among the available studies. Of the two largest studies, MADIT-CRT and RAFT, one reported a mortality difference while the other did not. The RAFT trial had individuals with more severe illness, a higher baseline death rate, and a longer follow-up period concluding that CRT is likely to improve mortality for individuals with NYHA class II heart failure. A subanalysis of the RAFT study found that women in particular benefitted from CRT-D, and had a significantly reduced incidence of death and heart failure hospitalization as compared to men ( $p < 0.001$ ) (de Waard, et al., 2019). Robust evidence to support biventricular resynchronization therapy in individuals with asymptomatic left ventricular dysfunction or NYHA Class I symptoms is inconclusive resulting in the inability to draw strong conclusions regarding the impact on health outcomes (Santangeli, et al., 2011; Al-Majed, et al., 2011; Adabag, et al., 2011; Zareba, et al., 2011; Versteeg, et al., 2011; Pouleur, et al., 2011; Solomon, et al., 2010; Tang, et al., 2010; Moss, et al., 2009; Linde, et al., 2008; Abraham, et al., 2004).

**Patient Selection Criteria:** Biventricular pacing is an established method of CRT, and is most effective for individuals experiencing heart failure with reduced ejection fraction (EF), left bundle branch block (LBBB), and a wide QRS. Pacing is also supported in individuals with a low EF receiving a new or replacement device and who require  $\geq 40\%$  ventricular pacing. However, approximately 30-50% of individuals do not improve with biventricular pacing due to anatomical variances, a narrow QRS, non-LBBB presentation, or other factors (Sharma and Vijayaraman, 2021). Since some individuals do not respond favorably after undergoing CRT, studies addressing optimal patient selection criteria for CRT are ongoing.

**QRS Duration:** Some individuals with narrower QRS complexes have echocardiographic evidence of left ventricular mechanical dyssynchrony and may also benefit from CRT. Results of published

trials are insufficient at this time to demonstrate that the use of CRT in heart failure patients with a narrow QRS complex (i.e., < 120 ms) benefits patient outcomes.

The Evaluation of Resynchronization Therapy for Heart Failure (LESSER-EARTH) trial was a randomized, double-blind, 12-center study that was designed to compare the effects of active and inactive cardiac resynchronization therapy in individuals with severe left ventricular dysfunction and a QRS duration < 120 ms (Thibault, et al., 2013). The trial was interrupted prematurely by the Data Safety and Monitoring Board because of futility and safety concerns after 85 individuals were randomized. The authors reported that in individuals with a LVEF  $\leq$  35%, symptoms of heart failure, and a QRS duration < 120 ms, CRT did not improve clinical outcomes or left ventricular remodeling and was associated with potential harm (Thibault, et al., 2013).

Stavrakis et al. (2012) conducted a meta-analysis of randomized clinical trials to evaluate the impact of QRS duration on the efficacy of CRT. Only trials that reported subgroup data according to QRS duration were included. Five trials involving 6501 subjects (4437 with QRS  $\geq$  150 ms and 2064 with QRS < 150 ms) were included. Three trials, enrolling individuals with mild to moderate HF, compared CRT-implantable cardioverter defibrillator with CRT, whereas CRT versus medical therapy was compared in the other two trials, which included individuals with advanced HF. In individuals with intrinsic QRS duration  $\geq$  150 ms, pooled analysis of the five trials revealed a significant 42% reduction in the incidence of the primary endpoint of death or hospitalization for HF with the use of CRT compared to control (HR = 0.58, 95% CI: 0.50-0.68;  $p < 0.00001$ ), but not in individuals with QRS < 150 ms (HR = 0.95, 95% CI: 0.83-1.10;  $p = 0.51$ ). These results were consistent across all degrees of HF severity. In individuals with intrinsic QRS duration < 150 ms, pooled analysis of the five trials showed no significant benefit from CRT (with or without ICD) compared to control (HR = 0.95, 95% CI: 0.83-1.10;  $p = 0.51$ ). The lack of benefit was consistent between the two subgroups based on the severity of heart failure.

Sipahi et al. (2011) conducted a meta-analysis of published randomized controlled trials that evaluated whether individuals with modest prolongation of the QRS complex benefited from CRT. This study identified five trials enrolling a total of 5813 subjects that reported on outcomes stratified by QRS duration. There was some variability in the definition of QRS categories, but the authors were able to categorize studies into those with moderately prolonged QRS, generally 120-149 ms, and severely prolonged QRS, generally  $\geq$  150 ms. For individuals with a moderately prolonged QRS, there was no significant benefit for CRT in reducing composite outcomes of adverse cardiac events (Risk ratio [RR]: 0.95, 95% CI: 0.82 to 1.10,  $p = 0.49$ ). In contrast, for individuals with a severely prolonged QRS, there was a 40% relative reduction in the composite outcomes (RR: 0.60, 95% CI: 0.53 to 0.67,  $p < 0.001$ ). Multiple limitations to these findings were reported including use of summary versus individual data in the meta-analysis; use of heterogeneous enrollment criteria by the five included trials with variable composite outcome measures; unknown morphology of the QRS complex in participants with a QRS duration less than 150 ms; and unknown percentages of study participants with RBBB (right bundle branch block). The authors reported that further analysis of individual subject-specific data from all relevant clinical trials can further refine the QRS cutoffs for different types of conduction abnormalities.

In a prospective randomized clinical trial, Beshai et al. (2007) enrolled 172 subjects who had a standard indication for an ICD. Subjects received a CRT-D device and were randomly assigned to the CRT group or to a control group (no CRT) for six months. The primary end point was the proportion of individuals with an increase in peak oxygen consumption of at least 1.0 ml per kilogram of body weight per minute during cardiopulmonary exercise testing at six months. At six months, the CRT group and the control group did not differ significantly in the proportion of individuals with the primary end point (46% and 41%, respectively). In a pre-specified subgroup with a QRS interval of  $\geq$  120 ms, the peak oxygen consumption increased in the CRT group ( $p = 0.02$ ), but it was unchanged in a subgroup with a QRS interval of  $\leq$  120 ms ( $p = 0.45$ ). There

were 24 heart failure events requiring intravenous therapy in 14 individuals in the CRT group (16.1%) and 41 events in 19 individuals in the control group (22.3%), but the difference was not significant. The authors reported that CRT did not improve peak oxygen consumption in individuals with moderate-to-severe heart failure, providing evidence that individuals with heart failure and narrow QRS intervals may not benefit from CRT.

In a prospective pilot study, Bleeker et al. (2006a) studied the effects of CRT in heart failure individuals with narrow QRS complex (<120 ms) and evidence of LV dyssynchrony on tissue Doppler imaging (TDI). The study participants included a total of 33 consecutive subjects with narrow QRS complex and 33 consecutive subjects with wide QRS complex (control group). Patient inclusion criteria included: LV dyssynchrony  $\geq 65$  ms on TDI, NYHA functional Class III/IV heart failure, and LVEF  $\leq 35\%$ . Baseline characteristics, particularly LV dyssynchrony, were comparable between individuals with narrow and wide QRS complex ( $p=NS$ ). No significant relationship was observed between baseline QRS duration and LV dyssynchrony ( $p=NS$ ). The improvement in clinical symptoms and LV reverse remodeling was comparable between individuals with narrow and wide QRS complex (mean NYHA functional class reduction 0.9 versus 1.1;  $p=NS$ ) and mean LV end-systolic volume reduction 39 versus 44 ml ( $p=NS$ ). The authors reported that, "CRT appears to be beneficial in individuals with narrow QRS complex and severe LV dyssynchrony on TDI, with similar improvement in symptoms and comparable LV reverse remodeling. These effects need confirmation in studies with larger populations." The authors noted that color-coded TDI measures the velocity of the myocardium, which may not always equal active myocardial contraction. Large, comparative studies are needed to define which technique is most accurate in the assessment of LV dyssynchrony.

**QRS Morphology:** In a retrospective study, Dupont et al. (2012) evaluated the relative impact of QRS morphology and duration in echocardiographic responses to CRT and clinical outcomes. Baseline characteristics, clinical and echocardiographic response, and outcomes of all individuals who received CRT at a single center were evaluated. Subjects were stratified into four groups according to their baseline QRS morphology and QRS duration. A total of 496 subjects were included in the study; 216 (43.5%) had LBBB and a QRS  $150 \geq$  ms, 85 (17.1%) had LBBB and QRS < 150 ms, 92 (18.5%) had non-LBBB and a QRS  $\geq 150$  ms, and 103 (20.8%) had non-LBBB and QRS < 150 ms. Echocardiographic response (change in ejection fraction) was better in individuals with LBBB and QRS  $\geq 150$  than in those with LBBB and QRS < 150 ms, non-LBBB and QRS  $\geq 150$ , and non-LBBB and QRS > 150 ms ( $p < 0.0001$ ). In a multivariate stepwise model with change in ejection fraction as the dependent variable, the presented classification was the most important independent variable ( $p = 0.0003$ ). Long-term survival was better in LBBB individuals with QRS  $\geq 150$  ( $p = 0.02$ ), but this difference was not significant after adjustment for other baseline characteristics ( $p = 0.15$ ) suggesting that comorbid conditions may confound the treatment responses. The authors stated that "due to the lack of sufficiently powered trials in these subgroups, guideline committees have the difficult task of using this and similar studies to refine patient selection for CRT".

In a meta-analysis, Sipah et al. (2012) evaluated the effect of CRT on clinical events (including death and heart failure hospitalizations) with regards to bundle branch block morphologies. Four randomized controlled trials totaling 5356 people met the inclusion criteria. The authors reported that in individuals with a LBBB, CRT was very effective in reducing adverse events with a relative risk reduction of 36% ( $p = 0.00001$ ). However, no benefit was observed in individuals with other types of conduction abnormalities and a QRS duration > 120 milliseconds.

**Atrial Fibrillation:** The use of CRT in atrial fibrillation (AF) is a growing area of study. Evidence in the published peer-reviewed literature is generally supportive of CRT in individuals with AF with reduced ejection fraction on guideline-directed medical therapy, when criteria for CRT are otherwise met, and atrioventricular nodal ablation or pharmacological rate control will allow near

100% ventricular pacing with CRT (Heidenreich, et al., 2022; Steinberg, et al., 2022; Brignole, et al., 2021).

### **Other Cardiac Resynchronization and Pacing Technologies**

To further evaluate potential solutions for CRT “nonresponders”, studies have investigated alternative lead placement strategies, including triple-site (triventricular) and conduction system pacing.

#### **Conduction System Pacing in Cardiac Resynchronization Therapy (CRT)**

In conventional biventricular pacing, the pacing leads are placed in the right ventricle and in the coronary sinus (a large vein on the posterior surface of the heart) which then paces the left ventricle, causing the ventricles to beat synchronously. Conventional biventricular CRT is an established treatment for heart failure patients with low ejection fraction and ventricular dyssynchrony, and is effective in the majority of individuals. However, around 30% of individuals have a suboptimal response or do not respond to biventricular pacing CRT. This may be due to the patient’s anatomy, atypical conduction disease, and/or coronary sinus lead dislodgement. Alternative strategies to achieve resynchronization have been studied, including conduction system pacing (CSP). Conduction system pacing is a technique of pacing that involves implanting permanent pacing leads at different sites along the cardiac conduction system, and includes His bundle pacing and left bundle branch pacing. These techniques are proposed to engage the intrinsic cardiac conduction system, with the intent to mimic the native ventricular activation sequence.

**His Bundle Pacing (HBP):** HBP was initially performed using standard pacing leads by reshaping the stylet or using a deflectable stylet to precisely position the lead at a site near the electrophysiology mapping catheter demonstrating the largest His deflection. This approach was technically challenging and time consuming. Case reports and review articles report that HBP may be an alternative approach in an attempt to achieve cardiac resynchronization in technically challenging cases where the standard endovascular approach via the coronary sinus is not possible. HBP has been associated with atrial oversensing, higher capture thresholds, and increased risk for lead complications requiring revision (Lewis, et al., 2019; Vijayaraman, et al., 2019; Vijayaraman, 2018).

**Left Bundle Branch Pacing (LBBP):** Similar to His bundle pacing, LBBP (or left bundle branch area pacing [LBBAP]) is another conduction system pacing strategy used as an alternative to conventional lead placement in CRT. LBBP is a more recent approach which involves placing the pacing lead deep in the interventricular septum at the LBB region to capture the LV septum or proximal left conduction system. The premise is this placement will bypass the pathological or disease-vulnerable region in the conduction system such as the atrioventricular (AV) node or the His bundle, where AV block and bundle branch block likely occur (Chen, et al., 2019; Vijayaraman, et al., 2019). The limitations and complications of LBBP are reportedly similar to HBP; notably, cases of lead dislodgement and interventricular septal perforation have been reported in the literature.

**U.S. Food and Drug Administration (FDA):** In June 2018, the FDA granted Premarket Approval (PMA) to expand the indication for use of the Medtronic SelectSecure 3830 lead, to include pacing at the bundle of His.

In October 2022, the FDA approval for the SelectSecure 3830 lead was expanded to include pacing at the left bundle branch area as an alternative to right ventricular pacing.

**Literature Review:** There is a growing body of evidence in the peer-reviewed literature assessing the impact of CRT with His bundle pacing or left bundle branch pacing on long-term health outcomes, compared to conventional biventricular pacing with traditional coronary sinus or epicardial LV leads. Evidence is in the form of randomized controlled trials, case studies, small case series, retrospective studies, noncomparative observational feasibility studies, and meta-analyses. While the available evidence is less robust than for conventional biventricular pacing, studies suggest that conduction system pacing for CRT shortens QRS duration, and leads to improvements in NYHA functional class, echocardiographic parameters including left ventricular ejection fraction (LVEF), heart failure hospitalization rates, and mortality. As such, CRT via conduction system pacing may be clinically appropriate in select individuals when biventricular pacing is indicated but coronary sinus or left ventricular lead placement was attempted and was unsuccessful, or in individuals with LBBB in whom effective CRT cannot be achieved with traditional lead placement (Pujol-Lopez, et al., 2025; Diaz, et al., 2024; Ferreira Felix, et al., 2024; Li, et al., 2024; Palmisano, et al., 2024; Pestrea, et al., 2024; Verstappen, et al., 2024; Yasmin, et al., 2024; Gui, et al., 2022; Wang, et al., 2022; Tan, et al., 2021; Vijayaraman, et al., 2021; Vinther, et al., 2021; Wu, et al., 2021; Zweerink, et al., 2021; Huang, et al., 2020; Boczar, et al., 2019, 2018; ECRI, 2019; Huang, et al., 2019; Upadhyay, et al., 2019a; Vijayaraman, et al., 2019; Sharma, et al., 2018, 2016; Vijayaraman, 2018; Bhatt, et al., 2017; Huang, et al., 2017; Teng, et al., 2016; Lustgarten, et al., 2015).

Whinnett et al. (2023) conducted a randomized crossover trial to evaluate the effects of atrioventricular (AV) optimized His pacing CRT in select individuals with heart failure. The study, conducted in the United Kingdom, included 167 participants (90% male; 82% White). The study inclusion criteria were symptomatic heart failure and left ventricular ejection fraction (LVEF)  $\leq$  40%; PR interval  $\geq$  200 milliseconds (ms), and either narrow QRS ( $\leq$  140 ms) or right bundle branch block (RBBB, of any QRS duration). Excluded from the study were individuals with permanent or persistent atrial fibrillation; or paroxysmal AF with fewer than six months of maintained sinus rhythm. Participants were randomized to the "pacing" or "no pacing" groups. His bundle pacing was attempted in all subjects, with either selective or non-selective capture accepted. When His bundle capture was not possible, an LV lead was placed. Subjects also received an RA lead and a third lead which was either an RV defibrillator lead (where indicated) or an LV coronary sinus lead (used for backup pacing in the "no pacing" period, and/or as an alternative pacing lead if the His lead failed). After six months, subjects crossed over to the opposite treatment group. Twenty five (15%) participants were lost to follow up. The primary outcome measure was peak oxygen uptake on cardiopulmonary exercise testing. Other outcome measures included quality of life; LV dimensions; LVEF; plasma BNP; and incidence of ventricular arrhythmias. The authors found that His bundle pacing did not increase peak exercise oxygen consumption (+0.25 ml/kg/min, 95% confidence interval [CI] -0.23 to 0.73,  $p=0.3$ ). The Minnesota Living with Heart Failure Questionnaire (MLHFQ) score improved significantly (-3.7, 95% CI -7.1 to -0.3,  $p=0.03$ ) although the generic quality of life score (EQ-5D VAS) did not show a statistically significant improvement (+1.9, 95% CI -1.6 to 5.5,  $p=0.28$ ). Left ventricular dimensions, LVEF, plasma BNP and incidence of ventricular arrhythmias did not change significantly with His bundle pacing. There were 19 heart failure admissions in each period/group (pacing and no pacing), and a total of 11 deaths were reported (six with pacing on and five with pacing off). The authors noted the study was not powered to detect a difference in these endpoints. Further limitations included the underrepresentation of non-male and non-white participants; limited treatment time and follow up; and crossover design (i.e., lack of separate control group).

Chen et al. (2022) conducted a multicenter prospective nonrandomized observational study ( $n=100$ ) to evaluate the feasibility and efficacy of CRT with left bundle branch pacing (LBBP-CRT) compared with optimized biventricular pacing with adaptive algorithm (BVP-aCRT) in individuals with heart failure. Subjects were divided into each group per physician and patient choice. Left

bundle branch pacing was performed on the LBBP-CRT group with pacing lead placement deep in the interventricular septum. The LBBP lead was programmed as pacing only or pacing prior to LV or RV lead if AV block occurred due to intraprocedural RBB injury. The LBBP lead was programmed back to pacing only once RBB injury resolved during follow up. In the BVP-aCRT group, pacing leads were placed in the RV apex and coronary sinus. Post-procedure, the devices in the BVP-aCRT group underwent adaptive optimization algorithm programming (aCRT; available on select devices). The study inclusion criteria were: symptomatic heart failure with NYHA class II-IV; LVEF  $\leq 35\%$ ; sinus rhythm; QRS duration (QRSd)  $\geq 150$  ms; typical LBBB; age  $> 18$  years; life expectancy  $> 1$  year. Excluded from the study were persons with P-R interval  $> 200$  ms, persistent atrial fibrillation, or intraventricular conduction defect. Outcome measures included implantation success rate; QRSd; pacing threshold; LVEF; echocardiographic measurements; NYHA class; and complications. Follow ups occurred at six and 12 months. The implant success rate for LBBP and BVP was 98.00% and 91.07%, respectively. Five subjects in the BVP-aCRT group crossed over to the LBBP-CRT group, and one subject in the LBBP-CRT group crossed over to the BVP-aCRT group. A significant reduction in QRSd was observed in both groups ( $p < 0.001$ ), with LBBP achieving the greatest reduced QRSd compared to BVP-aCRT ( $126.54 \pm 11.67$  ms vs  $102.61 \pm 9.66$  ms, respectively;  $p < 0.001$ ). Pacing threshold at implantation was lower in the LBBP-CRT group than the BVP-aCRT group ( $0.92 \pm 0.20$  V/0.5ms vs  $1.45 \pm 0.39$  V/0.5ms, respectively;  $p < 0.001$ ). The LBBP-CRT group had a significantly higher LVEF at six-month follow up compared to the BVP-aCRT group ( $47.58 \pm 12.02\%$  vs  $41.24 \pm 10.56\%$ , respectively;  $p = 0.008$ ). CRT with LBBP demonstrated a greater improvement in absolute LVEF at six and 12 months, compared to BVP-aCRT ( $18.52 \pm 13.19\%$  vs  $12.89 \pm 9.73\%$ , respectively;  $p = 0.020$ ; and  $20.90 \pm 11.80\%$  vs  $15.20 \pm 9.98\%$ , respectively;  $p = 0.015$ ). There was no significant difference between the groups overall in response rate, however higher super-response rate (a  $> 20\%$  improvement and a normalization of LVEF [ $> 50\%$ ]) was seen in the LBBP-CRT group as compared to the BVP-aCRT group at six months ( $53.06\%$  vs  $36.59\%$ , respectively;  $p = 0.016$ ) and 12 months ( $61.22\%$  v.  $39.22\%$ , respectively;  $p = 0.028$ ). Both groups demonstrated significant improvement in clinical heart function when evaluating the percentage of NYHA classification III-IV subjects, at follow up as compared to the subjects' baseline (all  $p < 0.05$ ); the percentage was significantly lower in the LBBP-CRT group compared to the BVP-aCRT group at 12 months ( $4.08\%$  vs  $19.61\%$ , respectively;  $p = 0.028$ ). Both groups has a significant decrease in echocardiographic measurements (all  $p < 0.05$ ). Right bundle branch injury occurred during lead placement in 10 (20%) of LBBP-CRT subjects. Dislodgement of the LV lead occurred in one BVP-aCRT subject. Two subjects in the LBBP-CRT group and five subjects in BVP-aCRT group reported a heart failure hospitalization (no significant between-group difference). Author-noted limitations of the study included a relatively small cohort, non-randomized group allocation with risk of considerable selection bias, and overrepresentation of subjects with dilated cardiomyopathy, thus limiting the generalizability of results to persons with heart failure with atypical LBBB and other etiologies. Additionally, the comparator was BVP CRT utilizing an adaptive optimization algorithm, rather than conventional biventricular pacing, which may further limit the generalizability of the study results.

Qian et al. (2019) conducted a systematic review and meta-analysis to evaluate the efficacy of HBP in individuals with heart failure and LV dyssynchrony. The successful rate of implantation, QRS duration, pacing threshold, LV function at baseline and follow-up, and mortality rates were extracted and summarized. Eleven studies including 494 subjects were included in this analysis. The average age of the participants was 71.9 years and 63.2% of subjects were male. Individuals with ischemic etiology accounted for 32.8% of the population. Four studies reported 173 individuals with atrial fibrillation (AF) and cardiomyopathy undergoing atrioventricular (AV) node ablation. The other seven studies focused on CRT candidates including de novo implantation, CRT nonresponders, individuals with pacing-induced cardiomyopathy, and failed LV lead placement. The overall successful rate for implantation was 82.4%. The main indications for HBP were CRT candidates and cardiomyopathy with atrial fibrillation undergoing atrioventricular node ablation. Permanent HBP resulted in narrow QRS duration of  $116.3 \pm 13.9$  ms after implantation. LV

functions, including echocardiographic parameters and clinical outcomes, significantly improved at follow-up ( $p < 0.001$ ). However, there was a trend of increased capture and bundle branch block correction thresholds at follow-up compared to baseline ( $p = 0.01$  and  $0.02$ , respectively). During a mean follow-up of 23.7 months, 5.9% of the subjects experienced heart failure-related hospitalization and the mortality rate was 9.1%. The authors reported limitations of this meta-analysis include the limited sample size and most of the studies were cohort studies with inherent limitations that reduced the internal validity compared to randomized controlled trials. There was limited data on the effect size of HBP on outcomes as the studies included were observational and did not all have comparative arms. Next, some data, including pacing pulse width and follow-up time, were variable and inconsistent, which may influence the study uniformity. In addition, there was no uniformity in measuring QRS durations with selective and nonselective HBP. The authors concluded that although HBP has shown promising results in small and nonrandomized studies in several clinical situations, long-term safety and pacing threshold are needed.

### **Triple-site CRT (Triventricular Pacing)**

Triple-site cardiac resynchronization or triventricular pacing involves the addition of another ventricular pacing lead. The typical triventricular configuration involves implanting the right ventricular and atrial leads as in conventional CRT, with the third ventricular lead joined in parallel with a Y-connector and connected to the left ventricular port of the CRT system. An alternate approach is using two RV leads and one LV lead.

Triventricular pacing has been proposed as an alternative approach to improve the response rate in CRT recipients. It has been suggested that failure of response to biventricular pacing is probably due to a combination of factors including placement of the pacing lead over a zone of slow conduction, the presence of scar within the left ventricle, variable electrical response of the diseased ventricle to pacing, or suboptimal positioning of the pacing leads with regard to the area of latest contraction (Rogers, et al., 2012).

**Literature Review:** Elliott et al. (2022) conducted a meta-analysis of six randomized controlled trials (RCTs;  $n = 415$  subjects) to evaluate the efficacy of multi-lead pacing compared to conventional biventricular CRT. Multi-lead pacing with two left ventricular (LV) leads and one right ventricular (RV) lead was utilized in four studies; one study used two RV leads and one LV lead; and one study used both configurations. Included were RCTs comparing standard biventricular CRT and multi-lead pacing CRT with follow up  $\geq$  three months. Observational studies, nonrandomized studies, case reports, narrative reviews, and studies with only acute hemodynamic data were excluded. Outcome measures included echocardiographic outcomes; symptomatic outcomes using the six-minute walk test (6MWT), the Minnesota Living with Heart Failure Questionnaire (MLWHF) and New York Heart Association (NYHA) class; and mortality. Analysis demonstrated a statistically significant improvement in MLWHF score for multi-lead pacing versus conventional CRT ( $p = 0.05$ ), however the difference was not significant when only those individuals receiving LV-only multi-lead pacing were included ( $p = 0.25$ ). There were no statistically significant differences between the groups in the remaining outcomes. The authors noted significant disadvantages to multi-lead pacing, including technical challenges, higher rates of battery depletion, and prolonged procedure times. Limitations of the meta-analysis included heterogeneity among the included studies in terms of inclusion criteria, study design, outcome reporting, and lead configuration. There was also a consistent underrepresentation of women across the included studies. The authors concluded the findings did not support the use of multi-lead pacing for CRT, although there may be a potential benefit to select individuals (e.g., in atrial fibrillation or ischemic cardiomyopathy). Further RCTs to evaluate multi-lead pacing CRT in these subgroups are needed.

Gould et al. (2022) conducted the STRIVE HF (Standard care vs. TRIVentricular pacing in Heart Failure;  $n = 95$ ) randomized controlled trial to evaluate whether triventricular (TriV) pacing was

feasible and superior to standard BiV pacing in heart failure patients with left bundle branch block (LBBB) with a moderately prolonged QRS duration (120–150 ms). Subjects in the TriV group underwent placement of two left ventricular (LV) leads and one right ventricular (RV) lead which were connected to a TriV device (Paradym TriV CRT-D) via an internal parallel Y-port. Subjects in the BiV group underwent placement of a quadripolar LV lead and CRT-defibrillator (CRT-D) device. The devices in both groups were programmed similarly. The study included individuals with LBBB, QRS duration 120-150 ms, and age  $\geq$  18 years. Pregnant persons were excluded from the study. The primary outcome measure was the feasibility of TriV pacing. Other outcomes included reverse remodeling; N-terminal (NT)-pro hormone BNP (NTpro-BNP) value; six-minute walk test (6MWT); device shock therapy; quality of life scores; hospitalizations; adverse events; and mortality. Follow up occurred after six months. Successful device implantation occurred in 91.3% of subjects in the TriV group, and 95.9% of subjects in the BiV group. Pacing was maintained in 90% of the TriV subjects and 97.7% of the BiV subjects. Both groups showed a significant increase in left ventricular ejection fraction (LVEF) (TriV  $p=0.018$ , BiV  $p=0.007$ ), and reduction in left ventricular end diastolic volume ( $p<0.001$  each). Procedure time was significantly longer in the TriV group compared to the BiV group ( $192.6 \pm 107.6$  vs  $133.9 \pm 50.9$  min, respectively;  $p<0.001$ ). Mean LV pacing thresholds at implant were significantly higher in the TriV group versus the BiV group ( $1.3 \pm 0.5$  vs  $1.0 \pm 0.5$  V, respectively;  $p=0.004$ ). Battery longevity was significantly lower in the TriV group ( $5.5 \pm 2.3$  vs  $8.6 \pm 2.7$  years, respectively;  $p<0.001$ ). There were no significant between-group differences in the remaining outcomes. TriV pacing was deactivated in six individuals after the study period due to threshold rises. There was one lead displacement reported in each group, and there was a limited coronary sinus dissection in the TriV group. Six deaths occurred during the study: two in the TriV group and four in the BiV group (one of which was thought to be procedure-related). The authors concluded that there was insufficient evidence to demonstrate that TriV pacing improved CRT response or provided any clinical benefit to individuals with LBBB and intermediate QRS prolongation. Limitations of the study included short duration of follow up, unblinding of subjects and investigators during follow up, lack of power calculation, and differences in leads used.

Zhang et al. (2017) conducted a meta-analysis of randomized controlled trials (RCTs) and comparative observational studies ( $n=251$ ) comparing the benefits of triple-site ventricular (Tri-V pacing) versus Bi-V pacing on the left ventricular (LV) remodeling, quality of life, and exercise capacity in individuals with heart failure (HF). The meta-analysis included one RCT, two randomized crossover studies, and two nonrandomized comparative studies. Two different pacing modalities were used. One type used one lead in the right ventricle and leads in two different tributaries in the left ventricle. The other used two leads in the right ventricle. Individuals in the triple-site pacing group had greater improvement in LVEF ( $p<0.001$ ) and NYHA classes ( $p=0.001$ ) compared with the control group. There were no significant differences in left ventricular geometry, six-minute walk distance, or Minnesota Living With Heart Failure Questionnaire score between the two groups. The subgroup analyses showed there might be a greater improvement in LVEF in the Tri-V pacing group in individuals with QRS duration  $\geq 155$  ms ( $p<0.001$ ). The studies were limited by small sample size, short-term follow-up and lack of randomization. No study in this meta-analysis had power to assess the benefits of Tri-V pacing in terms of mortality, mobility, or other clinical outcomes.

There is a paucity of evidence in the peer-reviewed literature supporting the long-term safety and efficacy of triple-site resynchronization, compared to conventional biventricular pacing.

### **Professional Societies/Organizations**

**American College of Cardiology (ACC)/American Heart Association (AHA)/American Society of Echocardiography (ASE)/Heart Failure Society of America (HFSA)/Heart Rhythm Society (HRS)/Society for Cardiovascular Angiography and Interventions (SCAI)/Society of Cardiovascular Computed Tomography (SCCT)/Society for**

**Cardiovascular Magnetic Resonance (SCMR):** The 2025 ACC/AHA/ASE/HFSA/HRS/SCAI/SCCT/SCMR Appropriate Use Criteria for implantable cardioverter defibrillators (ICD), cardiac resynchronization therapy (CRT), and pacing provided an updated review of common clinical scenarios where ICDs, CRT devices, cardiac contractility modulation, leadless pacing, and conduction system pacing therapies may be considered. The clinical applications for these therapies were derived from common or anticipated uses, clinical practice guidelines, individual studies, and meta-analyses. The indications were developed by a multidisciplinary writing team and scored by a separate independent rating panel on a scale of 1 to 9 to designate care that is considered "Appropriate" (median 7 to 9), "May Be Appropriate" (median 4 to 6), and "Rarely Appropriate" (median 1 to 3).

As concerns CRT in heart failure, the team made the following assumptions:

- "Electrocardiogram (ECG) criteria for left bundle branch block (LBBB), right bundle branch block (RBBB), and intraventricular conduction delay (IVCD) are accurately determined.
- Non-LBBB is defined as RBBB or nonspecific intraventricular conduction block (not transient or rate-related).
- QRS duration is accurately measured.
- Left ventricular ejection fraction (LVEF) is accurately measured.
- All assessments are made after  $\geq 3$  months of optimized guideline-directed medical therapy (GDMT).
- If persistent atrial fibrillation (AF) is present, it should be assumed that CRT pacing can be maximized with a high percentage of pacing ( $\geq 98\%$ ) to optimize CRT delivery" (Russo, et al., 2025).

The following CRT indications were rated as Appropriate Care (median score 7-9):

Ischemic cardiomyopathy, left ventricular ejection fraction (LVEF)  $\leq 35\%$ , sinus rhythm (SR) for the following:

- QRS 120-149 milliseconds (ms), left bundle branch block (LBBB), New York Heart Association (NYHA) Class II, III-ambulatory IV (7)
- QRS  $\geq 150$  ms, LBBB, NYHA Class I (7) II-ambulatory IV (9)
- QRS  $\geq 150$  ms, non-LBBB, NYHA Class III-ambulatory IV (7)

Ischemic cardiomyopathy, LVEF  $\leq 35\%$ , persistent or permanent atrial fibrillation, LBBB, and QRS  $\geq 150$  ms (7)

Nonischemic cardiomyopathy, LVEF  $\leq 35\%$ , SR for the following:

- QRS 120-149 ms, LBBB, NYHA Class II-ambulatory IV (7)
- QRS  $\geq 150$  ms, LBBB, NYHA Class I (7), II-ambulatory IV (9)
- QRS  $\geq 150$  ms, non-LBBB, NYHA Class III-ambulatory IV (7)

Nonischemic cardiomyopathy, LVEF  $\leq 35\%$ , persistent or permanent atrial fibrillation, LBBB, and QRS  $\geq 150$  ms (8)

Pre-existing or anticipated right ventricular (RV) pacing with a clinical indication for ICD or pacemaker implantation, intrinsic narrow QRS, LVEF  $\leq 35\%$  when RV pacing anticipated is  $> 40\%$ , NYHA Class I-II (7), III-ambulatory IV (8).

Conduction system pacing (His bundle pacing or left bundle branch area pacing) for the following:

- sinus node dysfunction, first-degree AV block ( $> 250$  ms), normal QRS, anticipated substantial RV pacing, LVEF  $< 50\%$  (7)

- AV block, anticipated substantial RV pacing for:
  - second-degree AV block, Mobitz type I, narrow QRS, LVEF  $\leq$  35% (7)
  - second-degree AV block, Mobitz type II, wide QRS, LVEF < 50% (7)
  - intermittent third-degree AV block, LVEF  $\leq$  35% (7)
  - third-degree AV block, narrow junctional escape rhythm, LVEF < 50% (7)
  - third-degree AV block, wide complex ventricular escape rhythm, LVEF < 50% (7)
  - third-degree AV block, no escape rhythm, LVEF < 50% (7)
  - individual undergoing AV junction ablation, LVEF < 50% (7)
- failed CRT or nonresponder, anticipated substantial RV pacing for:
  - Failed CRT coronary sinus/left ventricular lead implantation, LVEF  $\leq$  35% (8) or 36-50% (7)
  - CRT nonresponders with LBBB, LVEF  $\leq$  35% (8) or 36-50% (7)
- anticipated substantial RV pacing for:
  - atrial fibrillation with slow ventricular response, LVEF < 50% (7)
  - sinus rhythm with long first-degree AV block (eg, PR >300 ms), LVEF  $\leq$  35% (7)

The remaining CRT-related indications presented in the document received scores below 7 (Russo, et al., 2025).

**Heart Rhythm Society (HRS)/Asia Pacific Heart Rhythm Society (APHRS)/Latin American Heart Rhythm Society (LAHRS):** In 2023 these societies published a clinical practice guideline on cardiac physiologic pacing for the avoidance and mitigation of heart failure. The guideline defined cardiac physiologic pacing (CPP) as “as any form of cardiac pacing intended to restore or preserve synchrony of ventricular contraction”, achieved via conduction system pacing (CSP; including His bundle pacing [HBP] and left bundle branch area pacing [LBBAP]), or CRT via biventricular (BiV) pacing using a coronary sinus branch or epicardial LV pacing lead. Scientific evidence was systematically reviewed and interpreted to develop several recommendations, which were then assigned a class of recommendation and a level of evidence using the ACC/AHA recommendation system described above. Among the highest-rated recommendations were the following:

Class of Recommendation: 1; Level of Evidence: A

- In patients with LVEF  $\leq$  35%, sinus rhythm, LBBB with QRS duration  $\geq$  150 ms, and NYHA class II–IV symptoms on guideline-directed medical therapy (GDMT), CRT with BiV pacing is indicated to improve symptoms and reduce morbidity and mortality.
- In patients with select characteristics (e.g., female) who have LVEF  $\leq$  35%, sinus rhythm, LBBB with QRS duration 120–149 ms, and NYHA class II–IV symptoms on GDMT, CRT with BiV pacing is recommended to reduce mortality and HF events and to improve LVEF.

Class of Recommendation: 1; Level of Evidence: B-R

- In patients undergoing CRT implant, a quadripolar LV lead is recommended to assist with lead stability, lower capture thresholds, avoid phrenic nerve pacing, and decrease need for lead repositioning.

Class of Recommendation: 2a; Level of Evidence: A

- In patients who have LVEF  $\leq$  35%, sinus rhythm, a non-LBBB pattern with QRS duration  $\geq$  150 ms, and NYHA class III or ambulatory class IV symptoms on GDMT, CRT with BiV pacing can be useful to improve functional class, cardiac structure, and LVEF.

Class of Recommendation: 2a; Level of Evidence: B-R

- In patients with LVEF  $\leq$  35%, sinus rhythm, LBBB with QRS duration 120–149 ms, and NYHA class II–IV symptoms on GDMT, CRT with BiV pacing is reasonable to reduce mortality and HF and to improve LVEF.
- In patients with an indication for permanent pacing with an LVEF 36%–50% who are anticipated to require substantial ventricular pacing, CPP is reasonable to reduce the risk of pacing-induced cardiomyopathy (Note: Level of Evidence B-R is for CRT, and B-NR for HBP, LBBAP).
- In patients with an indication for permanent pacing with LVEF  $>$ 35% who are anticipated to require less than substantial ventricular pacing, it is reasonable to choose a traditional RV lead placement and minimize right ventricular pacing.
- In patients with atrial fibrillation undergoing atrioventricular junction ablation with LVEF  $\leq$  50%, CRT with BiV pacing is reasonable to improve heart failure hospitalization, reverse structural remodeling, and improve quality of life, exercise capacity, LVEF, and potentially mortality.

Regarding the evidence to support the use of biventricular pacing/CRT versus conduction system pacing (CSP), the authors noted “The strength of evidence for CRT in heart failure (HF) is substantially greater than what is available to support CSP. Multiple randomized controlled trials have shown a beneficial effect of CRT in reducing HF symptoms and hospitalization, improving left ventricular function, and increasing survival. The majority of data on CSP are observational, and long-term data on lead survival are lacking. Ongoing and planned studies are likely to provide future guidance on the use of CSP compared to CRT” (Chung, et al., 2023).

**American Heart Association (AHA)/American College of Cardiology (ACC)/Heart Failure Society of America (HFSA) Guideline for the Management of Heart Failure:** The updated AHA/ACC/HFSA guidelines for the management of heart failure (HF) were published in 2022. To develop the guidelines, the committee used evidence-based methodologies to assign each recommendation a Class of Recommendation and a Level of Evidence:

#### Class (Strength) of Recommendation

- Class 1 (Strong)  
Benefit  $\ggg$  Risk  
Intervention is recommended; is indicated/useful/effective/beneficial
- Class 2a (Moderate)  
Benefit  $\gg$  Risk  
Intervention is reasonable; can be useful/effective/beneficial
- Class 2b (Weak)  
Benefit  $\geq$  Risk  
Intervention may be reasonable; may be considered; its usefulness/ effectiveness is unknown/unclear/uncertain or not well-established
- Class 3: No Benefit (Moderate)  
Benefit = Risk  
Intervention is not recommended/indicated/useful/effective/beneficial; it should not be performed/ administered
- Class 3: Harm (Strong)  
Risk  $>$  Benefit  
Intervention is potentially harmful; causes harm; is associated with excess morbidity/mortality; should not be performed/administered

#### Level of Evidence (LOE)

- Level A  
High-quality evidence from more than one RCT  
Meta-analyses of high-quality RCTs

- One or more RCTs corroborated by high-quality registry studies
- Level B-R (Randomized)
  - Moderate-quality evidence from one or more RCTs
  - Meta-analyses of moderate-quality RCTs
- Level B-NR (Nonrandomized)
  - Moderate-quality evidence from one or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies
  - Meta-analyses of such studies
- Level C-LD (Limited Data)
  - Randomized or nonrandomized observational or registry studies with design or execution limitations
  - Meta-analyses of such studies
  - Physiological or mechanistic studies in human subjects
- Level C-EO (Expert Opinion)
  - Consensus of expert opinion based on clinical experience

To reduce total mortality and hospitalizations, and improve symptoms and quality of life (QOL) in patients with heart failure with reduced ejection fraction (HFrEF), the committee made the following recommendations concerning cardiac resynchronization therapy (CRT) (Heidenreich, et al, 2022):

- Strong recommendation:
  - For individuals with left ventricular ejection fraction (LVEF)  $\leq$  35%, sinus rhythm, left bundle branch block (LBBB) with a QRS duration  $\geq$  150 ms, and New York Heart Association (NYHA) class II, III, or ambulatory IV symptoms on guideline-directed medical therapy (GDMT), CRT is indicated (Class of Recommendation: 1; Level of Evidence: B-R)
- Moderate recommendation:
  - For individuals with LVEF  $\leq$  35%, sinus rhythm, non-LBBB pattern with a QRS duration  $\geq$  150 ms, and NYHA class II, III, or ambulatory class IV symptoms on GDMT, CRT can be useful (Class of Recommendation: 2a; Level of Evidence: B-R)
  - For individuals with high-degree or complete heart block and LVEF of 36% to 50%, CRT is reasonable (Class of Recommendation: 2a; Level of Evidence: B-R)
  - For individuals with LVEF  $\leq$  35%, sinus rhythm, LBBB with a QRS duration of 120 to 149 ms, and NYHA class II, III, or ambulatory IV symptoms on GDMT, CRT can be useful (Class of Recommendation: 2a; Level of Evidence: B-NR)
  - For individuals with atrial fibrillation (AF) and LVEF  $\leq$  35% on GDMT, CRT can be useful if: a) the patient requires ventricular pacing or otherwise meets CRT criteria and b) atrioventricular nodal ablation or pharmacological rate control will allow near 100% ventricular pacing with CRT (Class of Recommendation: 2a; Level of Evidence: B-NR)
  - For individuals with LVEF  $\leq$  35% on GDMT and undergoing placement of a new or replacement device implantation with anticipated requirement for significant ( $>$  40%) ventricular pacing, CRT can be useful (Class of Recommendation: 2a; Level of Evidence: B-NR)
- Weak recommendation:
  - For individuals with LVEF  $\leq$  35%, sinus rhythm, a non-LBBB pattern with QRS duration of 120 to 149 ms, and NYHA class III or ambulatory class IV on GDMT, CRT may be considered (Class of Recommendation: 2b; Level of Evidence: B-NR)

- For individuals with LVEF  $\leq$  30%, ischemic cause of HF, sinus rhythm, LBBB with a QRS duration  $\geq$  150 ms, and NYHA class I symptoms on GDMT, CRT may be considered (Class of Recommendation: 2b; Level of Evidence: B-NR)
- Not recommended:
  - For individuals with QRS duration  $<$ 120 ms, CRT is not recommended (Class of Recommendation: 3 – no benefit; Level of Evidence: B-R)
  - For individuals with NYHA class I or II symptoms and non-LBBB pattern with QRS duration  $<$  150 ms, CRT is not recommended (Class of Recommendation: 3 – no benefit; Level of Evidence: B-NR)
  - For individuals whose comorbidities or frailty limit survival with good functional capacity to  $<$  1 year, ICD and cardiac resynchronization therapy with defibrillation (CRT-D) are not indicated (Class of Recommendation: 3 – no benefit; Level of Evidence: C-LD)

**European Society of Cardiology (ESC) Guidelines on Cardiac Pacing and Cardiac Resynchronization Therapy:**

The updated 2021 ESC guidelines on cardiac pacing and CRT include expanded recommendations for CRT, and new sections which included alternative pacing strategies/sites (Glikson, et al., 2021). Guideline recommendations are classified as Class I, Class IIa, Class IIb, and Class III. The classification system is described as follows:

- Class I: Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.
- Class II: Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.
  - Class IIa: Weight of evidence/opinion is in favor of usefulness/efficacy.
  - Class IIb: Usefulness/efficacy is less well established by evidence/opinion.
- Class III: Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.

The weight of evidence supporting each recommendation is classified as follows:

- Level of evidence A: Data derived from multiple randomized clinical trials or meta-analyses.
- Level of evidence B: Data derived from a single randomized clinical trial or large non-randomized clinical trials.
- Level of evidence C: Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

Recommendations for CRT in patients in sinus rhythm (SR):

- CRT is recommended for symptomatic patients with heart failure (HF) with LVEF  $\leq$  35%, QRS duration  $\geq$  150 ms, and left bundle branch block (LBBB) QRS morphology despite optimal medical treatment (OMT) in order to improve symptoms and reduce morbidity and mortality (Class I, Level A)
- CRT should be considered for symptomatic patients with HF with LVEF  $\leq$  35%, QRS duration 130 – 149 ms, and LBBB QRS morphology despite OMT, in order to improve symptoms and reduce morbidity and mortality (Class IIa, Level B)
- CRT should be considered for symptomatic patients with HF LVEF  $\leq$  35%, QRS duration  $\geq$  150 ms, and non-LBBB QRS morphology despite OMT, in order to improve symptoms and reduce morbidity (Class IIa, Level B)
- CRT may be considered for symptomatic patients with HF with LVEF  $\leq$  35%, QRS duration 130 – 149 ms, and non-LBBB QRS morphology despite OMT, in order to improve symptoms and reduce morbidity (Class IIb, Level B)
- CRT is not indicated in patients with HF and QRS duration  $<$ 130 ms without an indication for RV pacing (Class III, Level A)

Recommendations for CRT in patients with persistent or permanent atrial fibrillation (AF):

- Patients with HF with permanent AF who are candidates for CRT:
  - CRT should be considered for patients with HF and LVEF  $\leq$  35% in NYHA class III or IV despite OMT if they are in AF and have intrinsic QRS  $\geq$  130 ms, provided a strategy to ensure biventricular capture is in place, in order to improve symptoms and reduce morbidity and mortality (Class IIa, Level C)
  - Atrioventricular junction (AVJ) ablation should be added in the case of incomplete biventricular pacing (<90 – 95%) due to conducted AF (Class IIa, Level B)
- Patients with symptomatic AF and an uncontrolled heart rate who are candidates for AVJ ablation (irrespective of QRS duration):
  - CRT is recommended in patients with HF with reduced ejection fraction (<40%) (Class I, Level B)
  - CRT rather than standard right ventricular (RV) pacing should be considered in patients with HF with mildly reduced ejection fraction (40 - 49%) (Class IIa, Level C)
  - RV pacing should be considered in patients with HF with preserved ejection fraction ( $\geq$  50%) (Class IIa, Level B)
  - CRT may be considered in patients with HF with preserved ejection fraction ( $\geq$  50%) (Class IIb, Level C)

Recommendation for upgrade from RV pacing to CRT:

- Patients who have received a conventional pacemaker or an ICD and who subsequently develop symptomatic HF with LVEF  $\leq$  35% despite OMT, and who have a significant proportion of RV pacing, should be considered for upgrade to CRT (Class IIa, Level B)

Recommendation for patients with HF and atrioventricular block (AVB):

- CRT rather than RV pacing is recommended for patients with HF with reduced ejection fraction (<40%) regardless of NYHA class who have an indication for ventricular pacing and high-degree AVB in order to reduce morbidity. This includes patients with AF (Class I, Level A) (Glikson, et al., 2021).

**American Heart Association (AHA)/American College of Cardiology (ACC) Guideline for the Diagnosis and Treatment of Patients With Hypertrophic Cardiomyopathy:** The 2020 AHA/ACC clinical practice guideline for the care of patients with hypertrophic cardiomyopathy (HCM) stated that cardiac resynchronization therapy (CRT) for symptom reduction is reasonable in select adult patients who have NYHA class II to ambulatory class IV HF, left bundle branch block (LBBB), LV ejection fraction (LVEF) < 50%, who are either receiving an ICD, or in whom symptoms persist despite guideline-directed medical therapy (Class of Recommendation: 2a; Level of Evidence: C-LD) (Ommen, et al., 2020). The 2024 update to this guideline did not change these recommendations (Ommen, et al., 2024).

**American College of Cardiology (ACC)/American Heart Association (AHA)/Heart Rhythm Society (HRS) 2018 Guideline on the Evaluation and Management of Patients With Bradycardia and Cardiac Conduction Delay:** The 2018 ACC/AHA/HRS document makes the following recommendations for permanent pacing techniques in persons with atrioventricular block:

- In patients with atrioventricular block who have an indication for permanent pacing with a LVEF between 36% and 50% and are expected to require ventricular pacing more than 40% of the time, it is reasonable to choose pacing methods that maintain physiologic

ventricular activation (e.g., cardiac resynchronization therapy [CRT] or His bundle pacing) over right ventricular pacing (Class of Recommendation: 2a; Level of Evidence: B-R)

- In patients with atrioventricular block who have an indication for permanent pacing with a LVEF between 36% and 50% and are expected to require ventricular pacing less than 40% of the time, it is reasonable to choose right ventricular pacing over pacing methods that maintain physiologic ventricular activation (e.g., CRT or His bundle pacing) (Class of Recommendation: 2a; Level of Evidence: B-R)
- In patients with atrioventricular block at the level of the atrioventricular node who have an indication for permanent pacing, His bundle pacing may be considered to maintain physiologic ventricular activation (Class of Recommendation: 2b; Level of Evidence: B-R)

The guideline described His bundle pacing as a “promising pacing option”. Supportive evidence consisted of small nonrandomized studies. The authors noted that “more studies are needed to better characterize His bundle pacing and compare it to RV and CRT pacing in atrioventricular block patients”.

**American College of Cardiology Foundation (ACCF), American Heart Association (AHA) and Heart Rhythm Society (HRS) Guideline for Device-Based Therapy for Cardiac Rhythm Abnormalities:** The 2012 ACCF/AHA/HRS focused update incorporated into the ACCF/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities addresses recommendations for CRT (Epstein, et al., 2013). Guideline recommendations are classified as Class I, Class IIa, Class IIb, and Class III. The classification system is described as follows:

- Class I: Benefit >>> Risk; Procedure/Treatment should be performed/administered
- Class IIa: Benefit >> Risk; Additional studies with focused objectives needed. It is reasonable to perform procedure/administer treatment.
- Class IIb: Benefit  $\geq$  Risk; Additional studies with broad objectives needed; additional registry data would be helpful. Procedure/treatment may be considered.
- Class III: No Benefit or Harm
  - Class of Recommendation (COR) III: No Benefit
    - Procedure/Test: not helpful
    - Treatment: no proven benefit
  - COR III: Harm
    - Procedure/Test: excess cost w/o benefit or harmful
    - Treatment: harmful to patients

The weight of evidence supporting each recommendation is classified as follows:

- Level A: Multiple populations evaluated. Data derived from multiple randomized clinical trials or meta-analyses.
- Level B: Limited populations evaluated. Data derived from a single randomized trial or nonrandomized studies.
- Level C: Very limited populations evaluated. Only consensus opinion of experts, case studies, or standard of care.

The updated guideline proposes several changes in recommendations for CRT, compared with the 2008 document. The most significant changes are limitation of the Class I indication to individuals with QRS duration  $\geq 150$  ms; limitation of the Class I indication to individuals with left bundle-branch block (LBBB) pattern; expansion of Class I indication to New York Heart Association (NYHA) class II (and with LBBB with QRS duration  $\geq 150$  ms); and the addition of a Class IIb recommendation for individuals who have LVEF  $\leq 30\%$ , ischemic etiology of heart failure (HF), sinus rhythm, LBBB with a QRS duration  $\geq 150$  ms, and NYHA class I symptoms.

The following recommendations for CRT placement are included in the 2012 guideline:

#### Class I

- CRT is indicated for patients who have LVEF  $\leq$  35%, sinus rhythm, LBBB with a QRS duration  $\geq$  150 ms, and NYHA class II, III, or ambulatory IV symptoms on guideline directed medical therapy (GDMT) (Level of Evidence: A for NYHA class III/IV; Level of Evidence: B for NYHA class II).

#### Class IIa

- CRT can be useful for patients who have LVEF  $\leq$  35%, sinus rhythm, LBBB with a QRS duration 120 to 149 ms, and NYHA class II, III, or ambulatory IV symptoms on GDMT (Level of Evidence: B).
- CRT can be useful for patients who have LVEF  $\leq$  35%, sinus rhythm, a non-LBBB pattern with a QRS  $\geq$  150 ms, and NYHA class III/ambulatory class IV symptoms on GDMT (Level of Evidence: A).
- CRT can be useful in patients with atrial fibrillation and LVEF  $\leq$  35% on GDMT if the patient requires ventricular pacing or otherwise meets CRT criteria and b) AV nodal ablation or pharmacologic rate control will allow near 100% ventricular pacing with CRT (Level of Evidence: B).
- CRT can be useful for patients on GDMT who have LVEF  $\leq$  35% and are undergoing new or replacement device placement with anticipated requirement for significant ( $>$  40%) ventricular pacing (Level of Evidence: C).

#### Class IIb

- CRT may be considered for patients who have LVEF  $\leq$  30%, ischemic etiology of heart failure, sinus rhythm, LBBB with a QRS duration of  $\geq$ 150 ms, and NYHA class I symptoms on GDMT (Level of Evidence: C).
- CRT may be considered for patients who have LVEF  $\leq$  35%, sinus rhythm, a non-LBBB pattern with QRS duration 120 to 149 ms, and NYHA class III/ambulatory class IV on GDMT (Level of Evidence: B).
- CRT may be considered for patients who have LVEF  $\leq$  35%, sinus rhythm, a non-LBBB pattern with a QRS duration  $\geq$  150 ms, and NYHA class II symptoms on GDMT (Level of Evidence: B).

#### Class III: No Benefit

- CRT is not recommended for patients with NYHA class I or II symptoms and non-LBBB pattern with QRS duration less than 150 ms (Level of Evidence: B).
- CRT is not indicated for patients whose comorbidities and/or frailty limit survival with good functional capacity to less than 1 year (Level of Evidence: C).

## Health Equity Considerations

Health equity is the highest level of health for all people; health inequity is the avoidable difference in health status or distribution of health resources due to the social conditions in which people are born, grow, live, work, and age.

Social determinants of health are the conditions in the environment that affect a wide range of health, functioning, and quality of life outcomes and risks. Examples include safe housing, transportation and neighborhoods; racism, discrimination and violence; education, job opportunities and income; access to nutritious foods and physical activity opportunities; access to clean air and water; and language and literacy skills.

Although overall utilization of cardiac resynchronization therapy (CRT) has increased in the U.S. over the years, significant disparities exist, with lower use of CRT in women compared with men, and in under-represented racial and ethnic groups. A 2016 study involving the Nationwide Inpatient Sample database (2002-2010) of 374,202 cardiac resynchronization therapy procedures revealed significant and persistent gender and racial disparities favoring men (71.4%) and white individuals (79.6%), respectively (Sridhar, et al., 2016).

## Medicare Coverage Determinations

	Contractor	Determination Name/Number	Revision Effective Date
NCD	National	No Determination found	
LCD	Palmetto GBA	Cardiac Resynchronization Therapy (CRT) (L39080)	12/12/2021

Note: Please review the current Medicare Policy for the most up-to-date information. (NCD = National Coverage Determination; LCD = Local Coverage Determination)

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## Revision Details

Type of Revision	Summary of Changes	Date
Annual Review	<ul style="list-style-type: none"> <li>No clinical policy statement changes.</li> </ul>	12/15/2025
Annual Review	<ul style="list-style-type: none"> <li>Title changed from "Cardiac Resynchronization Therapy (CRT) and Advanced Cardiac Pacing Technologies" to "Cardiac Resynchronization Therapy (CRT)".</li> <li>Revised policy statements for biventricular pacing.</li> <li>Added policy statements for CRT for cardiomyopathy with persistent or permanent atrial fibrillation; and for conduction system pacing.</li> <li>Removed wireless pacing CRT from policy statement.</li> </ul>	6/15/2025
Focused Review	<ul style="list-style-type: none"> <li>Remove leadless pacemaker from policy statement.</li> </ul>	9/1/2024
Annual Review	<ul style="list-style-type: none"> <li>Revised statement for biventricular pacemaker for all other indications.</li> <li>Removed policy statement for body surface potential mapping.</li> </ul>	1/15/2024

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