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Biventricular Pacemakers (Cardiac Resynchronization Therapy) for the Treatment of Heart Failure

Policy # 00009

Original Effective Date: 06/05/2002

Current Effective Date: 04/23/2014

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- Benefits are available in the member's contract/certificate, and
- Medical necessity criteria and guidelines are met.

Based on review of available data, the Company may consider biventricular pacemakers with or without an accompanying implantable cardiac defibrillator (ICD) (i.e., a combined biventricular pacemaker/implantable cardiac defibrillator [ICD]) as a treatment of heart failure to be **eligible for coverage**.

Patient Selection Criteria

Coverage eligibility for biventricular pacemakers with or without an accompanying implantable cardiac defibrillator (ICD) as a treatment of heart failure for New York Heart Association (NYHA) class III or IV will be considered when all of the following criteria are met:

- Left ventricular ejection fraction (LVEF) \leq 35%; and
- Sinus rhythm; and
- QRS duration of \geq 120–130* msec, and
- Patients treated with a stable pharmacological medical regimen prior to implant, such as an angiotensin-converting enzyme (ACE) inhibitor (or an angiotensin receptor blocker) and a beta blocker, digoxin, and/or diuretics.

Patient Selection Criteria

Coverage eligibility for biventricular pacemakers with or without an accompanying implantable cardiac defibrillator (ICD) as a treatment of heart failure for New York Heart Association (NYHA) class II will be considered when all of the following criteria are met:

- Left ventricular ejection fraction (LVEF) \leq 30%
- Sinus rhythm
- QRS duration of \geq 120–130* msec, and
- Patients treated with a stable pharmacological medical regimen prior to implant, such as an angiotensin-converting enzyme (ACE) inhibitor (or an angiotensin receptor blocker) and a beta blocker, digoxin, and/or diuretics.

* The FDA-labeled indications for QRS duration vary by device. For some devices, FDA approval is based on QRS duration of \geq 130 (e.g., InSync[®] device)[†] while for others, it is based on QRS duration \geq 120 msec (e.g., CONTAK CD[®] CRT-D System)[‡]. These differences in QRS duration arise from differences in the eligibility criteria in the trials on which the FDA approval is based.

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When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of biventricular pacemakers, with or without an accompanying implantable cardiac defibrillator (ICD) (i.e., a combined biventricular pacemaker/implantable cardiac defibrillator [ICD]) as a treatment for patients with New York Heart Association (NYHA) class II, III or IV heart failure when patient selection criteria are not met to be **investigational**.*

Based on review of available data, the Company considers biventricular pacemakers, with or without an accompanying implantable cardiac defibrillator (ICD) (i.e., a combined biventricular pacemaker/implantable cardiac defibrillator [ICD]) as a treatment for patients with New York Heart Association [NYHA] class I heart failure to be **investigational**.*

Based on review of available data, the company considers biventricular pacemakers, with or without an accompanying implantable cardiac defibrillator (ICD) (i.e., a combined biventricular pacemaker/implantable cardiac defibrillator [ICD]), as a treatment for heart failure in patients with atrial fibrillation (AF) to be **investigational**.*

Based on review of available data, the Company considers an intrathoracic fluid monitoring sensor is considered **investigational*** as a component of a biventricular pacemaker.

Based on review of available data, the Company considers triple-site (triventricular) cardiac resynchronization therapy (CRT), using an additional pacing lead, to be **investigational**.*

Background/Overview

Cardiac resynchronization therapy, which consists of synchronized pacing of the left and right ventricles, is intended to treat patients with heart failure and dyssynchronous ventricular contractions. Treatment involves placement of a device that paces both ventricles and which coordinates ventricular pacing to maximize cardiac pumping function and LVEF.

It is estimated that 20–30% of patients with heart failure have intraventricular conduction disorders, resulting in a contraction pattern that is not coordinated and a wide QRS interval on the electrocardiogram (ECG). This abnormality appears to be associated with increased morbidity and mortality. Biventricular pacemakers using 3 leads (1 in the right atrium and 1 in each ventricle) have been investigated as a technique to coordinate the contraction of the ventricles, thus improving patients' hemodynamic status. Two strategies are being explored: incorporating biventricular pacing into automatic ICDs and the development of stand-alone biventricular pacemakers.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration

One stand-alone biventricular pacemaker (InSync Biventricular Pacing System, Medtronic)[†] has received approval by the U.S. FDA for the treatment of patients with NYHA class III or IV heart failure, on a stable

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pharmacologic regimen, who also have a QRS duration of 130 msec or longer and a LVEF of 35% or less. Biventricular pacemakers have also been combined with automatic ICDs. Both Guidant (CONTAK CD[®] CRT-D System)[†] and Medtronic (InSync[®] ICD Model 7272)[‡] have received FDA approval for combined CRT defibrillators for patients at high risk of sudden cardiac death due to ventricular arrhythmias and who have NYHA class III or IV heart failure with LVEF of 35% or less, QRS duration 130 msec or longer (120 msec or longer for the Guidant device), and remain symptomatic despite a stable, optimal heart failure drug therapy.

In September 2010, the FDA expanded the indications for CRT to include patients with class I and II heart failure. In addition to NYHA class I/II heart failure, indications for CRT in mild heart failure include a LVEF of less than 30% and a QRS duration of 130 msec or greater.

In 2005, the InSync Sentry system received FDA approval through the supplemental premarket approval (PMA) process. This combined biventricular pacemaker/ICD is also equipped to monitor intrathoracic fluid levels using bioimpedance technology, referred to as OptiVol Fluid Status monitoring. Bioimpedance measures, defined as the electrical resistance of tissue to flow of current, are performed many times per day using a vector from the right ventricular coil on the lead in the right side of the heart to the implanted pacemaker devices; changes in bioimpedance reflect intrathoracic fluid status and are evaluated based on a computer algorithm. For example, changes in a patient's daily average of intrathoracic bioimpedance can be monitored; differences in the daily average compared to a baseline are reported as the OptiVol Fluid Index. It has been proposed that these data may be used as an early warning system of cardiac decompensation or to provide additional feedback enabling a physician to further tailor medical therapy.

Rationale/Source

LITERATURE REVIEW

Biventricular Pacemakers and Combined Biventricular Pacemakers/Cardiac Defibrillators

Efficacy of Cardiac Resynchronization Therapy in Advanced Heart Failure (New York Heart Association Class III/IV)

Use of biventricular pacemakers with or without accompanying ICD for selected patients with advanced heart failure is supported by a large body of clinical trial evidence. For patients with the following characteristics, this treatment receives a class I recommendation in the 2005 American College of Cardiology/American Heart Association (ACC/AHA) guidelines for the diagnosis and management of patients with heart failure, supported by the "A" level of evidence:

- Left-ventricular ejection fraction \leq 35%
- Sinus rhythm
- New York Heart Association functional class III or IV despite optimal medical therapy
- Cardiac dyssynchrony as defined as a QRS $>$ 120 msec
- No contraindications for biventricular pacing

The current ACC/AHA guideline is accompanied by a review of the evidence, which states that more than 4,000 patients have been evaluated in randomized, clinical trials (RCTs) and that these trials establish benefit for CRT in this patient population in improving functional status and exercise capacity.



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A 2009 TEC Assessment of CRT in mild heart failure summarized 5 of the larger trials of CRT for advanced heart failure, showing that CRT improves quality of life (QoL) and functional status for patients with class III and class IV heart failure. Four of the 5 trials reported improvements in functional status for the CRT group. Similarly, 4 of the trials reported QoL measures, with all 4 showing significant improvements for the CRT group. Hospitalizations were reduced in 2 of the 4 trials, with an additional 2 trials reporting no difference in hospitalizations. The Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) trial, which had the highest enrollment and the longest follow-up, reported a significant improvement in mortality. The other trials reported lower mortality for the CRT group, which did not reach statistical significance.

A systematic review of 9 RCTs of CRT in class III/IV heart failure was published in 2004. This quantitative analysis revealed the following conclusions: 1) improvement of 3.5% in LVEF; 2) improved QoL, with weighted mean difference on the Minnesota Living with Heart Failure Questionnaire of 7.6 points (0–100 scale); 3) improved functional capacity and a reduction in all-cause mortality of 21%. This analysis also found some evidence that cardiac morphology may be improved, suggesting that CRT may prevent, delay, or even reverse the changes in morphology resulting from chronic heart failure (reverse remodeling).

Efficacy of CRT in Mild Heart Failure (NYHA Class I/II)

Evaluation of CRT in mild heart failure was originally based on a 2009 Technology Assessment Centers (TEC) Assessment. There is less evidence on treatment of mild heart failure compared to that for advanced heart failure, but clinical trial evidence is available. At least 4 RCTs enrolling over 3,000 patients, with follow-up ranging from 6 months to 2.4 years, have been published to date. A summary of the major RCTs in mild heart failure is provided.

MADIT-CRT Trial

The largest trial published to date was the Multicenter Automatic Implantation Trial – Cardiac Resynchronization (MADIT-CRT) trial, a single-blind trial that randomized 1,820 patients with NYHA class I/II heart failure to an ICD alone or an ICD-CRT device. The MADIT-CRT trial reported a reduction for the ICD-CRT group on the primary outcome, i.e., death or acute heart failure exacerbation. The primary endpoint was reached by 17.2% of patients in the ICD-CRT group compared to 25.3% of patients in the ICD-alone group. The first component of the composite outcome, acute heart failure events, occurred in 22.8% of patients in the ICD-alone group compared with 13.9% of patients in the ICD-CRT group (relative risk reduction [RRR]: 39%; absolute risk reduction [ARR]: 8.9%; number needed to treat [NNT]:11.2). This difference in acute heart failure events accounted entirely for the difference on the primary composite outcome. The death rate was similar between groups.

A follow-up publication from the MADIT-CRT trial was published in 2011 and analyzed the reduction in recurrent heart failure events. This analysis supplemented the original MADIT-CRT outcome of time to first heart failure event, by comparing total heart failure events during an average follow-up of 2.6 years. Over this time period, there was a 38% relative reduction in heart failure events in the CRT group (hazard ratio [HR] 0.62; 95% confidence interval [CI]: 0.45-0.85; $p = 0.003$). On subgroup analysis, the benefit was evident in patients with left bundle branch block (LBBB) (HR: 0.50; 95% CI: 0.33-0.76; $p = 0.001$) but not in patients without LBBB (HR: 0.99; 95% CI: 0.58-1.69; $p = 0.96$).

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RAFT Trial

A second, large RCT was the Resynchronization-Defibrillation for Ambulatory Heart Failure Trial or (RAFT) trial, which randomized 1,798 patients with class II/III heart failure to ICD-CRT or ICD alone, with a mean follow-up 40 +/- 20 months. Unlike most previous trials, this trial did not confine enrollment to patients with sinus rhythm but allowed patients with atrial arrhythmias to participate. However, the number of patients who were not in sinus rhythm was only 12.8% (229/1,798). The RAFT trial was included in a 2011 TEC Assessment. On formal quality assessment as part of the TEC Assessment, this trial met all quality indicators and was given a "good" quality rating.

The primary outcome, death from any cause or hospitalization for heart failure, was reduced in the ICD-CRT group compared to the ICD-alone group (33.2% vs. 40.3%, respectively; $p < 0.001$). There were significant reductions in both individual components of the primary outcome, overall mortality (20.8% vs. 26.1%; $p = 0.003$) and hospitalizations (19.5% vs. 26.1%, all respectively; $p < 0.001$). When restricted to patients with NYHA class II heart failure, the improvements in the outcomes of mortality and hospitalizations remained significant. The mortality for class II patients in the ICD-CRT group was 15.5% versus 21.1% in the ICD-alone group (HR: 0.71; 95% CI: 0.56-0.91; $p < 0.006$). Hospitalizations for class II patients occurred in 16.2% of patients in the ICD-CRT group compared to 21.1% in the ICD-alone group (HR: 0.70; 95% CI: 0.55-0.89; $p < 0.003$).

Subgroup analyses from the RAFT trial reported that female gender, QRS duration equal to or greater than 150 msec, LVEF less than 20%, and QRS morphologic features were predictive of benefit. Of these factors, the QRS duration was the strongest factor. Patients with a QRS duration equal to or greater than ≥ 150 msec had a relative risk (RR) for the primary outcome of approximately 0.50, compared with a RR of approximately 1.0 for patients with a QRS duration less than 150 msec ($p = 0.003$ for difference between RRs). There was a trend for greater improvement in patients with sinus rhythm compared to patients with atrial arrhythmias, but this difference did not reach statistical significance.

REVERSE Trial

The Resynchronization Reverses Remodeling in Systolic Left Ventricular Dysfunction (REVERSE) trial enrolled a total of 610 patients, all of whom received a CRT device. Patients were randomized to CRT-ON or CRT-OFF for a period of 12 months in double-blind fashion. The primary outcome was a composite measure that classified patients as improved, unchanged, or worse. There were no significant differences reported on this primary outcome. There was a decrease in hospitalizations for heart failure in the CRT-ON group (4.1%, 17/419) compared with the CRT-OFF group (7.9%, 15/191). Changes in functional status, as measured by the 6-minute walk, were similar between groups. Quality of life, as measured by the Minnesota Living with Heart Failure Questionnaire, was also similar between groups.

MIRACLE ICD Trial

The Multicenter InSync ICD Randomized Clinical Evaluation MIRACLE ICD study was the smallest of the 3 studies, enrolling 186 patients with class II heart failure and an indication for an ICD in an unblinded fashion. Patients were randomized to ICD/CRT-ON versus ICD/CRT-OFF and followed for 6 months. There was no difference in the primary outcome of peak oxygen uptake between groups. There were also no differences reported between groups on the secondary outcomes of functional status, as measured by the



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6-minute walk, QoL, as measured by the Minnesota Living with Heart Failure Questionnaire, and NYHA heart failure class.

Systematic Reviews

Numerous systematic reviews and meta-analyses have been published on CRT for heart failure. The majority compare CRT to medical management and report that outcomes are improved for patients with advanced heart failure and for patients with mild heart failure. For example, a meta-analysis of 25 trials of CRT was published in February 2011 by Al-Majed et al. This study focused on the analysis of trials with class I/II heart failure patients, identifying 6 trials treating 4,572 patients. There was a significant mortality benefit associated with CRT on combined analysis (6 trials, 4,572 participants; RR 0.83 [95% CI: 0.72 to 0.96]). This mortality benefit was driven largely by the results of the RAFT trial, which had the most number of events and was given the greatest weight in combined analysis. There was also a significant reduction in heart failure hospitalizations associated with CRT use (4 trials, 4,349 participants; RR, 0.71 [CI: 0.57 to 0.87]). There were no significant benefits reported for QoL, functional status, or progression to more advanced stages of heart failure.

Adverse Effects of CRT Placement

Complications in the main RCTs were not uniformly reported; however, each trial contained some information on short- and long-term complications. Short-term complication rates ranged from 4–22%, with lead dislodgement and hematoma at the access site most common. Long-term complications were reported by 2 of the trials, with rates of 16% and 35%. The majority of these long-term complications were lead dislodgement.

A systematic review and meta-analysis was published in 2011 that focused on complications from CRT treatment. This review included 7 trials of CRT treatment that reported on in-hospital mortality and complications related to device placement. In all 7 CRT trials, the device was placed percutaneously without a thoracotomy. In-hospital mortality occurred at a rate of 0.3%, and 30-day mortality was 0.7%. The most common complications were related to placement of the left ventricular (LV) lead. Lead dislodgement occurred in 5.9% of patients. Other LV lead placement complications included coronary vein dissection in 1.3% and coronary vein perforation in 1.3%. Pneumothorax occurred in 0.9% of patients, and hematoma at the insertion site occurred in 2.4% of patients.

Conclusions

There is a large body of clinical trial evidence that supports the use of CRT in patients with NYHA class III/IV heart failure. These trials establish that CRT treatment leads to reduced mortality, improved functional status, and improved QoL.

For patients with milder heart failure, at least 4 RCTs of CRT have been published in the literature. A mortality benefit was reported by one of the 4 trials, the RAFT trial. This trial was free of major bias and reported a fairly large absolute difference in overall mortality of 5.3%. None of the other 3 RCTs reported a mortality difference. While 2 of the other 3 trials were underpowered to detect differences in mortality, the MADIT-CRT was approximately the same size as the RAFT trial and did not show any improvement in mortality. It is possible that the sicker patient population and longer follow-up in RAFT accounted for the



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mortality difference. Among other outcome measures, hospitalizations for heart failure showed consistent improvements, but QoL and functional status did not.

Use of CRT in Patients with Atrial Fibrillation

There is controversy about whether CRT leads to health outcome benefits for patients with AF. Many experts feel that if CRT is to be used, it needs to be combined with ablation of the atrioventricular (AV) node, in order to avoid transmission of atrial impulses through the node that might result in rapid ventricular rates, thus undermining the efficacy of CRT.

An RCT was published in 2011 that compared CRT to right ventricular pacing alone in patients with AF. A total of 186 patients had AV nodal ablation and implantation of a CRT device. Patients were then randomized to echo-optimized CRT or right ventricular pacing alone and followed for a median of 20 months. The primary outcome measure was a composite of death from heart failure, hospitalization for heart failure, or worsening heart failure. This combined endpoint occurred in 11% of the CRT group compared with 26% of the RV pacing group (HR: 0.37; 95% CI: 0.18-0.73; $p = 0.005$). For the individual outcome measures, there was not a significant reduction in mortality (HR: 1.57; 95% CI: 0.58-4.27; $p = 0.37$), but there were significant reductions in hospitalizations (HR: 0.20; 95% CI: 0.06-0.72; $p = 0.013$) and worsening heart failure (HR: 0.27; 95% CI: 0.12-0.58; $p = 0.37$). There were no differences in outcomes on subgroup analysis, including analysis by ejection fraction, NYHA class, and/or QRS duration.

A post-hoc analysis of patients with AF enrolled in the RAFT RCT was published by Healey et al. in 2012. Randomization in the RAFT trial was stratified for the presence of AF, resulting in 114 patients with AF in the CRT plus defibrillator group and 115 patients with AF in the defibrillator group alone. There was no difference between groups in the primary outcome of death or hospitalization due to heart failure (HR: 0.96, 95% CI: 0.65-1.41, $p = 0.82$). There were also no differences in cardiovascular death or functional status. There was a trend for patients in the CRT group to have fewer hospitalizations for heart failure compared to the defibrillator-alone group, but the difference did not reach statistical significance.

A systematic review published in 2011 compared outcomes of CRT in patients with and without AF. This analysis included 23 observational studies enrolling 7,495 patients, of whom 1,912 had AF. Outcomes in patients with AF were less favorable on all measures. This included overall mortality (RR: 1.5; 95% CI: 1.08 to 2.09; $p = 0.015$), nonresponse to CRT (RR: 1.32; 95% CI: 1.12 to 1.55; $p = 0.001$), change in the Minnesota Living with Heart Failure QoL score (mean difference: -4.1; 95% CI: -1.7 to -6.6; $p = 0.001$), and change in the 6-minute walk distance (mean difference: -14.1meters, 95% CI: -28.2 to 0.0; $p = 0.05$). Five studies compared outcomes of patients with AF who had AV nodal ablation to patients who did not have ablation. Pooled analysis from these studies indicated that AV nodal ablation was associated with a lower rate of non-response (RR: 0.40; 95% CI: 0.28 to 0.58; $p < 0.001$).

A second systematic review that evaluated the role of AV node ablation in patients with AF treated with CRT was published in 2012. This review included non-randomized studies that reported outcomes of CRT and medical therapy. Six studies were included, enrolling a total of 768 patients, 339 of whom underwent AV node ablation and 429 who did not. AV nodal ablation was associated with improvements in the



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outcomes of all-cause mortality (RR: 0.42; 95% CI: 0.26 to 0.68), cardiovascular mortality (RR: 0.44; 95% CI: 0.24 to 0.81), and change in NYHA class (mean difference: -0.34; 95% CI: -0.56 to -0.13; $p = 0.002$).

Conclusions

There is insufficient evidence to determine whether CRT improves outcomes for patients with AF and heart failure. One systematic review of observational studies suggests that patients with AF do not achieve the same degree of benefit as do patients with sinus rhythm. However, this comparison does not determine whether patients with AF have a greater benefit from CRT compared to medical therapy. For patients with AF who are undergoing CRT, one RCT and a systematic review of non-randomized studies conclude that when CRT is used in patients with AF, AV nodal ablation is associated with improved outcomes compared to no AV nodal ablation.

Selecting Patients for CRT Treatment

For patients who meet indications for CRT treatment, there is a large variability in the magnitude of response. Some patients do not respond at all, while others have very substantial benefit. As a result, there is interest in better defining the clinical features that predict response in order to better target therapy toward those who will benefit most.

The Predictors of Response to Cardiac Resynchronization Therapy (PROSPECT) study was a prospective, multicenter study that evaluated the ability of echocardiographic parameters to predict response to CRT. Results of this trial indicated that the 12 individual echocardiographic parameters varied widely in their ability to predict response. The sensitivity of these individual measures ranged from 6-74% and the specificity ranged from 35-91%. The authors concluded that it was unlikely that these echocardiographic measures could improve patient selection for CRT.

Ventricular Dyssynchrony

A small RCT that compared outcomes of CRT in patients with ventricular dyssynchrony versus those without was published in 2011. A total of 73 patients with class II/IV were evaluated, 44 of whom were found to have dyssynchrony on echocardiography. These 44 patients were randomized to a combined CRT-defibrillator or a defibrillator alone. Outcomes measures were peak O₂ consumption (VO₂max), NYHA class, and echocardiographic parameters. At 6 months of follow-up, more patients in the CRT group had an increase of at least 1 mL/kg/min in VO₂max (62% vs. 50% $p = 0.04$). There were significant within-group improvements in NYHA class and echocardiographic measures, but the between-group comparisons with the no-CRT group did not reach statistical significance.

Several observational studies of patients who meet criteria for treatment have shown that measures of dyssynchrony measured by various methods are correlated with treatment response, as defined by improvements in LV end-systolic volume, ejection fraction, or clinical criteria. Although correlations have been found, studies vary due to the method used to measure dyssynchrony, the cutoff value used, and the criteria used for clinical response. Without clinical trial evidence, it is not possible to determine which method and which cutoff will select patients who otherwise meet criteria for therapy who would be better off without a biventricular pacemaker.



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QRS Duration

One RCT was identified that selected patients who had a narrow QRS complex on EKG and echocardiographic evidence (Doppler and M-mode) of dyssynchrony. The Resynchronization Therapy in Normal QRS Trial [RethinQ study] randomized 172 patients to receive a CRT device, turned on or not, and followed up for 6 months. CRT-treated patients were not more likely to have improvement than non-CRT patients (46 vs. 41%, respectively, met endpoint of improvement in exercise capacity [peak VO₂]). A subset of patients with QRS duration greater than or equal to 120–130 msec showed improvement ($p = 0.02$), whereas patients with QRS less than 120 msec did not ($p = 0.45$). This study confirmed that patients with a QRS duration less than 120 msec do not benefit from CRT.

Several meta-analyses of the association of QRS duration with outcomes have been published. The first of these was published in 2011 and evaluated whether patients with modest prolongations of the QRS complex benefited from CRT. This study identified 5 trials enrolling 5,813 patients 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 msec, and severely prolonged QRS, generally 150 msec or greater. For patients with a moderately prolonged QRS, there was no significant benefit for CRT in reducing composite outcomes of adverse cardiac events (RR: 0.95; 95% CI: 0.82 to 1.10; $p = 0.49$). In contrast, for patients 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; $p < 0.001$). There were no differences in outcomes on sensitivity analysis according to NYHA class and ICD status.

Other meta-analyses have come to similar conclusions, reporting benefit in patients with a QRS > 150 , and little to no benefit in patients with shorter QRS duration. In one of these studies, the benefit of CRT was confined to patients with left bundle-branch block (LBBB). There was no benefit demonstrated for patients with right bundle-branch block (RBBB) or intraventricular conduction delay. These authors suggest that QRS morphology may be as important, or more important, than QRS duration in prediction response to CRT.

Conclusions

The optimal selection of patients for CRT treatment remains an active area of investigation. The presence of dyssynchrony on echocardiography may risk stratify patients, but is not a good discriminator of responders versus non-responders. In contrast, a QRS duration of greater than 150 msec, or the presence of LBBB, appears to discriminate well between responders and non-responders and represents another potential factor on which patients may be selected for CRT treatment. The evidence on this question is primarily from subgroup analyses of RCTs but is consistent across multiple studies and is supported by quantitative pooling of these subgroup analyses in a meta-analysis.

Triple-site Cardiac Resynchronization Therapy (Triventricular Pacing)

Triple-site CRT, or triventricular pacing, is a variation of conventional CRT that uses an additional pacing lead. The rationale behind triventricular pacing is that a third pacing lead may improve electromechanical synchrony, thereby leading to better outcomes. Two RCTs have been published that compared triple-site CRT with conventional CRT. Rogers et al. performed a double-blind RCT in 43 patients referred for CRT.



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All patients had 3 leads implanted, but patients in the conventional CRT arm had their device programmed to biventricular pacing. The triventricular group had greater improvements in the 6-minute walk distance compared to the conventional CRT group (increase of 91 m vs. 65 m, $p = 0.008$), and greater improvement on the Minnesota Living with Heart Failure scale (reduction of 24 points vs. 18 points, $p < 0.0001$). Complications did not differ between groups; however, since all patients had 3 leads implanted, this was not a valid comparison of complications for biventricular versus triventricular pacing.

A second RCT was published by Lenarczyk et al. in 2012. This was a report of the first 100 patients randomized to triple-site or conventional CRT in the Triple-Site versus Standard Cardiac Resynchronization Therapy Randomized Trial (TRUST CRT). After a follow-up of 1 year, more patients in the conventional arm were in NYHA class III or IV heart failure compared to the triple-site CRT group (30% vs. 12.5%, $p < 0.05$). Implantation success was similar in the triple-site and conventional groups (94% vs. 98%, respectively, $p = NS$), but the triple-site implantation was associated with longer time for implantation and a higher fluoroscopic exposure. In addition, more patients in the triple-site group required additional procedures (33% vs. 16%, $p < 0.05$).

Conclusions

Two small RCTs with limited follow-up report improved functional status and QoL with triple-site CRT compared to conventional CRT. However, triple-site CRT was also associated with higher radiation exposure and a greater number of additional procedures post-implantation. Further studies are needed to better define the benefit/risk ratio for triple-site CRT compared to conventional CRT.

Combined Automatic Implantable Cardiac Defibrillators/Biventricular Pacemakers/Intrathoracic Fluid Monitors

Intrathoracic fluid status monitoring has been proposed as a more sensitive monitoring technique of the fluid status leading to prompt identification of impending heart failure, permitting early intervention and, it is hoped, a decreased rate of hospitalization. There is a lack of evidence from RCTs on the efficacy of fluid monitoring compared to usual care. The available evidence consists of uncontrolled studies that evaluate the correlation of fluid status information with cardiac events.

A prospective cohort of 558 patients from 34 centers identified the number of “threshold crossing events” and the percent of days with such events as predictors of hospitalization for severe heart failure using multivariate regression. Over a mean of 326 days, 953 threshold crossing events in 351 patients resulted in 63 hospitalizations among 49 patients. Each subsequent event was associated with a 36% increased risk of hospitalization; however, the extent to which the presence of threshold crossing events influenced the decision to hospitalize is not known.

A similar retrospective study, that evaluated “threshold crossings” as a predictor of arrhythmogenic events, was published in 2011. This analysis included 282 patients with NYHA class III or IV heart failure followed for a mean of 10 months. Patients were categorized into those that had “threshold crossings” ($n = 145$, 51%) and those that did not ($n = 137$, 49%). Tachyarrhythmic events were more common in patients with threshold crossings than in patients without (3,241 vs. 1,484 events; $p < 0.0001$).



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Medtronic, the manufacturer of the OptiVol[®] Fluid Status Monitoring feature of the InSync Sentry system, has announced several ongoing clinical trials of the device as follows. The Optilink HF trial is designed to evaluate fluid status monitoring with the OptiVol[®] device combined with wireless transmission through the CareLink Network. Patients with NHYA class II or III heart failure are eligible, and the target enrollment is 1,000 patients. The primary outcome is a composite of all-cause death or cardiovascular hospitalization. The trial is scheduled to report the first results in May 2014.

The Medtronic Impedance Diagnostics in Heart Failure (MID-HeFT) study was a retrospective study designed to investigate the feasibility of predicting heart failure hospitalization based on intrathoracic bioimpedance and to validate impedance measurements as a surrogate measure of pulmonary congestion based on pulmonary capillary wedge pressure. The device that was used was a modified pacemaker and thus was not incorporated into a biventricular pacemaker/ICD. A total of 9 abstracts are derived from this study. One abstract included 33 patients. Among the 10 patients with 26 hospitalizations for heart failure during an 18-month follow-up, thoracic bioimpedance gradually decreased prior to the hospitalization, in many instances before the onset of clinical symptoms.

The Fluid Accumulation Status Trial (FAST) is a prospective trial investigating the use of the algorithm used to analyze the collected bioimpedance data. The early results of this trial have been presented at the 13th Heart Failure Society meeting in September 2009. Data presented at that time reported that fluid monitoring was more sensitive in predicting acute heart failure exacerbations, compared to weight monitoring. To date, there have not been any publications in the peer-reviewed literature on this study, and no data on other health outcomes are available at this time.

The Sensitivity of the InSync Sentry for Prediction of Heart Failure (SENSE-HF) study is designed to prospectively evaluate the sensitivity of the OptiVol fluid trends feature in predicting heart failure hospitalizations with signs and/or symptoms of pulmonary congestion and then to define OptiVol clinical guidelines for patient management. The SENSE-HF study was completed in March 2009. Baseline characteristics of the PARTNERS-HF study have been published; study outcomes have not been published in the peer-reviewed literature.

The Combined Heart Failure Diagnostics Identify Patients at Higher Risk of Subsequent Heart Failure Hospitalization (PARTNERS-HF) is a prospective, nonrandomized postmarketing study conducted in up to 100 U.S. centers that was completed in March 2008. The goal of the trial is to characterize the relationship between a variety of diagnostic data derived from the implanted biventricular/ICD devices. Data from this study were presented at the 2008 Annual Heart Failure Society Meeting. Researchers reported at this time that patients with a fluid index that crossed threshold were twice as likely to develop acute heart failure events, compared to patients whose fluid index did not cross the threshold.

Conclusions

The evidence is not sufficient to determine whether intrathoracic fluid monitoring improves outcomes for patients who receive a CRT device. The available evidence indicates that intrathoracic monitoring may be a more sensitive measure for predicting heart failure exacerbations compared to weight monitoring. However, there is no published data that report improved outcomes associated with fluid monitoring. Although



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numerous trials have been undertaken, as of April 2012, there were no RCT publications in the peer-reviewed literature that report on outcomes and/or the utility of intrathoracic fluid monitoring in the management of patients with heart failure.

Clinical Input Received through Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, input was received from 1 physician specialty society and 8 academic medical centers while this policy was under review in 2012. There was consensus agreement with the medically necessary statements. For patients with class I heart failure, there was mixed input as to whether CRT should be medically necessary. Regarding the duration of the QRS complex, there was acknowledgement that the literature supported use mainly in patients with a QRS greater than 150 msec, but most reviewers disagreed with restricting CRT use to patients with a QRS greater than 150 msec because that was not currently the accepted standard of care. For patients with AF, the input was mixed on whether biventricular pacing improves outcomes.

Summary

Evidence from clinical trials and systematic reviews supports the benefit of CRT treatment for patients with NYHA class III/IV heart failure. For this group, there are improvements in mortality, functional status and QoL. As a result, CRT treatment may be considered medically necessary for patients with NYHA class III/IV heart failure who have an ejection fraction < 35%, sinus rhythm, a QRS duration of at least 120 msec, and who are treated with an optimal pharmacologic regimen.

For patients with milder heart failure, RCT evidence from at least one large, high-quality trial reports a mortality benefit for patients with class II heart failure, but other RCTs do not report a mortality benefit. Several studies report a decrease in hospitalizations for class II patients, but no studies provide evidence of treatment benefit on functional status or QOL outcomes. Despite the lower level of evidence available for mild compared to advanced heart failure, it can be concluded that the benefit of CRT outweighs the risk for these patients. Therefore, CRT treatment may be considered medically necessary for class II heart failure patients who meet other clinical criteria for treatment. The evidence on class I heart failure is not sufficient to permit conclusions, as only a small number of class I patients have been included in some of the trials, and no benefit has been demonstrated for this specific subgroup. As a result, CRT is considered investigational for class I heart failure.

Treatment of patients with AF and heart failure is controversial. Available evidence establishes that patients with heart failure probably do not derive the same magnitude of benefit as do patients with sinus rhythm and that CRT with AV nodal ablation is probably superior to CRT without AV nodal ablation in patients with heart failure. However, the evidence is insufficient to determine whether CRT treatment is superior to no treatment for this patient group. In addition, clinical input in 2012 was mixed as to whether patients with AF should be treated with CRT. Therefore, CRT remains investigational for patients with AF.

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The optimal selection of patients for CRT treatment remains uncertain. Accumulating evidence indicates that benefit is concentrated in patients with a QRS duration of greater than 150 msec. This factor offers a potential method to better select patients for CRT and potentially avoid treatment in patients who will not benefit. Clinical input in 2012 demonstrated support for continued use of QRS threshold of 120 msec, rather than restricting treatment to patients with QRS greater than 150 msec. Other factors for selecting patients, such as ventricular dyssynchrony on echocardiography, have not been shown to be good discriminators of responders versus non-responders.

References

1. Blue Cross Blue Shield Association, Medical Policy Reference Manual, "Biventricular Pacemakers for the Treatment of Congestive Heart Failure", 2.02.10, 4:2013.
2. Hunt SA. ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure). *J Am Coll Cardiol* 2005; 46(6):e1-82.
3. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Cardiac Resynchronization Therapy for Mild Congestive Heart Failure. TEC Assessments 2009; Volume 24, Tab 8.
4. Bristow MR, Saxon LA, Boehmer J et al. Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. *N Engl J Med* 2004; 350(21):2140-50.
5. McAlister FA, Ezekowitz JA, Wiebe N et al. Systematic review: cardiac resynchronization in patients with symptomatic heart failure. *Ann Intern Med* 2004; 141(5):381-90.
6. Moss AJ, Hall WJ, Cannom DS et al. Cardiac-resynchronization therapy for the prevention of heart-failure events. *N Engl J Med* 2009; 361(14):1329-38.
7. Goldenberg I, Hall WJ, Beck CA et al. Reduction of the risk of recurring heart failure events with cardiac resynchronization therapy: MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy). *J Am Coll Cardiol* 2011; 58(7):729-37.
8. Tang AS, Wells GA, Talajic M et al. Cardiac-resynchronization therapy for mild-to-moderate heart failure. *N Engl J Med* 2010; 363(25):2385-95.
9. Linde C, Abraham WT, Gold MR et al. Randomized trial of cardiac resynchronization in mildly symptomatic heart failure patients and in asymptomatic patients with left ventricular dysfunction and previous heart failure symptoms. *J Am Coll Cardiol* 2008; 52(23):1834-43.
10. Abraham WT, Young JB, Leon AR et al. Effects of cardiac resynchronization on disease progression in patients with left ventricular systolic dysfunction, an indication for an implantable cardioverter-defibrillator, and mildly symptomatic chronic heart failure. *Circulation* 2004; 110(18):2864-8.
11. Adabag S, Roukoz H, Anand IS et al. Cardiac resynchronization therapy in patients with minimal heart failure: a systematic review and meta-analysis. *J Am Coll Cardiol* 2011; 58(9):935-41.
12. Al-Majed NS, McAlister FA, Bakal JA et al. Meta-analysis: cardiac resynchronization therapy for patients with less symptomatic heart failure. *Ann Intern Med* 2011; 154(6):401-12.
13. Bertoldi EG, Polanczyk CA, Cunha V et al. Mortality reduction of cardiac resynchronization and implantable cardioverter-defibrillator therapy in heart failure: an updated meta-analysis. Does recent evidence change the standard of care? *J Card Fail* 2011; 17(10):860-6.
14. Nery PB, Ha AC, Keren A et al. Cardiac resynchronization therapy in patients with left ventricular systolic dysfunction and right bundle branch block: a systematic review. *Heart Rhythm* 2011; 8(7):1083-7.
15. Tu R, Zhong G, Zeng Z et al. Cardiac resynchronization therapy in patients with mild heart failure: a systematic review and meta-analysis of randomized controlled trials. *Cardiovasc Drugs Ther* 2011; 25(4):331-40.
16. Wells G, Parkash R, Healey JS et al. Cardiac resynchronization therapy: a meta-analysis of randomized controlled trials. *CMAJ* 2011; 183(4):421-9.
17. van Rees JB, de Bie MK, Thijssen J et al. Implantation-related complications of implantable cardioverter-defibrillators and cardiac resynchronization therapy devices: a systematic review of randomized clinical trials. *J Am Coll Cardiol* 2011; 58(10):995-1000.
18. Brignole M, Botto G, Mont L et al. Cardiac resynchronization therapy in patients undergoing atrioventricular junction ablation for permanent atrial fibrillation: a randomized trial. *Eur Heart J* 2011; 32(19):2420-9.
19. Healey JS, Hohnloser SH, Exner DV et al. Cardiac resynchronization therapy in patients with permanent atrial fibrillation: results from the Resynchronization for Ambulatory Heart Failure Trial (RAFT). *Circ Heart Fail* 2012; 5(5):566-70.

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20. Wilton SB, Leung AA, Ghali WA et al. Outcomes of cardiac resynchronization therapy in patients with versus those without atrial fibrillation: a systematic review and meta-analysis. *Heart Rhythm* 2011; 8(7):1088-94.
21. Ganesan AN, Brooks AG, Roberts-Thomson KC et al. Role of AV Nodal Ablation in Cardiac Resynchronization in Patients With Coexistent Atrial Fibrillation and Heart Failure A Systematic Review. *J Am Coll Cardiol* 2012; 59(8):719-26.
22. Yu CM, Abraham WT, Bax J et al. Predictors of response to cardiac resynchronization therapy (PROSPECT)--study design. *Am Heart J* 2005; 149(4):600-5.
23. Chung ES, Leon AR, Tavazzi L et al. Results of the Predictors of Response to CRT (PROSPECT) trial. *Circulation* 2008; 117(20):2608-16.
24. Diab IG, Hunter RJ, Kamdar R et al. Does ventricular dyssynchrony on echocardiography predict response to cardiac resynchronisation therapy? A randomised controlled study. *Heart* 2011; 97(17):1410-6.
25. Hawkins NM, Petrie MC, MacDonald MR et al. Selecting patients for cardiac resynchronization therapy: electrical or mechanical dyssynchrony? *Eur Heart J* 2006; 27(11):1270-81.
26. Beshai JF, Grimm RA, Nagueh SF et al. Cardiac-resynchronization therapy in heart failure with narrow QRS complexes. *N Engl J Med* 2007; 357(24):2461-71.
27. Thibault B, Harel F, Ducharme A et al. Cardiac Resynchronization Therapy in Patients With Heart Failure and a QRS Complex <120 Milliseconds: The Evaluation of Resynchronization Therapy for Heart Failure (LESSER-EARTH) Trial. *Circulation* 2013; 127(8):873-81.
28. Sipahi I, Carrigan TP, Rowland DY et al. Impact of QRS duration on clinical event reduction with cardiac resynchronization therapy: meta-analysis of randomized controlled trials. *Arch Intern Med* 2011; 171(16):1454-62.
29. Bryant AR, Wilton SB, Lai MP et al. Association between QRS duration and outcome with cardiac resynchronization therapy: A systematic review and meta-analysis. *J Electrocardiol* 2013; 46(2):147-55.
30. Stavrakis S, Lazzara R, Thadani U. The benefit of cardiac resynchronization therapy and QRS duration: a meta-analysis. *J Cardiovasc Electrophysiol* 2012; 23(2):163-8.
31. Sipahi I, Chou JC, Hyden M et al. Effect of QRS morphology on clinical event reduction with cardiac resynchronization therapy: meta-analysis of randomized controlled trials. *Am Heart J* 2012; 163(2):260-7 e3.
32. Rogers DP, Lambiasi PD, Lowe MD et al. A randomized double-blind crossover trial of triventricular versus biventricular pacing in heart failure. *Eur J Heart Fail* 2012; 14(5):495-505.
33. Lenarczyk R, Kowalski O, Sredniawa B et al. Implantation feasibility, procedure-related adverse events and lead performance during 1-year follow-up in patients undergoing triple-site cardiac resynchronization therapy: a substudy of TRUST CRT randomized trial. *J Cardiovasc Electrophysiol* 2012; 23(11):1228-36.
34. Perego GB, Landolina M, Vergara G et al. Implantable CRT device diagnostics identify patients with increased risk for heart failure hospitalization. *J Interv Card Electrophysiol* 2008; 23(3):235-42.
35. Sekiguchi Y, Tada H, Yoshida K et al. Significant increase in the incidence of ventricular arrhythmic events after an intrathoracic impedance change measured with a cardiac resynchronization therapy defibrillator. *Circ J* 2011; 75(11):2614-20.
36. Brachmann J, Bohm M, Rybak K et al. Fluid status monitoring with a wireless network to reduce cardiovascular-related hospitalizations and mortality in heart failure: rationale and design of the OptiLink HF Study (Optimization of Heart Failure Management using OptiVol Fluid Status Monitoring and CareLink). *Eur J Heart Fail* 2011; 13(7):796-804.
37. Foreman B, Fishel RS, Odryzynski NL et al. Intra-thoracic impedance: A surrogate measure of thoracic fluid – Fluid Accumulation Status Trial (FAST). *J Card Fail* 2004; 10(suppl):251.
38. Yu CM, Wang L, Stadler R et al. Impedance based prediction of CHF admission precedes symptoms in heart failure patients. *Pacing Clin Electrophysiol* 2004; 1(suppl):S213.
39. Whellan DJ, O'Connor CM, Ousdigian KT et al. Rationale, design, and baseline characteristics of a Program to Assess and Review Trending Information and Evaluate Correlation to Symptoms in Patients with Heart Failure (PARTNERS HF). *Am Heart J* 2008; 156(5):833-9, 39 e2.
40. PARTNERS HF: Program to Access and Review Trending Information and Evaluate Correlation to Symptoms in Patients With Heart Failure. Sponsored by Medtronic Cardiac Rhythm Disease Management. 2010. Available online at: <http://clinicaltrials.gov/ct2/show/results/NCT00279955>.

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HCPCS	C1721, C1785, C1786, C2619, C2621
ICD-9 Diagnosis	428.0 thru 428.9
ICD-9 Procedure	00.50, 00.51, 00.52, 00.53, 00.54

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04/18/2002 Medical Policy Committee review
06/05/2002 Managed Care Advisory Council approval
06/24/2002 Format revision. No substance change to policy.
06/01/2004 Medical Director review. Format revision. Clinical criteria revision.
06/15/2004 Medical Policy Committee review
06/28/2004 Managed Care Advisory Council approval
11/02/2004 Medical Director review. Clinical criteria revision
11/16/2004 Medical Policy Committee review
11/29/2004 Managed Care Advisory Council approval
04/05/2005 Medical Director review
04/18/2005 Medical Director review
04/22/2005 Medical Director review
04/27/2005 Medical Policy Committee review. Clinical criteria revision. Combination automatic implantable cardiac defibrillators (AICD) and biventricular pacemakers criteria further defined; "patients with New York Heart Association (NYHA) Class III or IV CHF, with a QRS duration of >120-130 msec". FDA labeled indication for the InSync device and CONTAK CD® CRT-D System added. Investigational statement added to address cases not meeting clinical criteria.
04/04/2007 Medical Director review
04/18/2007 Medical Policy Committee approval. Policy statements revised indicating that intrathoracic bioimpedance is considered investigational as a component of a biventricular pacemaker; patient selection criteria for combined biventricular pacemaker/ACID revised to indicate that a combined



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	device would be considered medically necessary in patients who meet the criteria for a biventricular pacemaker alone. Rationale /Source and Background/Overview updated.
04/02/2008	Medical Director review
04/16/2008	Medical Policy Committee approval. No changes to policy statement.
04/02/2009	Medical Director review
04/15/2009	Medical Policy Committee approval. No changes to policy statement.
04/08/2010	Medical Policy Committee approval
04/21/2010	Medical Policy Implementation Committee approval. Added statement "Based on review of available data, the Company considers biventricular pacemakers with or without an accompanying implantable cardiac defibrillator as a treatment of NYHA class I or II heart failure to be investigational to the policy.
04/07/2011	Medical Policy Committee approval
04/13/2011	Medical Policy Implementation Committee approval. Sinus rhythm added to the list of patient selection criteria.
04/12/2012	Medical Policy Committee review
04/25/2012	Medical Policy Implementation Committee approval. Cardiac resynchronization therapy use in patients with NYHA class II heart failure meeting specific criteria now may be considered eligible for coverage; all other uses in mild heart failure (e.g., class I) considered investigational. The term "congestive" was removed from the title and text.
02/04/2013	Coding revised
04/04/2013	Medical Policy Committee review
04/24/2013	Medical Policy Implementation Committee approval. Title changed. Cardiac resynchronization as a treatment of heart failure in patients with atrial fibrillation added as investigational.
04/03/2014	Medical Policy Committee review
04/23/2014	Medical Policy Implementation Committee approval. Additional investigational statement added for triple-site (triventricular) CRT.
Next Scheduled Review Date:	04/2015

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