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CONTAK RENEWAL® 3

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System Guide

CONTAK RENEWAL® 3
MODELS H170/H175

CONTAK RENEWAL® 3 HE
MODELS H177/H179

**Cardiac Resynchronization
Therapy Defibrillator**

RESTRICTED DEVICE:
Federal law (USA) restricts
this device to sale, distribution,
and use by, or on the lawful
order of a physician trained or
experienced in device implant
and follow-up procedures.

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INFORMATION FOR USE

CHAPTER 1

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DEVICE DESCRIPTION

The Guidant CONTAK RENEWAL[®] 3 cardiac resynchronization therapy defibrillator (CRT-D), Models H170 and H175, and CONTAK RENEWAL[®] 3 HE CRT-D, Models H177 and H179, provide ventricular tachyarrhythmia and cardiac resynchronization therapies. Ventricular tachyarrhythmia therapy is for the treatment of ventricular tachycardia (VT) and ventricular fibrillation (VF), rhythms that are associated with sudden cardiac death (SCD). Cardiac resynchronization therapy is for the treatment of heart failure (HF) and uses biventricular electrical stimulation to synchronize ventricular contractions. The device also uses accelerometer-based adaptive-rate bradycardia therapy similar to Guidant's commercially available VENTAK[®] family of implantable cardioverter defibrillators (ICDs). The pulse generator has independently programmable outputs and accepts one IS-1¹ atrial lead, one LV-1 or one IS-1 coronary venous pace/sense lead, and one DF-1/IS-1 cardioversion/defibrillation lead. The pulse generator and the leads constitute the implantable portion of the CONTAK RENEWAL 3 system. The device's small, physiologic shape minimizes pocket size and device migration.

Cardioversion/defibrillation therapies include a range of low- and high-energy shocks using either a biphasic or monophasic waveform. The CONTAK RENEWAL 3 device uses the Guidant TRIAD[®] electrode system for defibrillation energy delivery. By using the metallic housing of the pulse generator as an active electrode, combined with the Guidant ENDOTAK[®] two-electrode defibrillation lead, energy is sent via a dual-current pathway from the distal shocking electrode to the proximal electrode and to the pulse generator case. The CONTAK RENEWAL 3 device also offers a wide variety of antitachycardia pacing schemes to terminate slower, more stable ventricular tachyarrhythmias. Bradycardia pacing with cardiac resynchronization therapy, including adaptive-rate features, is available to detect and treat bradyarrhythmias and to support the cardiac rhythm after defibrillation therapy.

The ZOOM[®] Programming System, which includes the Model 2920 Programmer/Recorder/Monitor (PRM), the Model 2845 CONSULT Software Application, and an accessory telemetry wand, constitutes the external portion of the CONTAK RENEWAL 3 system. The external components allow interrogation and programming of the pulse generator as well as access to the device's diagnostic features. The CONTAK RENEWAL 3 system can be programmed to provide a variety of therapy options. It also can provide noninvasive diagnostic testing and therapy history data.

1. IS-1 refers to the international standard ISO 5841.3:2000. LV-1 refers to the Guidant LV[®] proprietary connector. DF-1 refers to the international standard ISO 11318:2002.

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Related Manuals and Information Tools

The Operator's Manual for the Guidant Programmer/Recorder/Monitor provides information specific to the programmer, such as setting up the system, maintenance, and handling. Physician's manuals for the leads provide specific information and instructions regarding the implanted leads. The Physician's Technical Manual is packaged with the pulse generator and provides the information needed to implant the device at nominal parameter settings. All information in the Physician's Technical Manual is also included in this manual.

INDICATIONS AND USAGE

Guidant Cardiac Resynchronization Therapy Defibrillators (CRT-Ds) are indicated for patients with moderate to severe heart failure (NYHA III/IV) who remain symptomatic despite stable, optimal heart failure drug therapy, and have left ventricular dysfunction (EF \leq 35%) and QRS duration \geq 120 ms.

Guidant Cardiac Resynchronization Therapy Defibrillators (CRT-Ds) have demonstrated the following outcomes in the indicated population specified above:

- Reduction in risk of all-cause mortality or first all-cause hospitalization

NOTE: Hospitalization is defined as administration of IV inotropes or vaso-active drugs > 4 hours (outpatient or inpatient), or admission to a hospital that includes or extends beyond a calendar date change.

- Reduction in risk of all-cause mortality
- Reduction of heart failure symptoms

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CONTRAINDICATIONS

The CONTAK RENEWAL 3 CRT-D is contraindicated for use in the following:

- Patients whose ventricular tachyarrhythmias may have reversible cause, such as 1) digitalis intoxication, 2) electrolyte imbalance, 3) hypoxia, or 4) sepsis, or
- Patients whose ventricular tachyarrhythmias have a transient cause, such as 1) acute myocardial infarction, 2) electrocution, or 3) drowning.

WARNINGS

General

- **Labeling knowledge.** Read this manual thoroughly before implanting the pulse generator to avoid damage to the system. Such damage can result in injury to or death of the patient.
- **Avoid shock during handling.** Program the pulse generator Tachy Mode to Off during implant, explant, or postmortem procedures to avoid inadvertent high voltage shocks.
- **Defibrillator paddles.** Always have sterile external and internal defibrillator paddles or an equivalent (e.g., R2² pads) immediately available during conversion testing. If not terminated in a timely fashion, an induced tachyarrhythmia can result in the patient's death.
- **Resuscitation availability.** Ensure that an external defibrillator and medical personnel skilled in cardiopulmonary resuscitation (CPR) are present during post-implant device testing should the patient require external rescue.
- **Magnetic resonance imaging (MRI) exposure.** Do not expose a patient to MRI device scanning. Strong magnetic fields may damage the device and cause injury to the patient.
- **Diathermy.** Do not subject a patient with an activated implanted pulse generator to diathermy since diathermy may damage the pulse generator.

2. Trademark of the R2 Corporation.

Programming and Device Operation

- **Atrial tracking modes.** Do not use atrial tracking modes in patients with chronic refractory atrial tachyarrhythmias. Tracking of atrial arrhythmias could result in VT or VF.
- **Atrial only modes.** Do not use atrial only modes in patients with heart failure because such modes do not provide cardiac resynchronization therapy.
- **Ventricular sensing.** Left ventricular lead dislodgment to a position near the atria can result in atrial oversensing and left ventricular pacing inhibition. See Sensitivity Adjustment on page 10-4 for more information.
- **Slow VT.** Physicians should use medical discretion when implanting this device in patients who present with slow VT. Programming therapy for slow monomorphic VT may preclude CRT delivery at faster rates if these rates are in the tachyarrhythmia zones. See CRT Delivery Zone and Tachyarrhythmia Zones on page 3-5 for more information.

Implant Related

- **Do not kink leads.** Kinking leads may cause additional stress on the leads, possibly resulting in lead fracture.
- **Patch leads.** Do not use defibrillation patch leads with the CONTAK RENEWAL 3 system, or injury to the patient may occur.
- **Separate pacemaker.** Do not use the CRT-D device with a separate pacemaker system. This combination could result in CRT-D/pacemaker interaction.
- **Emulator.** The emulator is not intended for use as a permanent lead electrode and must be removed from the patient. It is for one-time use only. Do not resterilize.

PRECAUTIONS

Sterilization, Storage, and Handling

- **For single use only—do not resterilize devices.** Do not resterilize the device or the accessories packaged with it because Guidant cannot ensure that resterilization is effective.

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- **If package is damaged.** Guidant sterilizes the pulse generator blister trays and contents with ethylene oxide gas before final packaging. When the pulse generator is received, it is sterile, provided the container is intact. If the packaging is wet, punctured, opened, or otherwise damaged, return the device to Guidant.
- **Storage temperature and equilibration.** Recommended storage temperatures are 0–50°C (32–122°F). Allow the device to reach room temperature before programming or implanting the device because temperature extremes may affect initial device function.
- **Device storage.** Store the pulse generator in a clean area, away from magnets, kits containing magnets, and sources of electromagnetic interference (EMI) to avoid device damage.
- **Use before date.** Implant the device system before the USE BEFORE date on the package label because this date reflects a validated shelf life. For example, if the date is January 1, do not implant on or after January 1.

Implantation and Device Programming

- **Lead system.** Do not use any lead with this device without first verifying connector compatibility. Using incompatible leads can damage the connector or result in potential adverse consequences, such as undersensing of cardiac activity or failure to deliver necessary therapy.
- **STAT PACE settings.** Do not leave the device programmed in STAT PACE settings; these settings may significantly reduce the lifetime of the device due to the high output.
- **Drug-resistant SVTs.** Determine if the device and programmable options are appropriate for patients with drug-resistant supraventricular tachyarrhythmias (SVTs), because drug-resistant SVTs can initiate unwanted tachyarrhythmia therapy or can cause inhibition of cardiac resynchronization therapy.
- **AV Delay.** For delivery of cardiac resynchronization therapy, the programmed setting for the AV Delay must be less than the patient's intrinsic intracardiac AV interval.
- **Adaptive-rate pacing.** The clinical benefit of adaptive-rate pacing in heart failure patients has not been studied. The use of adaptive-rate pacing should be used with medical discretion only if the patient develops an indication for rate-

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responsive pacing, such as chronotropic incompetence. Patients with heart failure may have hemodynamic compromise at rapid sensor-driven rates, and the physician may wish to program less aggressive adaptive-rate parameters in accordance with patient condition.

- **Atrial Tachy Response (ATR).** ATR should be programmed Off unless the patient has a history of atrial tachyarrhythmias. The delivery of CRT is compromised because AV synchrony is disrupted.
- **Threshold test.** During the left ventricular threshold test, right ventricular backup pacing is unavailable.
- **Left ventricular pacing only.** The clinical effect of left ventricular pacing alone for heart failure patients has not been studied.
- **Do not bend the lead near the lead–header interface.** Improper insertion can cause insulation damage near the terminal ring that could result in lead failure.
- **Shock waveform polarity.** Never change the shock waveform polarity by physically switching the lead anodes and cathodes in the pulse generator header—use the programmable Polarity feature. Device damage or nonconversion of the arrhythmia post-operatively may result if polarity is switched physically.
- **Absence of an LV lead.** Absence of an electrode or plug in the LV lead port may affect device performance. If an LV lead is not used, be sure to insert a plug.
- **Electrode connections.** Fully insert each IS-1 or LV-1 pace/sense lead into its lead port and then tighten the setscrews onto the electrodes. If the lead is not fully inserted, the setscrews might damage the lead body.
- **Tachy Mode to Off.** Ensure that the pulse generator’s Tachy Mode is Off when not in use, before handling it, and before using electrosurgery to prevent inappropriate shocks. For tachyarrhythmia therapy, verify that the Tachy Mode is on.
- **Atrial oversensing.** Care must be taken to ensure that artifacts from the ventricles are not present on the atrial channel or atrial oversensing may result. If ventricular artifacts are present in the atrial channel, the atrial lead may need to be repositioned to minimize its interaction.

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- **Defibrillation lead impedance.** Never implant the device with a lead system that has less than 15- Ω total shock lead impedance. Device damage may result. If a shocking lead impedance is less than 20 Ω , reposition the shocking electrodes to allow a greater distance between the shocking electrodes.
- **ATR Entry Count.** Exercise care when programming the Entry Count to low values in conjunction with a short duration. This combination allows mode switching with very few fast atrial beats. If the entry count were programmed to 2 and the duration to 0, for example, ATR mode switching could occur on two fast atrial intervals. In these instances, a short series of premature atrial events could cause the device to mode switch.
- **ATR Exit Count.** Exercise care when programming the Exit Count to low values. If the Exit Count were programmed to 2, for example, a few cycles of atrial undersensing could cause termination of mode switching.
- **Left ventricular lead configuration.** Proper programming of the LV coronary venous lead configuration is essential for proper LV lead function. Program the lead configuration in accordance with the number of electrodes on the LV lead; otherwise, erratic LV sensing, loss of LV pacing, or ineffective LV pacing might occur.
- **Left Ventricular Protection Period (LVPP).** Use of a long LVPP reduces the maximum left ventricular pacing rate and may inhibit cardiac resynchronization therapy at higher pacing rates.
- **Shunting energy.** Do not allow any object that is electrically conductive to come into contact with the lead or device during induction because it may shunt energy and result in less energy getting to the patient, and may damage the implanted system.
- **Sensing adjustment.** Following any sensing range adjustment or any modification of the sensing lead, always verify appropriate sensing for HF/bradycardia pacing and tachycardia detection.

Follow-up Testing

- **Conversion testing.** Successful conversion of ventricular fibrillation or ventricular tachycardia during arrhythmia conversion testing is no assurance that conversion will occur post-operatively. Be aware that changes in the patient's condition, drug regimen, and other factors may change the

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defibrillation threshold (DFT), which may result in nonconversion of the arrhythmia post-operatively.

Pulse Generator Explant and Disposal

- **Incineration.** Be sure that the pulse generator is removed before cremation. Cremation and incineration temperatures might cause the pulse generator to explode.
- **Device handling.** Program the pulse generator Tachy Mode to Off, disable the magnet feature, and disable the Beep When ERI Is Reached beeper before explanting, cleaning, or shipping the device to prevent unwanted shocks, overwriting of important therapy history data, and audible tones.
- **Explanted devices.** Return all explanted pulse generators and leads to Guidant.

Environmental and Medical Therapy Hazards

- **Avoiding electromagnetic interference (EMI).** Advise patients to avoid sources of EMI because EMI may cause the pulse generator to deliver inappropriate therapy or inhibit appropriate therapy. Examples of EMI sources are: electrical power sources, arc welding equipment and robotic jacks, electrical smelting furnaces, large RF transmitters such as RADAR, radio transmitters including those used to control toys, electronic surveillance (anti-theft) devices, and an alternator on a car that is running.

Hospital and Medical Environments

- **Do not use internal defibrillation** paddles unless the pulse generator is disconnected from the leads because it may shunt energy causing injury to the patient, and may damage the pulse generator.
- **External defibrillation.** Use of external defibrillation can damage the pulse generator. To help prevent defibrillation damage to the pulse generator: position the defibrillation paddles as far from the pulse generator as possible, position the defibrillation paddles perpendicular to the implanted pulse generator–lead system, and set energy output of defibrillation equipment as low as clinically acceptable.

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Following any external defibrillation episode, verify pulse generator function since external defibrillation may have damaged the pulse generator. To verify proper function: interrogate the device, perform a manual capacitor re-formation, verify battery status, check the shock counters, and ensure that programmable parameters did not change.

- **Electrical interference** or “noise” from devices such as electrosurgical and monitoring equipment may interfere with establishing or maintaining telemetry for interrogating or programming the device. In the presence of such interference, move the programmer away from electrical devices and ensure that the wand cord and cables are not crossing one another.
- **Electrosurgical cautery.** Do not use electrosurgery devices until the pulse generator’s tachyarrhythmia therapy is deactivated. If active, the pulse generator may deliver an inappropriate shock to the patient. Remember to reactivate the pulse generator after turning off the electrosurgery equipment.
- **Ionizing radiation therapy may adversely affect device operation.** During ionizing radiation therapy (e.g., radioactive cobalt, linear accelerators, and betatrons), the pulse generator must be shielded with a radiation-resistive material, regardless of the distance of the device to the radiation beam. Do not project the radiation port directly at the device. After waiting a minimum of one hour following radiation treatment (to allow for a device memory check to occur), always evaluate device operation including interrogation and sensing and pacing threshold testing. At the completion of the entire course of treatments, perform device interrogation and follow-up, including sensing and pacing threshold testing and capacitor re-formation.
- **Lithotripsy may damage the pulse generator.** If lithotripsy must be used, avoid focusing near the pulse generator site.
- **Therapeutic ultrasound energy may damage the pulse generator.** If therapeutic ultrasound energy must be used, avoid focusing near the pulse generator site.
- **Radio frequency ablation.** Exercise caution when performing radio frequency ablation procedures in device patients. If the pulse generator Tachy Mode is programmed On during the procedure, the device may inappropriately declare a tachycardia episode and deliver therapy, or may cause inhibition of pacing therapy. Minimize risks by following these steps:

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- Program the Tachy Mode to Off to avoid inadvertent tachycardia detection (sensing) or therapy.
- Avoid direct contact between the ablation catheter and the implanted lead and pulse generator.
- Keep the current path (electrode tip to ground) as far away from the pulse generator and leads as possible.
- Have external defibrillation equipment available.
- Consider the use of external pacing support for pacemaker-dependent patients.

Home and Occupational Environments

- **Static magnetic fields.** Advise patients to avoid equipment or situations where they would have extended exposure to strong (>10 gauss or 1 mTesla) magnetic fields since the pulse generator mode could change. To prevent mode change in the presence of magnets, the Change Tachy Mode With Magnet feature may be programmed Off. Examples of magnetic sources are: industrial transformers and motors, magnetic resonance imaging (MRI) devices, large stereo speakers, telephone receivers if held within 0.5 inches (1.27 cm) of the pulse generator, and magnetic wands such as those used for airport security and in the game "Bingo."

Electronic Article Surveillance (EAS)

- Advise patients to avoid lingering near anti-theft devices, such as those found in entrances and exits of department stores and public libraries, and to walk through them at a normal pace, because such devices may cause inappropriate pulse generator operation.

Cellular Phones

- Advise patients to hold cellular phones to the ear opposite the side of the implanted device. Patients should not carry a cellular phone in a breast pocket or on a belt over or within 6 inches (15 cm) of the implanted devices since some cellular phones may cause the pulse generator to deliver inappropriate therapy or inhibit appropriate therapy.

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ADVERSE EVENTS

Observed Adverse Events

The CONTAK RENEWAL 3, CONTAK RENEWAL, and CONTAK CD devices provide the same cardiac resynchronization therapy (biventricular pacing) and have the same Indications for Use. Therefore, the Comparison of Medical, Pacing, and Defibrillation Therapies in Heart Failure (COMPANION) clinical trial data (based on CONTAK CD devices) used to support expanding Guidant CRT-D indications to the COMPANION patient population, are also applicable to CONTAK RENEWAL and CONTAK RENEWAL 3.

The primary difference between CONTAK CD devices and CONTAK RENEWAL/CONTAK RENEWAL 3 devices is that CONTAK CD utilizes an electrically common RV and LV sensing/pacing circuit whereas CONTAK RENEWAL and CONTAK RENEWAL 3 incorporate an independent RV and LV sensing/pacing circuit. Additional clinical analysis was conducted with CONTAK RENEWAL, in a European study, to provide confirmation that the independent sensing and pacing capability did not adversely affect the ability of the device to detect ventricular tachyarrhythmias or provide continuous biventricular pacing therapy.

The Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) Study was a prospective, open-label, randomized, controlled, multi-center, unblinded study conducted at 128 sites and enrolled a total of 1638 patients, of which 1520 were randomized. Patients were randomly assigned 1:2:2 to receive optimal pharmacological therapy (OPT, 308 patients) or a cardiac resynchronization therapy pacemaker (CRT-P, 617 patients) or a cardiac resynchronization therapy pacemaker with defibrillator (CRT-D, 595 patients). Of the 1520 patients randomized, 903 were randomized to OPT and CRT-D. This summary focuses on data and analyses for the CRT-D and OPT groups, only, with the exception of the Exercise Performance results, which are based on pooled CRT-D and CRT-P data.

A total of 498 device or procedure-related adverse events were reported in 290 out of 595 (48.7%) patients randomized to CRT-D for an average of 0.84 events per patient.

- Phrenic/diaphragmatic stimulation (58 patients, 10.7%)
- Loss of LV capture (36 patients, 6.7%)
- Pocket hematoma (31 patients, 5.7%)
- Inappropriate shock above rate cutoff due to SVT (23 patients, 4.3%)

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- Multiple counting of ventricular events (17 patients, 3.1%)
- Pocket infection (14 patients, 2.6%)
- Loss of atrial capture (14 patients, 2.2%)
- Inappropriate shock due to oversensing (11 patients, 2.0%)
- Loss of RV capture (8 patients, 1.5%)
- Pacemaker-mediated tachycardia (6 patients, 1.1%)

The following types of procedure-related adverse events with a prevalence greater than 1% were reported:

- Post surgical wound discomfort (63 patients, 10.6%)
- Coronary sinus dissection (14 patients, 2.4%)
- Pneumothorax (10 patients, 1.7%)
- Hypotension (9 patients, 1.5%)
- AV block (7 patients, 1.2%)
- Physical trauma (7 patients, 1.2%)
- Physiological reaction (6 patients, 1.0%)

Deaths

There were a total of 182 deaths (77 OPT, 105 CRT-D) that occurred during the trial and recorded through November 30, 2002. Of the 182 deaths, 134 were classified as cardiac in nature (58 OPT, 76 CRT-D). The remaining 48 deaths were classified as either vascular, non-cardiac or were unknown/unclassified.

Procedure related mortality was defined as any death that occurred within 30 days of the implant procedure and/or including events during, or as a result of, events from pre-operative anesthesia through discharge from the operating room, electrophysiology lab, or an office visit. Three (3) (0.5%) deaths in the CRT-D arm were considered to be procedure related. Since OPT patients did not undergo an implant procedure, 30 day mortality from the time of randomization was 1.0% and 1.2% for OPT and CRT-D respectively. These rates were not statistically significant between OPT and CRT-D groups ($p=0.779$).

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Potential Adverse Events

Based on the literature and implantable cardioverter defibrillator (ICD) implant experience, the following alphabetical list includes potential adverse events associated with implantation of an ICD system:

- Acceleration of arrhythmias
- Air embolism
- Allergic reaction
- Bleeding
- Cardiac tamponade
- Chronic nerve damage
- Conductor coil fracture
- Death
- Electrolyte Imbalance/Dehydration
- Elevated thresholds
- Erosion/extrusion
- Extracardiac stimulation (e.g., phrenic, diaphragm, chest wall)
- Fibrotic tissue formation (e.g., keloid formation)
- Fluid accumulation
- Formation of hematomas or cysts
- Heart block
- Inability to defibrillate or pace
- Inappropriate therapy (e.g., shocks, ATP, pacing)
- Incomplete lead connection with pulse generator
- Infection
- Lead displacement/dislodgment
- Lead fracture
- Lead insulation breakage or abrasion
- Lead tip deformation and/or breakage
- Local tissue reaction
- Muscle and nerve stimulation
- Myocardial trauma (e.g., cardiac perforation, irritability, injury)
- Myopotential sensing

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- Oversensing/undersensing
- Pacemaker-mediated tachycardia
- Pericardial rub, effusion
- Pneumothorax
- Random component failures
- Shunting current or insulating myocardium during defibrillation with internal or external paddles
- Thrombosis/thromboemboli
- Valve damage
- Venous occlusion
- Venous trauma (e.g., perforation, dissection, erosion)

Patients susceptible to frequent shocks despite antiarrhythmic medical management may develop psychologic intolerance to an implantable system that may include the following:

- Dependency
- Depression
- Fear of premature battery depletion
- Fear of shocking while conscious
- Fear that shocking capability may be lost
- Imagined shocking

In addition to the implantation of a cardiac resynchronization therapy system, potential adverse events associated with implantation of a coronary venous lead system are listed below in alphabetical order:

- Allergic reaction to contrast media
- Breakage/failure of implant tools
- Coronary venous occlusion
- Coronary venous trauma (e.g., perforation, dissection, erosion)
- Prolonged exposure to fluoroscopic radiation
- Renal failure from contrast media used to visualize coronary veins

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CLINICAL STUDIES

Clinical Study Populations

Guidant CRT-Ds have been demonstrated to be safe and effective in all-cause mortality and symptom reduction in patients who have moderate to severe heart failure (NYHA III/IV) including left ventricular dysfunction ($EF \leq 35\%$) and QRS duration ≥ 120 ms and remain symptomatic despite stable, optimal heart failure drug therapy, based on the Guidant sponsored COMPANION clinical study. (Guidant devices were the only devices studied in the COMPANION clinical trial. The trial demonstrated these devices to be safe and effective in the COMPANION population).

Guidant ICDs have been demonstrated to be safe and effective in patient populations including, but not limited to, those with:

- Prior myocardial infarction and an ejection fraction (EF) $\leq 30\%$, based on the Guidant sponsored MADIT II clinical study. (Guidant devices were the only devices studied in the MADIT II clinical trial. The trial demonstrated these devices to be safe and effective in the MADIT II population.)
- Prior myocardial infarction, left ventricular ejection fraction of $\leq 35\%$, and a documented episode of nonsustained VT, with an inducible ventricular tachyarrhythmia, based on the Guidant sponsored MADIT clinical study. (Guidant devices were the only devices studied in the MADIT clinical trial. The trial demonstrated these devices to be safe and effective in the MADIT population.)

Clinical Study Summary

The COMPANION clinical study was designed to determine whether combined all-cause mortality or all-cause hospitalization in heart failure patients receiving optimal pharmacologic therapy (OPT) can be reduced by combining OPT and 1) biventricular pacing therapy alone (CRT-P) or 2) biventricular pacing with defibrillation (CRT-D). All-cause mortality or all-cause hospitalization (time to first event) analyzed from the time of randomization, was the primary endpoint of the study.

Guidant conducted the COMPANION trial in part to demonstrate the safety and effectiveness of Guidant CRT-D and CRT-P devices in the COMPANION patient population. Trial objectives included establishing that OPT combined with biventricular pacing with defibrillation [CONTAK CD] is superior to OPT alone in

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improving exercise performance (Sub-study), reducing combined all-cause mortality or all-cause hospitalization (Primary endpoint), reducing cardiac morbidity (Secondary endpoint) and reducing all-cause mortality (Secondary endpoint).

The clinical study began January 20, 2000 and was conducted at 128 centers within the United States.

COMPANION Study Design

COMPANION was a prospective, randomized [1:2:2 to OPT, CRT-P (delivered by the CONTAK TR device), or CRT-D (delivered by the CONTAK CD device)], controlled, multi-center study. Randomization was stratified by centers and by beta-blocker use to assure proper balance between the treatment groups within each center. Each randomized patient remained counted as a member of the original randomization assignment (intention-to-treat) regardless of subsequent crossover or protocol adherence.

Endpoints

This summary focuses on the CRT-D vs. OPT contrast, providing evidence of safety and effectiveness for Guidant CRT-Ds in the COMPANION patient population. The clinical data and analyses herein address the following study endpoints for CRT-D vs. OPT only:

Primary Endpoint

The primary endpoint, a composite endpoint of all-cause mortality or all-cause hospitalization (time to first event) analyzed from the time of randomization, was designed to show a 25% reduction in the CRT-D group from an OPT annual rate of 40%. All-cause mortality was defined as death from any cause, while all-cause hospitalization was defined as admission to hospital involving a calendar date change. Also, administration of IV inotropes or vasoactive drugs for more than 4 hours was considered a hospitalization.

Secondary Endpoints

All-cause mortality: The all-cause mortality (death from any cause) endpoint was designed to show a 25% reduction in mortality in the CRT-D arm from an OPT annual mortality rate of 24%. Difference in mortality was determined by contrasting patients randomized to CRT-D in addition to OPT versus patients randomized to OPT alone using a two-tailed test for treatment versus control.

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Cardiac morbidity: To determine whether the occurrence of cardiac morbid events is reduced in patients randomized to CRT-D compared to OPT.

Sub-study Primary Endpoint and Additional tertiary endpoints

Exercise performance: The co-primary endpoint, which consists of Peak VO₂ and Six-Minute Walk, is designed to demonstrate improvement in exercise performance with CRT (CONTAK TR and CONTAK CD pooled data) compared to OPT at six months post-baseline.

Quality of Life as measured by the Minnesota Living with Heart Failure Questionnaire[®] and NYHA Class.

Safety

CRT-D system-related complication-free rate is determined by measuring complications related to any of the implanted components or their associated implant procedure in those patients who were successfully implanted with the CRT-D system.

Primary Endpoint Kaplan Meier Analysis

The 12-month event rates were 68.0% for OPT and 55.9% for CRT-D. This demonstrates an absolute reduction of 12.1% for the composite endpoint of all-cause mortality or all-cause hospitalization at one year in patients implanted with CRT-D. The log-rank test for difference in time to first event for combined all-cause mortality or all-cause hospitalization resulted in a p-value of 0.010. This demonstrates that CRT-D significantly reduces the risk of the combined endpoint of all-cause mortality or all-cause hospitalization compared to OPT alone. Additionally, the results of the proportional hazards analysis displayed a 20% relative reduction in the risk of the combined endpoint event in CRT-D compared to OPT [Hazard Ratio (HR) 0.80 (95% Confidence Interval (CI): 0.68, 0.95), p = 0.010, adjusted p = 0.011].

SECONDARY MORTALITY ENDPOINT KAPLAN MEIER ANALYSIS

The log-rank test for difference in survival resulted in a p-value of 0.003. This demonstrates that CRT-D when combined with OPT reduces the risk of all-cause mortality compared to OPT alone. Additionally, the results of the proportional hazards analysis displayed a 36% relative reduction in the risk of a mortality event in the CRT-D arm compared to OPT [Hazard Ratio (HR) 0.64, (95% Confidence Interval (CI): 0.48, 0.86), p = 0.003, adjusted p = 0.004].

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Data Analysis and Results for Secondary Cardiac Morbidity Endpoint

During the trial, 49% of the OPT patients experienced cardiac morbid events compared to 32% of CRT-D patients. This demonstrates a 35% reduction in the risk of having cardiac morbid events in patients treated with CRT-D. Adjusting for the greater average follow-up time per patient in the CRT-D group, CRT-D patients experienced 51% fewer cardiac morbid events per year of patient follow-up than OPT patients (0.49 events/year for CRT-D compared to 1.01 events/year for OPT). Additionally, CRT-D patients spent 43% fewer days in the hospital for cardiac morbid events per year compared to OPT patients. OPT patients spent 7.5 days in the hospital associated with cardiac morbid events per patient year and CRT-D patients were in hospital for 4.3 days associated with cardiac morbid events per patient year.

CRT-D System Safety

Device safety was determined by a system complication-free rate. The system-related complication-free rate was defined as the number of patients who do not experience a system-related complication divided by the total number of patients who were successfully implanted with the investigational system. A total of 81 system-related complications were reported in 68 of the 541 (12.6%) patients implanted with a CONTAK CD system yielding a 87.4% with a lower 95% confidence boundary of 85.1% system-related complication-free rate. Three system-related complications resulting in invasive intervention were reported in more than 1% of the patient population. These complications were as follows:

- Loss of left ventricular capture (25 patients)
- Loss of atrial capture (9 patients)
- Phrenic/diaphragmatic stimulation (8 patients)

Sub-study Results

Maximal Oxygen Consumption (Peak VO_2)

Peak VO_2 was determined from a standardized protocol for exercise testing as a means of measuring a patient's capacity for performing physical activity. Peak VO_2 was improved by 1.2 ml/kg/min in CRT-D patients compared to 0.6 ml/kg/min in OPT patients at 6 months. This demonstrates a between group difference of 0.6 ml/kg/min ($p=0.074$).

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Effectiveness Endpoint: Six-Minute Walk Distance

The Six-Minute Walk test is a measure of a patient's ability to sustain exercise during an activity similar to that which a patient may typically perform on a daily basis. For this test, patients are instructed to walk as far as possible in 6 minutes in a level corridor. Six-minute walk distance was improved by 41 meters in CRT-D patients compared to 17 meters in OPT patients at 6 months. This demonstrates a between group difference of 24 meters ($p=0.017$).

Ancillary Effectiveness: New York Heart Association Class (NYHA)

The determination for New York Heart Association (NYHA) Class is based on mutual assessment, by the patient and physician, of the patient's heart failure symptoms both at rest and while performing ordinary physical activity. NYHA class improved by one or more classes in 58% of the CRT-D patients compared to 46.2% of the OPT patients at 6 months ($p=0.03$).

Ancillary Effectiveness: Quality of Life (QOL)

Quality of Life (QOL) was assessed using the 21-question Minnesota Living with Heart Failure questionnaire. Each question, answered by the patient, is ranked on a scale ranging from 0 to 5. A lower total score indicates an improved quality of life. QOL was improved by -23 points in CRT-D patients compared to -10 points OPT patients at 6 months. This demonstrates a -13 point between group difference ($p<0.0001$).

Additional Functional Capacity Data

In addition to the Exercise Performance sub-study, functional capacity was evaluated by means of NYHA Class, six-minute walk distance, and Minnesota Living with Heart Failure Questionnaire[®] QOL for the all patients randomized to OPT and CRT-D through 6-months of follow up.

The NYHA Class, six-minute walk distance, and QOL scores were significantly improved in the CRT-D group compared to the OPT group at 3 and 6 months. These findings are similar to those presented in the exercise performance sub-study and previous cardiac resynchronization therapy trials.

In conclusion, the ability of the CRT-D system to effectively deliver CRT therapy has been demonstrated. The result of this success was improved exercise performance, as measured by Peak VO_2 and Six-Minute Walk distance, for those patients

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receiving optimal pharmacological therapy (OPT) with CRT as compared to patients receiving optimal pharmacological therapy alone. Additionally, New York Heart Association (NYHA) Class and Quality of Life test scores improved for those patients receiving OPT + CRT compared to the control.

CONTAK CD Study

The VENTAK[®] CHF/CONTAK CD[®]/EASYTRAK[®] Biventricular Pacing Study (hereafter referred to as the CONTAK CD Study) was a prospective, randomized, controlled, multicenter, double-blind study conducted at 47 sites in the United States and enrolled a total of 581 patients. Of these, 57 patients initially underwent a thoracotomy procedure to receive the Guidant Model 1822 VENTAK CHF AICD; 7 patients underwent a repeat procedure to receive an EASYTRAK lead. An additional 510 patients initially underwent an implant procedure to receive the Model 1823 CONTAK CD CRT-D along with the EASYTRAK (Models 4510/4511/4512/4513) coronary venous, single-electrode pace/sense lead for a total of 517 patients who underwent an EASYTRAK lead implant procedure. In 69 patients the EASYTRAK lead implant attempt was unsuccessful.

Table 1-1 provides information on all adverse events reported from implant through the randomization period in patients attempted or implanted with the EASYTRAK lead. During this period, a total of 765 events were reported in 310 patients. Of these, 155 were classified as complications, and 610 were classified as observations.

Table 1-1. Adverse Events Through the Randomization Period (Sheet 1 of 3)

(765 Events in 517 patients implanted or attempted with the EASYTRAK lead, 2559 total device months)

	# Of Events (# of pts) ^a	% Compli- cations (Patients)	Complica- tions per 100 Device Months (Events)	% Obser- vations (Patients)	Observations per 100 Device Months (Events)
Total Adverse Events	765 (310)	23.4 (121)	6.0 (155)	51.8 (268)	23.5 (610)
PG-Related Events					
Migration of device	1 (1)	0.0 (0)	0.0 (0)	0.2 (1)	0.0 (1)
Pacemaker-mediated tachycardia (PMT)	3 (3)	0.0 (0)	0.0 (0)	0.6 (3)	0.1 (3)
Telemetry difficulty	1 (1)	0.2 (1)	0.0 (1)	0.0 (0)	0.0 (0)
LV Lead-Related Events					
Loss of capture	43 (41)	5.6 (29)	1.1 (29)	2.5 (13)	0.5 (14)
Inappropriate shock due to oversensing	1 (1)	0.0 (0)	0.0 (0)	0.2 (1)	0.0 (1)
Insulation breach observed	1 (1)	0.2 (1)	0.0 (1)	0.0 (0)	0.0 (0)

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Table 1-1. Adverse Events Through the Randomization Period (Sheet 2 of 3)
(765 Events in 517 patients implanted or attempted with the EASYTRAK lead, 2559 total device months)

	# Of Events (# of pts) ^a	% Compli- cations (Patients)	Complica- tions per 100 Device Months (Events)	% Obser- vations (Patients)	Observations per 100 Device Months (Events)
Multiple counting ^b	31 (22)	1.0 (5)	0.2 (5)	3.9 (20)	1.0 (26)
Phrenic nerve/diaphragm stimulation	15 (15)	0.4 (2)	0.1 (2)	2.5 (13)	0.5 (13)
RA Lead-Related Events					
Loss of capture	6 (6)	1.0 (5)	0.2 (5)	0.2 (1)	0.0 (1)
Oversensing	3 (3)	0.0 (0)	0.0 (0)	0.6 (3)	0.1 (3)
Undersensing	1 (1)	0.2 (1)	0.0 (1)	0.0 (0)	0.0 (0)
RV Lead-Related Events					
Loss of capture	10 (9)	0.6 (3)	0.1 (3)	1.2 (6)	0.3 (7)
Elevated DFTs	6 (6)	0.4 (2)	0.1 (2)	0.8 (4)	0.2 (4)
Inappropriate shock above rate cutoff	49 (38)	0.4 (2)	0.1 (2)	7.2 (37)	1.8 (47)
Inappropriate shock due to oversensing	5 (4)	0.0 (0)	0.0 (0)	0.8 (4)	0.2 (5)
Nonconversion of VF	1 (1)	0.2 (1)	0.0 (1)	0.0 (0)	0.0 (0)
Oversensing	2 (2)	0.0 (0)	0.0 (0)	0.4 (2)	0.1 (2)
Phantom shock	2 (2)	0.0 (0)	0.0 (0)	0.4 (2)	0.1 (2)
Phrenic nerve/diaphragm stimulation	5 (5)	0.4 (2)	0.1 (2)	0.6 (3)	0.1 (3)
Subtotal Device-Related Events	186 (135)	9.5 (49)	2.1 (54)	19.0 (98)	5.1 (132)
Procedure-Related Events					
AV block	7 (7)	0.0 (0)	0.0 (0)	1.4 (7)	0.3 (7)
Coronary sinus dissection	5 (5)	0.0 (0)	0.0 (0)	1.0 (5)	0.2 (5)
Coronary venous perforation	5 (5)	0.2 (1)	0.0 (1)	0.8 (4)	0.2 (4)
Hematoma	11 (10)	0.8 (4)	0.2 (4)	1.2 (6)	0.3 (7)
Hypotension	7 (7)	0.0 (0)	0.0 (0)	1.4 (7)	0.3 (7)
Infection, post-operative wound	7 (7)	0.6 (3)	0.1 (3)	0.8 (4)	0.2 (4)
Pneumothorax	7 (7)	0.8 (4)	0.2 (4)	0.6 (3)	0.1 (3)
Post surgical wound discomfort	10 (9)	0.2 (1)	0.0 (1)	1.5 (8)	0.3 (9)
Renal failure	5 (5)	0.2 (1)	0.0 (1)	0.8 (4)	0.2 (4)
Other ^c	18 (18)	1.2 (6)	0.2 (6)	2.3 (12)	0.5 (12)
Subtotal Procedure-Related Events	79 (71)	3.9 (20)	0.7 (17)	10.0 (51)	2.2 (56)
Cardiovascular-Related Events					
AV Block	3 (3)	0.0 (0)	0.0 (0)	0.6 (3)	0.1 (3)
Arrhythmia - SVT	49 (42)	0.2 (1)	0.0 (1)	7.9 (41)	1.8 (48)
Arrhythmia - VT	20 (17)	1.0 (5)	0.2 (5)	2.7 (14)	0.6 (15)
Arrhythmia - brady	16 (14)	0.2 (1)	0.0 (1)	2.5 (13)	0.6 (15)

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Table 1-1. Adverse Events Through the Randomization Period (Sheet 3 of 3)

(765 Events in 517 patients implanted or attempted with the EASYTRAK lead, 2559 total device months)

	# Of Events (# of pts) ^a	% Compli- cations (Patients)	Complica- tions per 100 Device Months (Events)	% Obser- vations (Patients)	Observations per 100 Device Months (Events)
Cardiac arrest	2 (2)	0.4 (2)	0.1 (2)	0.0 (0)	0.0 (0)
Chest pain	30 (20)	1.0 (5)	0.2 (5)	3.1 (16)	1.0 (25)
Coagulopathy	3 (3)	0.2 (1)	0.0 (1)	0.4 (2)	0.1 (2)
Congestive heart failure	140 (91)	3.5 (18)	0.7 (18)	16.1 (83)	4.7 (122)
Distal thromboemboli	3 (2)	0.0 (0)	0.0 (0)	0.4 (2)	0.1 (3)
Dizziness	17 (17)	0.0 (0)	0.0 (0)	3.3 (17)	0.7 (17)
Dyspnea (shortness of breath)	16 (13)	0.0 (0)	0.0 (0)	2.5 (13)	0.6 (16)
Fatigue	10 (10)	0.0 (0)	0.0 (0)	1.9 (10)	0.4 (10)
Hypertension	1 (1)	0.0 (0)	0.0 (0)	0.2 (1)	0.0 (1)
Hypotension	11 (9)	0.2 (1)	0.0 (1)	1.7 (9)	0.4 (10)
Myocardial infarction	2 (2)	0.0 (0)	0.0 (0)	0.4 (2)	0.1 (2)
Pacemaker syndrome	1 (1)	0.0 (0)	0.0 (0)	0.2 (1)	0.0 (1)
Palpitations	2 (2)	0.0 (0)	0.0 (0)	0.4 (2)	0.1 (2)
Pulmonary edema	6 (6)	0.4 (2)	0.1 (2)	0.8 (4)	0.2 (4)
Shock	4 (4)	0.2 (1)	0.0 (1)	0.6 (3)	0.1 (3)
Stroke syndrome or CVA	4 (4)	0.0 (0)	0.0 (0)	0.8 (4)	0.2 (4)
Syncope	9 (9)	0.0 (0)	0.0 (0)	1.7 (9)	0.3 (9)
Thrombosis	3 (3)	0.0 (0)	0.0 (0)	0.6 (3)	0.1 (3)
Vascular related	6 (6)	1.0 (5)	0.2 (5)	0.2 (1)	0.0 (1)
Subtotal Cardiovascular-Related Events	358 (200)	7.7 (40)	1.6 (42)	35.6 (184)	12.2 (316)
Total Noncardiovascular-Related Events	142 (92)	6.2 (32)	1.5 (39)	13.5 (70)	4.0 (103)

- The total number of patients for a given event represents the unique number of patients who experienced that event. The total may not be equal to the sum of patients with complications or observations because some patients experienced more than one event that fell into both categories.
- Sensing of the two ventricular intrinsic events when only one intrinsic event is present due to intraventricular conduction delay.
- Other procedure-related events occurred in three patients or fewer: Guide wire fracture (1), Hemorrhage (3), Finishing wire left in lead (1), Nonconversion of VF (1), Perforation, arterial (1), Perforation, cardiac (1), Perforation, venous (2), Pericardial effusion (3), Pericarditis (1), Physiological reaction (1).

A total of 109 deaths occurred during the study. These deaths occurred during the study periods as shown in Table 1-2 along with the cause of death as adjudicated by an independent events committee.

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Table 1-2. Deaths that Occurred During the Study
(All patients enrolled, N = 581)

Study Period	# of pt deaths	Cause of Death				
		Cardiac: Pump Failure	Cardiac: Arrhythmic	Cardiac: Other	Non-cardiac	Unknown
After unsuccessful implant procedure	2	1	1	0	0	0
Peri-operative (< = 30 days)	10	5	2	0	2	1
Randomized therapy phase ^a : No CRT	16	9	0	1	3	3
Randomized therapy phase ^a : CRT	11	4	1	2	2	2
Post-randomized therapy phase ^b	70	28	5	1	16	20
Total	109	47	9	4	23	26

a. Day 31 to 120 for Phase I patients, day 31 to 210 for Phase II patients.

b. Day 121 and beyond for Phase I patients, day 211 and beyond for Phase II patients.

Study Design

The CONTAK CD Study was a prospective, randomized, controlled, multicenter, double-blind study conducted at 47 sites in the United States and enrolled a total of 581 patients. All patients enrolled were intended to be implanted with a device capable of delivering both CRT and treating ventricular tachyarrhythmias. Patients were randomized to CRT Off (VVI lower rate 40) or CRT On (VDD). The study began as a crossover design (called "Phase I") and enrolled 248 patients with a primary end-point of functional status with three months of follow-up. The study was later modified to a parallel design (called "Phase II") and enrolled 333 patients with a longer, six-month follow-up. The data from the first three months of the crossover phase were pooled with data obtained from the six-month parallel phase. The visit schedule and testing requirements remained the same. Additionally, while the study originally used the VENTAK CHF AICD in conjunction with epicardial leads placed via thoracotomy, the CONTAK CD CRT-D and EASYTRAK lead (placed transvenously) were added to the protocol later in the study.

Inclusion/Exclusion Criteria

Patients enrolled in the study were required to meet the following inclusion criteria:

- Meet the general indication for ICD implant
- Symptomatic heart failure despite optimal drug therapy (ACE inhibitors with diuretic and/or digoxin, as determined to be indicated and tolerated by the patient's physician-investigator)
- Left ventricular ejection fraction \leq 35%

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- QRS duration \geq 120 ms
- Age \geq 18 years
- Normal sinus node function

Patients were excluded from the investigation if they met any of the following criteria:

- Meet the general indications for permanent antibradycardia pacing, including pacemaker dependence
- Have chronic, medically refractory atrial tachyarrhythmias
- Require concomitant cardiac surgery
- Are unable to undergo device implant, including general anesthesia if required
- Are unable to comply with the protocol and follow-up requirements, including exercise testing
- Have a life expectancy of less than six months due to other medical conditions
- Have amyloid disease (amyloidosis)
- Have hypertrophic obstructive cardiomyopathy
- Require in-hospital continuous intravenous inotropes
- Have pre-existing cardioversion/defibrillation leads other than those specified in this investigational plan (unless the investigator intends to replace them with permitted cardioversion/defibrillation leads)
- Women who are pregnant or not using medically accepted birth control
- Have a mechanical tricuspid prosthesis
- Involved in other cardiovascular clinical investigations of active therapy or treatment

Follow-up Schedule

Pre-implant visit	Initial assessment of patient eligibility; taking of patient history.
Implant	Implant of investigational devices and acute device testing. Randomization status (CRT or No CRT) was assigned for implementation after a 30-day Recovery Period.
Recovery Period	Minimum 30-day period over which the patient recovered from the implant procedure and had his/her heart failure medications adjusted, but with no CRT, regardless of the randomization assignment.

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Post-Recovery Visit	First visit after the Recovery Period in which patients underwent Special Testing ^a to establish their baseline condition, after which the randomization assignment was implemented (CRT or No CRT).
Three- and six-month visit	Evaluation of randomized therapy with Special Testing ^a and device function at three- and six-months after the Post-Recovery Visit.
Quarterly Visits	After the six-month visit, patients were seen for routine evaluation of device function and patient condition.

- a. Special Testing included a Symptom-Limited Treadmill Test with measurement of oxygen uptake (Peak VO₂), a Six-Minute Walk, Echocardiography, Holter monitoring, blood chemistry testing, and a Quality of Life (QOL) questionnaire.

Patient Groups

The CONTAK CD Study included patients with symptomatic heart failure despite optimal drug therapy as defined in the inclusion criteria. The population included patients who were NYHA Class II, III, or IV at the time of implant.

Based upon the clinical results from the covariate analyses in this study and the internal consistency of these clinical findings with those from other completed CRT studies, the patient subgroup with NYHA Class III/IV heart failure in this study was examined further.

- **All Patients:** All patients (NYHA Class II/III/IV at the time of implant) implanted with an investigational system (N = 501). Ten patients died and one withdrew before the post-recovery visit. Therefore, therapy effectiveness analyses used N = 490.
- **NYHA Class III/IV (Advanced Heart Failure):** This subgroup was defined as those patients with moderate to severe heart failure at the time of the Post-Recovery Visit (N = 227). A percentage of patients either had an improvement or worsening of their NYHA Class during the post-implant recovery period. The patients in the Advanced Heart Failure subgroup were only those who remained in NYHA Class III/IV at the end of the post-recovery period. This subgroup was determined from interaction analysis of preselected covariates with the functional status endpoints.

Endpoints

The CONTAK CD Study had three investigational elements consisting of:

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CRT Effectiveness:

Primary: Composite endpoint consisting of all-cause mortality, hospitalization for heart failure, and ventricular tachyarrhythmia requiring device intervention.

Secondary: Peak VO_2 derived from a symptom-limited exercise test and Quality of Life as measured by the Minnesota Living with Heart Failure Questionnaire[®].

Additional: Six-Minute Walk, NYHA Class, Echocardiographic Analysis, Change in Norepinephrine, and Change in Heart Rate.

Lead and System Effectiveness:

Lead: Left ventricular pacing thresholds, biventricular sensing, biventricular lead impedance, and lead placement success rate.

System: VF detection time and biventricular antitachycardia pacing (ATP) efficacy.

Lead and System Safety:

Lead: Incidence of lead-related adverse events.

System: Incidence of severe, device-related adverse events and operative mortality.

Study Results

Patient Accountability

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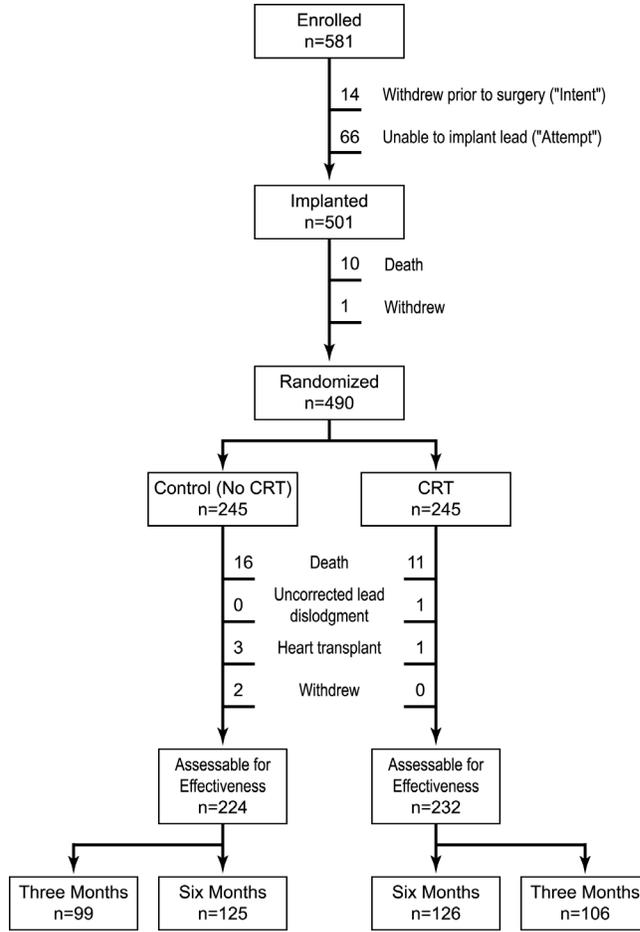


Figure 1-1. Enrollment and follow-up of randomized patients.

Baseline Characteristics

Table 1-3. Pre-Implant Assessment
(All Patients Implanted, N=501)

Characteristic		All Patients			NYHA Class III/IV		
		CRT (N = 248)	No CRT (N = 253)	P-val ^a	CRT (N = 117)	No CRT (N = 110)	P-val ^a
Age at Implant (years)	N	248	253		117	110	
	Mean +/- SD	66.0 +/- 10.5	66.3 +/- 10.5	0.73	66.1 +/- 10.5	65.8 +/- 10.5	0.80
	Range	26.1 - 82.6	29.5 - 86.3		26.1 - 82.5	38.3 - 85.3	
Gender [N (%)]	Male	210 (84.7)	211 (83.4)	0.70	90 (76.9)	86 (78.2)	0.82
	Female	38 (15.3)	42 (16.6)		27 (23.1)	24 (21.8)	
NYHA Class [N (%)]	II	80 (32.3)	83 (32.8)	0.66	20 (17.1)	11 (10.0)	0.08
	III	148 (59.7)	144 (56.9)		85 (72.6)	78 (70.9)	
	IV	20 (8.1)	26 (10.3)		12 (10.3)	21 (19.1)	
Concomitant Medications [N (%)]	ACE or ARB	212 (85.5)	224 (88.5)	0.31	95 (81.2)	98 (89.1)	0.10
	Beta Blocker	119 (48.0)	117 (46.2)	0.70	53 (45.3)	44 (40.0)	0.42
	Digoxin	172 (69.4)	171 (67.6)	0.67	84 (71.8)	75 (68.2)	0.55
	Diuretic	217 (87.5)	210 (83.0)	0.16	108 (92.3)	95 (86.4)	0.15
Qualifying LVEF (%)	N	248	253		117	110	
	Mean +/- SD	21.4 +/- 6.6	21.5 +/- 6.7	0.74	20.6 +/- 6.4	21.1 +/- 6.2	0.61
	Range	5.0 - 35.0	10.0 - 35.0		8.0 - 35.0	10.0 - 35.0	
PR Interval ^b (ms)	N	224	222		107	91	
	Mean +/- SD	205 +/- 42	202 +/- 49	0.44	204 +/- 41	200 +/- 54	0.60
	Range	88 - 336	104 - 400		136 - 336	110 - 400	
Qualifying QRS Duration ^b (ms)	N	226	224		109	93	
	Mean +/- SD	160 +/- 27	156 +/- 26	0.06	164 +/- 27	152 +/- 24	< 0.01
	Range	120 - 240	120 - 264		120 - 240	120 - 222	
Resting Heart Rate (bpm)	N	248	253		117	110	
	Mean +/- SD	73 +/- 12	75 +/- 14	0.37	75 +/- 13	74 +/- 15	0.61
	Range	43 - 108	48 - 120		43 - 108	50 - 120	
Systolic Blood Pressure (mmHg)	N	247	253		116	110	
	Mean +/- SD	118 +/- 21	118 +/- 21	0.95	116 +/- 20	117 +/- 23	0.72
	Range	79 - 197	70 - 190		79 - 191	74 - 190	
Diastolic Blood Pressure (mmHg)	N	247	253		116	110	
	Mean +/- SD	67 +/- 12	69 +/- 12	0.27	68 +/- 12	67 +/- 14	0.85
	Range	31 - 100	40 - 109		31 - 100	40 - 109	

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- a. P-values for comparing means were calculated with Student's t-test; p-values for comparing proportions were calculated with Pearson's chi-squared test.
- b. PR interval and QRS duration were not obtained for thoracotomy patients.

Table 1-4. Pre-Implant History
(All Patients Implanted, N = 501)

Characteristic		All Patients			NYHA Class III/IV		
		CRT (N = 248)	No CRT (N = 253)	P-val ^a	CRT (N = 117)	No CRT (N = 110)	P-val ^a
Primary Tachyarrhythmia [N (%)]	Monomorphic VT (MVT)	148 (59.7)	136 (53.8)	0.44	72 (61.5)	48 (43.6)	0.03
	Polymorphic VT (PVT)	16 (6.5)	20 (7.9)		7 (6.0)	7 (6.4)	
	Nonsustained VT	58 (23.4)	63 (24.9)		30 (25.6)	35 (31.8)	
	Ventricular Fibrillation (VF)	26 (10.5)	32 (12.6)		8 (6.8)	18 (16.4)	
	Other	0 (0.0)	2 (0.8)		0 (0.0)	2 (1.8)	
Other Arrhythmias [N (%)]	Paroxysmal Atrial Fibrillation	43 (17.3)	62 (24.5)	0.05	21 (17.9)	29 (26.4)	0.13
	Atrial Flutter	10 (4.0)	13 (5.1)	0.55	3 (2.6)	7 (6.4)	0.16
Arrhythmia/Conduction Disorder [N (%)]	LBBB	133 (53.6)	138 (54.5)	0.83	59 (50.4)	59 (53.6)	0.55
	RBBB	35 (14.1)	31 (12.3)		21 (17.9)	14 (12.7)	
	Non-Specific	80 (32.3)	84 (33.2)		37 (31.6)	37 (33.6)	
Etiology [N (%)]	Ischemic	167 (67.3)	178 (70.4)	0.47	76 (65.0)	78 (70.9)	0.34
	Non-Ischemic	81 (32.7)	75 (29.6)		41 (35.0)	32 (29.1)	

- a. P-values were calculated with Pearson's chi-squared test.

CRT Effectiveness

Heart Failure Progression (Composite Index)

The Composite Index (primary endpoint) was a combination of three events: all-cause mortality, hospitalization for heart failure, and VT/VF event requiring therapy (Table 1-5). A committee consisting of three heart failure specialists and an electrophysiologist reviewed and adjudicated all patient deaths and all hospitalizations, defined as an admission greater than 23 hours. Outpatient care, emergency room care, and clinic visits less than 23 hours were collected but not considered to be hospitalizations for the purposes of analysis.

Table 1-5. Composite Index
(All patients implanted and active 31 days post-implant)

Group	Heart Failure Mortality or Morbidity Event	CRT		No CRT		Relative Reduction with CRT
		N	%	N	%	
All Patients (N = 490)	Death from any cause	11	4.5	16	6.5	15% p = 0.35
	HF hospitalization	32	13.1	39	15.9	
	VT/VF	36	14.7	39	15.9	
NYHA Class III/IV (N = 227)	Death from any cause	11	9.4	11	10.0	22% p = 0.23
	HF hospitalization	23	19.7	27	24.5	
	VT/VF	21	17.9	22	20.0	

Twenty-seven patients died during the therapy phase. Mortality stratified by treatment group and cause, as adjudicated by the Events Committee, is shown in Table 1-6. The Kaplan-Meier curve, showing total survival by treatment group, is shown in Figure 1-2.

Table 1-6. Mortality Stratified by Treatment Group and Cause
(All patients implanted and active at 31 days post-implant, N = 490)

Deaths	Patients with CRT (N = 245)	Patients with No CRT (N = 245)
Cardiac, pump failure	4 (1.6%)	9 (3.7%)
Cardiac, arrhythmic	1 (0.4%)	0 (0.0%)
Cardiac, other	2 (0.8%)	1 (0.4%)
Noncardiac	2 (0.8%)	3 (1.2%)
Unknown	2 (0.8%)	3 (1.2%)
Total	11 (4.5%)	16 (6.5%)

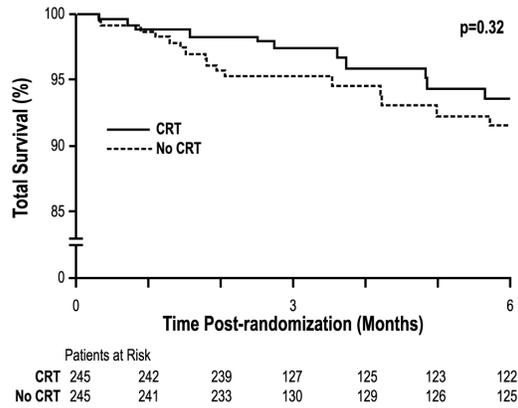


Figure 1-2. Kaplan-Meier curve.

Table 1-7 presents the reasons for hospitalization within the treatment period as determined by the Events Committee.

Table 1-7. Patients Hospitalized during Treatment Period^a
(All patients implanted and active at 31 days post-implant, N = 490)

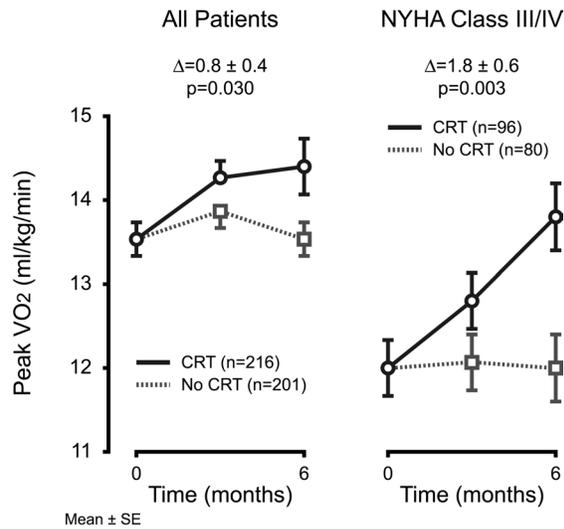
Reason for Hospitalization	All Patients			NYHA Class III/IV		
	CRT (N = 245)	No CRT (N = 245)	Total (N = 490)	CRT (N = 117)	No CRT (N = 110)	Total (N = 227)
Heart failure	32	39	71	23	27	50
Cardiac, other	20	25	45	14	14	28
Noncardiac	26	19	45	14	14	28
Total Hospitalizations	66	70	136	40	46	86

a. Represents number of patients with each category of hospitalization. Patients may have multiple hospitalizations that fall into different categories.

Peak VO₂

The Peak VO₂ was determined from a standardized protocol for exercise testing as a means of measuring a patient's capacity for performing physical activity. Figure 1-3 and the accompanying table provide the change in Peak VO₂.

A)



B)

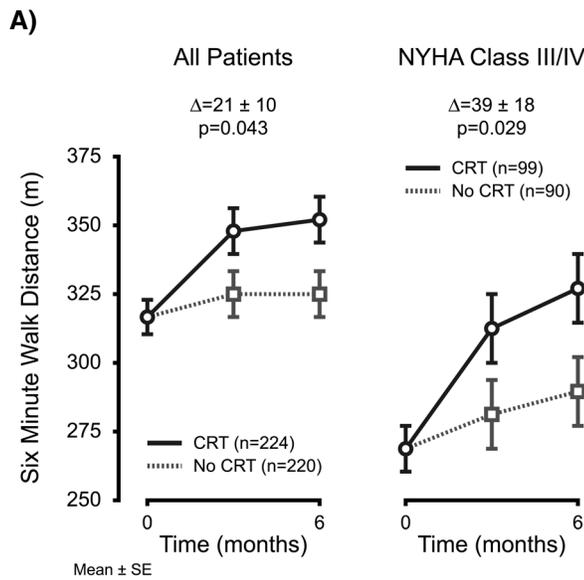
Peak VO ₂ (ml/kg/min)	All Patients			NYHA Class III/IV		
	CRT (N = 216)	No CRT (N = 201)	P-val ^a	CRT (N = 96)	No CRT (N = 80)	P-val ^a
Post-recovery Visit	13.5 +/- 0.2	13.5 +/- 0.2	-	12.0 +/- 0.3	12.0 +/- 0.3	-
3 Months	14.3 +/- 0.2	13.9 +/- 0.2	0.206	12.8 +/- 0.4	12.1 +/- 0.4	0.084
6 Months	14.4 +/- 0.3	13.6 +/- 0.3	0.030	13.8 +/- 0.5	12.0 +/- 0.5	0.003

a. P-values reflect the between-group differences with respect to baseline.

Figure 1-3. Change in Peak VO₂ (A). Change in Peak VO₂ table (B).

Six-Minute Walk

The Six-Minute Walk test is a measure of a patient's ability to sustain exercise during an activity similar to that which a patient may typically perform on a daily basis. For this test, patients are instructed to walk as far as possible in 6 minutes in a level corridor. Figure 1-4 and the accompanying table provide the change in Six-Minute Walk.



B)

Six Minute Walk Distance (meters)	All Patients			NYHA Class III/IV		
	CRT (N = 224)	No CRT (N = 220)	P-val ^a	CRT (N = 99)	No CRT (N = 90)	P-val ^a
Post-recovery Visit	317 +/- 5	317 +/- 5	-	268 +/- 9	268 +/- 9	-
3 Months	348 +/- 7	331 +/- 8	0.058	312 +/- 12	280 +/- 12	0.028
6 Months	353 +/- 8	332 +/- 8	0.043	327 +/- 14	288 +/- 15	0.029

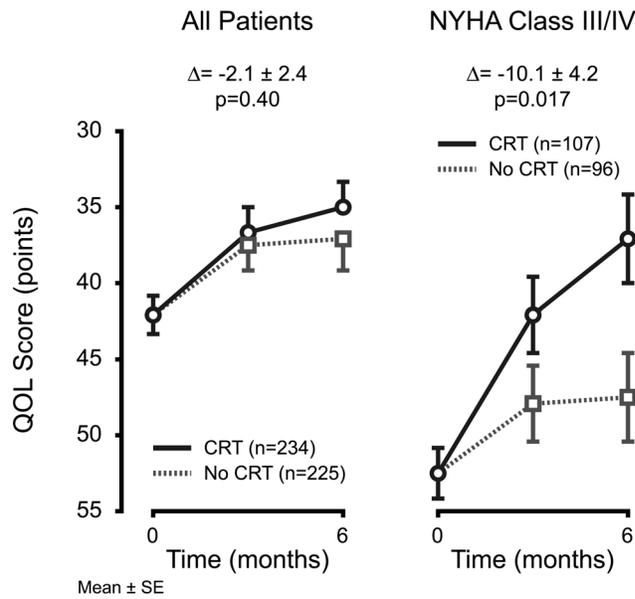
a. P-values reflect the between-group differences with respect to baseline.

Figure 1-4. Change in Six-Minute Walk (A). Change in Six-Minute Walk table (B).

Quality of Life

Quality of Life (QOL) was assessed using the 21-question Minnesota Living with Heart Failure questionnaire. Each question is answered by the patient, ranking each item on a scale ranging from 0 to 5. A lower total score indicates an improved quality of life. Figure 1-5 and the accompanying table provide the change in Quality of Life.

A)



B)

QOL (points)	All Patients			NYHA Class III/IV		
	CRT (N = 234)	No CRT (N = 225)	P-val ^a	CRT (N = 107)	No CRT (N = 96)	P-val ^a
Post-recovery Visit	41.8 +/- 1.1	41.8 +/- 1.1	-	52.7 +/- 1.5	52.7 +/- 1.5	-
3 Months	36.6 +/- 1.5	37.3 +/- 1.6	0.711	41.9 +/- 2.4	47.5 +/- 2.6	0.078
6 Months	34.8 +/- 1.8	36.9 +/- 1.8	0.395	37.2 +/- 3.1	47.3 +/- 3.2	0.017

a. P-values reflect the between-group differences with respect to baseline.

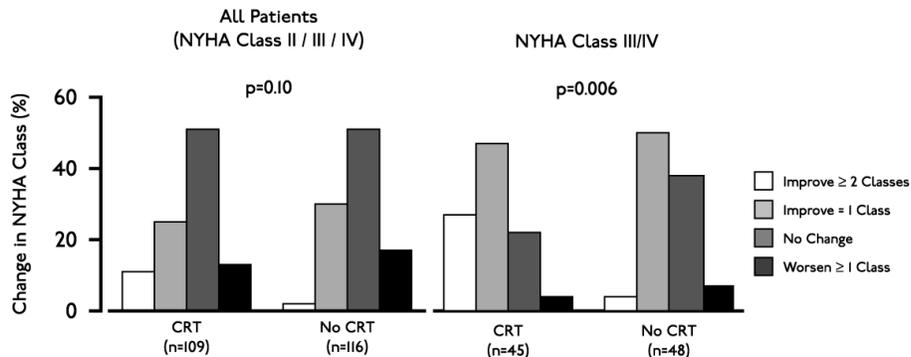
Figure 1-5. Change in Quality of Life (A). Change in Quality of Life table (B).

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NYHA Class

The determination of New York Heart Association (NYHA) Class is based on mutual assessment by the patient and the patient's physician of the patient's heart failure symptoms both at rest and while performing ordinary physical activity. NYHA Class was determined at each follow-up visit by a physician who was blinded to the patient's randomized therapy. Figure 1-6 and the accompanying table provide the change in NYHA Class results.

A)



B)

Change in NYHA Class	All Patients					NYHA Class III/IV				
	CRT (N = 109)		No CRT (N = 116)		P-val ^a	CRT (N = 45)		No CRT (N = 48)		P-val ^a
	N	%	N	%		N	%	N	%	
Improve 2 or More Classes	12	11.0	2	1.7	0.10	12	26.7	2	4.2	0.006
Improve 1 Class	27	24.8	35	30.2		21	46.7	24	50.0	
No Change	56	51.4	59	50.9		10	22.2	18	37.5	
Worsen 1 Class	13	11.9	19	16.4		2	4.4	4	8.3	
Worsen 2 or More Classes	1	0.9	1	0.9		0	0.0	0	0.0	

a. P-value was calculated from Mantel-Haenszel test and reflects the between-group differences with respect to baseline.

Figure 1-6. Change in NYHA Class (A). Change in NYHA Class table (B).

Echocardiography

Several echocardiography (echo) variables were identified to assist in measuring the possible hemodynamic impact of CRT as shown in Table 1-8. The limitation of this data is that patients are measured while at rest, and therefore, the data may not reflect any hemodynamic benefit that may be observed when patients are exercising and performing their daily activities.

Table 1-8. Echocardiography Results

Parameter	Timepoint	CRT		No CRT		Between Groups	
		N	Mean +/- SE	N	Mean +/- SE	Mean +/- SE	P-val
All Patients							
LVIDd (mm)	Post-recovery Visit	228	70.4 +/- 0.5	219	70.4 +/- 0.5	0	-
	Change at 6 Months	228	-3.4 +/- 0.6	219	-0.3 +/- 0.6	-3.1 +/- 0.9	< 0.001
LVIDs (mm)	Post-recovery Visit	228	58.3 +/- 0.5	219	58.3 +/- 0.5	0	-
	Change at 6 Months	228	-4.0 +/- 0.7	219	-0.7 +/- 0.7	-3.3 +/- 0.9	< 0.001
LVEF (%)	Post-recovery Visit	222	27.8 +/- 0.3	216	27.8 +/- 0.3	0	-
	Change at 6 Month	222	5.1 +/- 0.7	216	2.8 +/- 0.7	2.4 +/- 1.0	0.020
NYHA Class III/IV							
LVIDd (mm)	Post-recovery Visit	104	71.2 +/- 0.7	92	71.2 +/- 0.7	0	-
	Change at 6 Months	104	-4.9 +/- 1.0	92	-0.2 +/- 1.1	-4.7 +/- 1.5	0.001
LVIDs (mm)	Post-recovery Visit	104	59.2 +/- 0.7	92	59.2 +/- 0.7	0	-
	Change at 6 Months	104	-5.4 +/- 1.1	92	-0.6 +/- 1.1	-4.8 +/- 1.5	0.002
LVEF (%)	Post-recovery Visit	99	26.9 +/- 0.5	91	26.9 +/- 0.5	0	-
	Change at 6 Months	99	6.0 +/- 1.1	91	2.3 +/- 1.2	3.7 +/- 1.7	0.029

Measures of Sympathetic Tone

Mean Norepinephrine levels (Table 1-9) and Mean Heart Rate (Table 1-10) were examined as markers of how CRT may influence the excessive sympathetic drive associated with chronic heart failure.

Table 1-9. Mean Norepinephrine Results

Norepinephrine (pg/mL)	All Patients			NYHA Class III/IV		
	CRT (N = 228)	No CRT (N = 217)	P-val	CRT (N = 104)	No CRT (N = 90)	P-val
Post-recovery Visit	663 +/- 19	663 +/- 19	-	720 +/- 31	720 +/- 31	-
3 Months	651 +/- 31	681 +/- 32	0.479	685 +/- 55	743 +/- 60	0.463
6 Months	658 +/- 40	738 +/- 41	0.143	681 +/- 75	827 +/- 79	0.163

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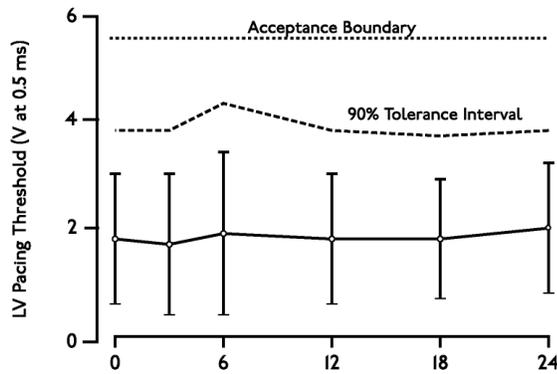
Table 1-10. Mean Heart Rate Results

Heart Rate (bpm)	All Patients			NYHA Class III/IV		
	CRT (N = 240)	No CRT (N = 233)	P-val	CRT (N = 113)	No CRT (N = 101)	P-val
Post-recovery Visit	72.3 +/- 0.6	72.3 +/- 0.6	-	74.5 +/- 1.0	74.5 +/- 1.0	-
3 Months	70.8 +/- 0.8	72.1 +/- 0.8	0.20	74.1 +/- 1.2	73.9 +/- 1.3	0.94
6 Months	69.4 +/- 1.0	70.2 +/- 1.0	0.58	70.6 +/- 1.6	72.5 +/- 1.6	0.40

EASYTRAK Lead and System Effectiveness

A)

All patients implanted with an EASYTRAK lead at first implant, N = 443



B)

Statistic ^a	Implant	3 Months	6 Months	12 Months	18 Months	24 Months
N	435	347	330	233	103	25
Mean +/- SD	1.8 +/- 1.2	1.7 +/- 1.3	1.9 +/- 1.5	1.8 +/- 1.2	1.8 +/- 1.1	2.0 +/- 1.2
Range	0.2 - 7.5	0.2 - 7.5	0.2 - 7.5	0.4 - 7.5	0.6 - 7.5	0.6 - 5.0
Upper Tolerance Limit	3.8	3.8	4.3	3.8	3.7	3.9

a. EASYTRAK lead models: 4511, 4512, and 4513.

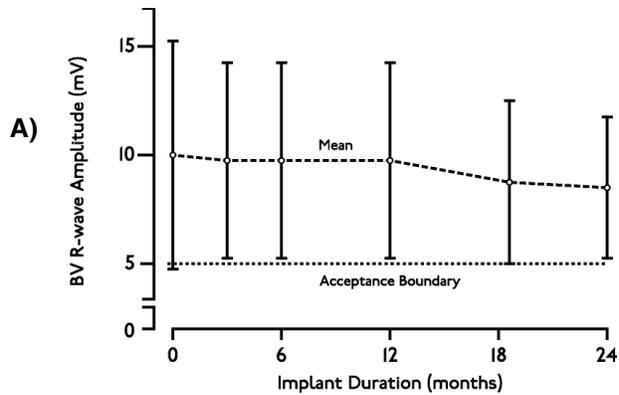
Figure 1-7. EASYTRAK lead threshold measurements (A). EASYTRAK lead threshold measurements table (B).

It was hypothesized that the upper tolerance limit of the chronic left ventricular pacing threshold of the EASYTRAK lead be less than 5.5 V to ensure that an adequate

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safety margin exists. Chronic left ventricular pacing thresholds shown in Figure 1-7 are well within this limit.

All patients implanted with an EASYTRAK lead at first implant, N = 443



B)

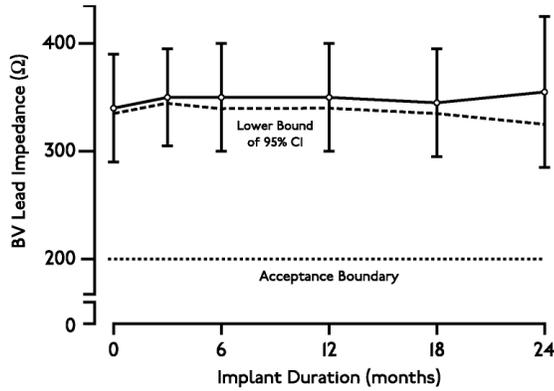
Statistic	Implant	3 Months	6 Months	12 Months	18 Months	24 Months
N	433	346	326	220	99	23
Mean +/- SD	10.0 +/- 5.2	9.9 +/- 4.4	9.9 +/- 4.5	9.8 +/- 4.4	8.9 +/- 3.5	8.5 +/- 3.3
Range	1.9 - 25.0	1.4 - 25.0	1.7 - 25.0	1.2 - 25.0	2.6 - 20.4	2.2 - 13.6

Figure 1-8. EASYTRAK biventricular-sensed R-wave amplitude (A). EASYTRAK biventricular-sensed R-wave amplitude table (B).

Mean chronic biventricular R-wave amplitudes are measured as a combination of the R-waves from both the right ventricle (commercially available ENDOTAK lead) and left ventricle (EASYTRAK lead). It was hypothesized that the mean biventricular R-wave amplitude be greater than 5 mV to ensure proper sensing. In Figure 1-8, the performance of the EASYTRAK lead system was significantly above this value ($p < 0.01$).

A)

All patients implanted with an EASYTRAK lead at first implant, N = 443



B)

Statistic	Implant	3 Months	6 Months	12 Months	18 Months	24 Months
N	436	355	336	237	107	26
Mean +/- SD	340 +/- 46	352 +/- 47	349 +/- 50	351 +/- 51	347 +/- 46	356 +/- 67
Range	243 - 550	248 - 519	186 - 534	237 - 513	254 - 507	267 - 520
95% CI	(336, 344)	(347, 357)	(344, 355)	(345, 358)	(338, 356)	(329, 383)

Figure 1-9. EASYTRAK biventricular pacing impedance (A). EASYTRAK biventricular pacing impedance table (B).

The impedance measured by the CONTAK CD device is the parallel combination of the left ventricular (EASYTRAK) and right ventricular (ENDOTAK) leads simultaneously. Therefore, the biventricular lead impedance will be substantially less than that of either lead alone. It was hypothesized that the lower limit of the 95% confidence interval of the mean chronic biventricular lead impedance would be greater than 200 Ω to ensure proper pulse generator function. The lower limit of the 95% confidence interval of the chronic biventricular lead impedance exceeds this value (Figure 1-9).

EASYTRAK Lead Placement Success Rate

The EASYTRAK lead was implanted in 448/517 (87%) of patients who underwent the implant procedure. Table 1-11 shows the reasons for inability to place the EASYTRAK lead. Table 1-12 provides the EASYTRAK lead implant success rate.

Table 1-11. Reasons for Unsuccessful EASYTRAK Lead Implant
(Patients with unsuccessful attempt to implant EASYTRAK lead, N = 69)

Reason	# of pts	%
Inability to locate or cannulate the coronary sinus	29	42
Dislodgment of EASYTRAK lead while removing guide catheter	13	18.8
Inability to advance the lead to a stable position	11	15.9
Inability to obtain adequate pacing thresholds	6	8.7
Procedure stopped due to coronary sinus dissection or perforation	5	7.2
Procedure stopped due to transient AV block	1	1.4
Procedure stopped due to venous perforation during subclavian stick	1	1.4
Reason not stated	1	1.4
Extracardiac stimulation	1	1.4
Inability to place an atrial pace/sense lead	1	1.4
Total	69	100

Table 1-12. Lead Placement Success Rate
(All patients implanted or attempted with EASYTRAK lead, N = 517)

Measurement	All Procedures
Number of patients implanted or attempted	517
Number of placements ^a of the EASYTRAK Lead	448
Rate	87%
95% CI	(84%, 90%)

a. Defined as an EASYTRAK implant procedure that is concluded with the implant of the investigational cardiac resynchronization system.

Although some situations such as patient anatomy and poor thresholds cannot be avoided, increased investigator experience with the EASYTRAK lead and accessories was associated with improved success, decreased total procedure time (measured skin-to-skin), and decreased fluoroscopy exposure time (Figure 1-10).



Figure 1-10. EASYTRAK success rate, procedure time, and fluoroscopy exposure time.

Biventricular Antitachycardia Pacing (ATP) Conversion Efficacy Performance

The conversion rate of induced monomorphic ventricular tachycardia (MVT) was 64% and that of spontaneous MVT was 88%.

Ventricular Tachyarrhythmia Detection Time

The VENTAK CHF and CONTAK CD devices sense events from both ventricles simultaneously. Ventricular tachyarrhythmia detection time was analyzed to determine if the additional lead had an adverse effect on sensing VT/VF. Guidant's ICDs typically have a detection time of two seconds. The VF detection time of 2.1 ± 0.6 seconds was statistically significantly lower than 6 seconds³ ($p < 0.01$), demonstrating that there was no statistically significant prolongation of induced VF detection times with the additional left ventricular lead. There were also no adverse events reported in which a VENTAK CHF or CONTAK CD failed to detect a spontaneous ventricular tachyarrhythmia.

3. Detection time at implant with legally marketed Guidant ICD devices is typically two seconds, and investigators have stated that an additional delay of 3 to 5 seconds would be a clinically significant event. The expected detection time is 2 seconds (95% CI: [0, 6 sec]).

EASYTRAK Lead and System Safety

EASYTRAK Lead Safety

Safety was established using the rate of adverse events that are either related to the EASYTRAK lead or to the implant procedure necessary to place the EASYTRAK lead.

An EASYTRAK lead implant procedure was performed in 517 patients with 448 patients (86.7%) being successfully implanted with the EASYTRAK lead.⁴ The upper boundary of the 95% confidence interval was hypothesized to be less than 23% at six months (Table 1-13).

Table 1-13. Lead-Related Adverse Events at Six Months

Patient Population	N	Event Rate (%)	95% CI
All Patients	517	12.2	(9.4, 15.0)
NYHA Class III/IV	201	17.4	(12.7, 22.7)

Fifty-three lead-related adverse events were reported during the clinical investigation of the EASYTRAK lead among the 448 patients who were implanted with an EASYTRAK lead. Twenty-seven procedure-related adverse events were reported among the 517 patients who underwent the implant procedure for an EASYTRAK lead. The overall lead-related adverse event rate was 14.5% (95% CI [11.5–17.5%]). Table 1-14 reports lead-related adverse events observed during the CONTAK CD Study.

Table 1-14. EASYTRAK Lead-Related Adverse Events Throughout the Study

(All patients implanted, N=448; All patients attempted, N=517)

Adverse Events	Total	% of pts (95% CI)
Lead-Related, N = 448		
Loss of capture/lead dislodgment	31 ^a	6.9 (4.6–9.3)
Ventricular oversensing	11	2.5 (1.0–3.9)
Extracardiac stimulation	9	2.0 (0.7–3.3)
Insulation breach	2	0.4 (0.0–1.1)
Procedure-Related, N = 517		
Transient AV block	6	1.2 (0.2–2.1)
Coronary venous dissection	5	1.0 (0.1–1.8)

4. For purposes of defining event rates, a denominator of 448 will be used for those adverse events that pertain to chronically implanted EASYTRAK leads, and a denominator of 517 will be used for those adverse events that pertain to the implant procedure of the EASYTRAK lead.

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Table 1-14. EASYTRAK Lead-Related Adverse Events Throughout the Study
(All patients implanted, N=448; All patients attempted, N=517)

Adverse Events	Total	% of pts (95% CI)
Coronary venous perforation	5	1.0 (0.1–1.8)
Transient renal failure	5	1.0 (0.1–1.8)
Pericardial effusion	2	0.4 (0.0–0.9)
Finishing wire left in lead	1	0.2 (0.0–0.6)
Right ventricular lead dislodgment	1	0.2 (0.0–0.6)
Guide wire fracture	1	0.2 (0.0–0.6)
Hypotension due to blood loss	1	0.2 (0.0–0.6)
Total (unique patients)	75	14.5 (11.5–17.5)

a. Twenty-six events were successfully corrected in a repeat procedure

The most common of the 53 lead-related adverse events (>1% incidence) included loss of left ventricular capture (31 patients, 6.9%), ventricular oversensing (11 patients, 2.5%), and extracardiac stimulation (9 patients, 2.0%). These events were typically resolved with surgical intervention.

The most common of the 27 procedure-related adverse events (> 1% incidence) included coronary venous trauma (10 patients, 2.0%), transient atrioventricular block (6 patients, 1.2%), and transient renal failure (5 patients, 1.0%). These events were typically resolved without intervention and no permanent long-term sequelae were reported.

Severe, Device-Related Adverse Events and Operative Mortality

Table 1-15. Adverse Events and Operative Mortality
(All patients attempted or implanted, N = 567)

Measurement	N	%	95% CI
Severe, Device-Related Adverse Events (Type I) ^a	7	1.2	(0.3, 2.1)
All-Cause Operative Mortality (< = 30 Days Post Implant)	12	2.1	(0.9, 3.3)

a. Percent is of patients with at least one event.

The incidence of severe, device-related events was reported in 7 of 567 patients (1.2%); this was significantly less than the hypothesized rate of 20% (p < 0.01) (Table 1-15). Table 1-16 reports system, device-related, severe adverse events observed during the CONTAK CD Study.

Table 1-16. System, Device-Related, Severe Adverse Events
(All patients attempted or implanted, N = 567)

Adverse Event	# of pts	% of pts (95% CI)
Telemetry difficulty; device explanted	2	0.4 (0.0–0.9)
Ventricular tachycardia during CPX testing	1	0.2 (0.0–0.5)
Coronary sinus perforation	1	0.2 (0.0–0.5)
Inappropriate shock due to oversensing	1	0.2 (0.0–0.5)
Lead dislodgment	1	0.2 (0.0–0.5)
Anaphylaxis in association with use of a pulmonary artery catheter	1	0.2 (0.0–0.5)

Operative mortality, defined as death from any cause within 30 days of implant, was reported in 12 of 567 patients (2.1%) undergoing the implant procedure. The outcome is significantly less than the hypothesized rate of 9% ($p < 0.01$). Table 1-17 reports the cause of death for operative mortality.

Table 1-17. Cause of Death for Operative Mortality
(All patients attempted or implanted, N = 567)

Cause of Death	Implants N = 501	Attempts N = 66	Total N = 567
Cardiac: pump failure	5	1	6
Cardiac: arrhythmic	2	1	3
Noncardiac	2	0	2
Unknown	1	0	1
Total	10	2	12

System Safety Profile

Analysis of system safety was performed on the complication-free rate of device-related adverse events, regardless of whether or not they were related to the investigational device (Figure 1-11). Table 1-18 outlines the device related complications. This study used an acceptance criterion such that the lower boundary of the 95% confidence interval could not be less than 70%.

Table 1-18. Device-Related Complications^a
(All patients implanted, N = 448; All patients attempted, N = 517)

Complication	# of pts	% of pts
All patients implanted (N = 448)		
Loss of LV capture	31	6.9
Loss of right atrial capture	7	1.6
Ventricular oversensing	6	1.3
Extracardiac stimulation	5	1.1
All patients attempted or implanted (N = 517)		
Infections	7	1.4

a. This table represents patients attempted or implanted with the EASYTRAK lead; most common (> 1%) device-related complications reported.

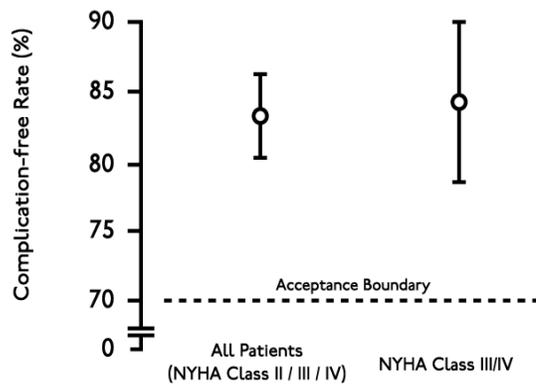


Figure 1-11. System safety.

System safety for the All Patients group and NYHA Class III/IV subgroup as determined by the device-related complication-free rate was within the 70% acceptance boundary for safety.

Verification of CRT Delivery

The delivery of biventricular pacing throughout the CONTAK CD Study was confirmed by comparing the programmed device output to the biventricular pacing threshold and demonstrating that capture was maintained in daily activities and during exercise.

The investigational plan recommended programming the device output to at least twice the biventricular pacing voltage threshold. Electrocardiograms (ECGs) from Holter Monitors during daily activities were received and analyzed to verify that total capture was maintained at the 3-month and 6-month visits and to ensure that the safety margin was adequate. Cardiopulmonary exercise tests (CPX) were performed on patients who were randomized to receive CRT therapy at 3- and 6- month visits.

- In 623 evaluations of safety margin at baseline, three-, and six-months, the device output was programmed to deliver a voltage approximately three times that necessary to stimulate both ventricles.
- A total of 1139 Holter monitors were placed throughout the study at baseline, three-, and six-months. The tests indicated only 4 instances (0.4%) of inappropriate pacing or sensing that were all corrected with device programming.
- A total of 316 CPX tests at the three- and six-month follow-up visits were performed in patients with CRT who also had interpretable ECG results. Of these, 277 (88%) had continuous CRT delivery throughout exercise. The remaining 39 patients (12%) had continuous CRT delivery until the sinus rate exceeded the maximum tracking rate (MTR).

Focused Confirmatory Study

Study Design

The Focused Confirmatory Study (FCS) was a prospective, multicenter study conducted in the United States in 127 patients who participated in an exercise performance study. The purpose of the FCS was:

- To confirm effectiveness results related to functional capacity measures, specifically the Peak VO₂ and 6-Minute Hall Walk, previously reported in the NYHA Class III/IV subgroup of the CONTAK CD Study.

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CRT was provided in the same manner for the FCS as for the CONTAK CD Study. The EASYTRAK lead, along with market approved right atrial and right ventricular leads were used to provide biventricular stimulation.

Study Patients

The patients in the FCS had the same heart failure indications as the patients in the NYHA Class III/IV subgroup of the CONTAK CD Study; i.e., patient inclusion criteria included NYHA Class III or IV while on drug therapy, QRS duration ≥ 120 ms, and Left Ventricular Ejection Fraction (LVEF) $\leq 35\%$.

A baseline physical assessment and functional measures were performed prior to CRT system implant. Patients were eligible for participation in the study if they were capable of walking between 150 and 425 meters. In addition to a Six-Minute Walk test, other special tests were performed prior to implant consisting of a symptom-limited treadmill test and completion of the Minnesota Living with Heart Failure Questionnaire to assess Quality of Life. CRT therapy was enabled immediately upon device implant. Patients were followed at one week, one month, three months, six months and every three months thereafter for a routine physical assessment and device evaluation. Special testing as defined above was repeated at three months and six months post-implant.

Prior to study entry, patients were stable on optimal heart failure medications (ACE inhibitors or substitute > 1 month and beta blockers > 3 months). Patients were excluded if they were indicated for either a pacemaker or ICD or if they were hospitalized for heart failure in the month prior to enrollment.

Baseline Demographics

The patient characteristics at study entry are summarized in Table 1-19.

Table 1-19. Preimplant Characteristics of Study Patients (N = 127)

Characteristics	All Patients Receiving CRT	Characteristic	All Patients Receiving CRT	
Age (years)	61 ± 12	QRS width (ms)	159 ± 27	
Male Gender (%)	69	LBBB/NSIVCD (%)	91	
NYHA Class III (%)	94	Heart failure medications (%)	91	
Ischemic Etiology (%)	49			• ACE inhibitor or ARB
LVEF (%)	23 ± 7			• Beta blockers
Resting heart rate (bpm)	73 ± 12			• Digoxin
		• Diuretics	98	

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Inclusion Criteria

Inclusion criteria included:

- Moderate or severe heart failure, defined as symptomatic heart failure for at least six months with NYHA Class III or IV symptoms at the time of enrollment, AND at least one of the following events in the previous 12 months:
 - Hospitalization for heart failure management
 - Outpatient visit in which intravenous (IV) inotropes or vasoactive infusion were administered continuously for at least 4 hours
 - Emergency room visit of at least twelve hours duration in which IV heart failure medications were administered (including diuretics)
- QRS \geq 120 ms and PR interval $>$ 150 ms from any two leads of a 12-lead ECG
- Left ventricular ejection fraction \leq 35%
- Left ventricular end diastolic dimension \geq 60 mm (required only if LVEF measured by echo)
- Age \geq 18 years
- Optimal pharmacologic therapy for heart failure
- Able to walk between 150 and 425 m in a Six-Minute Walk test

Major Differences Between CONTAK CD and Focused Confirmatory Study Patients

The CONTAK RENEWAL 3, CONTAK RENEWAL, and CONTAK CD devices provide the same cardiac resynchronization therapy (biventricular pacing) and have the same Indications for Use. Therefore, the CONTAK CD clinical trial data used to support CONTAK CD is also applicable to CONTAK RENEWAL and CONTAK RENEWAL 3. The primary difference between CONTAK CD devices and CONTAK RENEWAL and CONTAK RENEWAL 3 devices is that CONTAK CD utilizes an electrically common RV and LV sensing/pacing circuit whereas CONTAK RENEWAL and CONTAK RENEWAL 3 incorporate an independent RV and LV sensing/pacing circuit. Additional clinical analysis was also conducted with CONTAK RENEWAL to provide confirmation that the independent sensing and pacing capability did not adversely affect the ability of the device to detect ventricular tachyarrhythmias or provide continuous biventricular pacing therapy.

Some of the major differences between the study populations included:

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- Patients were excluded from the FCS if they were indicated for either a pacemaker or implantable cardioverter defibrillator (ICD). Patients in the CONTAK CD Study were excluded if they met the indications for a pacemaker; however, they were required to meet the general indications for an ICD.
- Patients were excluded from the FCS if they were hospitalized for heart failure in the month prior to enrollment; whereas, there was no exclusion for hospitalization for heart failure in the month prior to enrollment for the CONTAK CD patients.
- Patients in the FCS must have been on stable, optimal heart failure medications, including beta blocker therapy for three months, prior to study entry. Patients in the CONTAK CD Study could be optimized on drug therapy between the time from device implant until the treatment phase (either CRT or No CRT) began.
- Patients in the FCS had baseline measurements performed prior to implant. Patients in the CONTAK CD Study had baseline measurements performed post-implant, but before programming of the randomized therapy.
- Seventy-seven percent of patients in the FCS (98 of N = 127) were on beta blockers compared to 42% in the CONTAK CD Study (95 of N = 227).
- Forty-nine percent of the patients in the FCS (62 of N = 127) had ischemic etiology compared to 68% in the CONTAK CD Study (154 of N = 227).

Endpoints

The primary endpoints of the study were Peak VO₂ and Six-Minute Walk distance. The study was designed to show a mean change of at least 1ml/kg/min and a 95% lower confidence bound (LCB) at least 0.5 ml/kg/min. The study was also designed to detect a statistically significant improvement in the Six-Minute Walk distance at a one-sided significance level of 0.10. Additionally, two ancillary analyses of Quality of Life Score and NYHA Class had to demonstrate a change that was directionally favorable towards CRT using descriptive statistics.

Study Results

Peak VO₂

A statistically significant improvement from baseline of 0.94 ± 0.30 ml/kg/min with a 95% LCB of 0.45 was observed in Peak VO₂ after six months of CRT.

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Six-Minute Walk

Statistically significant improvements versus baseline were observed in Six-Minute Walk distance after six months of CRT with an observed mean improvement of 50.9 ± 10.4 m with a 95% LCB of 37.6 m.

Quality of Life

Consistent with the other analyses, a statistically significant improvement of 23.9 ± 2.6 points was observed in the Quality of Life score after six months of CRT with a 95% LCB of 19.7 points.

New York Heart Association Class

After six months of CRT, a statistically significant improvement in NYHA Class was observed with 60.4% of patients improving one or more NYHA Class.

CONTAK RENEWAL Study**Study Design**

The CONTAK RENEWAL Study was a prospective, multi-center, non-randomized evaluation conducted in Europe and enrolled a total of 45 patients. The purpose of the study was to verify that the CONTAK RENEWAL device performs according to specification.

Inclusion/Exclusion Criteria

Patients who were enrolled in the study were required to meet the following inclusion criteria:

- Symptomatic heart failure
- Left ventricular dysfunction
- Wide QRS
- At risk for sudden cardiac death
- 18 years or of legal age in order to give informed consent according to national laws
- Able to understand the nature of the procedure
- Available for follow-up on a regular basis at an approved investigational center

Patients were excluded from the investigation if they met any of the following criteria:

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- Life expectancy of less than six months due to other medical conditions
- For women: Pregnancy or absence of medically accepted birth control
- Inability or refusal to sign the Patient Informed Consent
- Inability or refusal to comply with the follow up schedule or protocol requirements
- Mechanical tricuspid prosthesis
- Currently enrolled in another investigational study, including drug investigations
- Hypertrophic Obstructive Cardiomyopathy
- Are unable to undergo device implant, including general anesthesia if required
- Have pre-existing leads other than those specified in the investigational plan (unless the investigator intended to replace them with the permitted leads)

Baseline Demographics

The patient characteristics at study entry are summarized in Table 1-20.

Table 1-20. Preimplant Characteristics of Study Patients

Characteristics ^a	Patient Data
N patients implanted	44
Gender	Male (91%), Female (9%)
Age (years)	65 ± 9
NYHA	II (14%), III (77%), IV (9%)
LVEF (%)	22 ± 6
BBB	LBBB/NSIVCD (86%),RBBB (14%)
Etiology	Ischemic (56%), Non-ischemic (44%)
QRS Width	172 ± 24 ms
PR Interval	211 ± 49 ms
Resting HR	70 ± 12 bpm

a. Continuous measures are reported as means ± standard deviations.

Ventricular Tachyarrhythmia Detection Time

The CONTAK RENEWAL device has independent Left Ventricular and Right Ventricular Sensing. Ventricular tachyarrhythmia detection time was analyzed to determine if the sensing configuration had any effect on sensing VT/VF. Based on previous clinical studies of the VENTAK AV family, upon which the ICD function of CONTAK CD and CONTAK RENEWAL are built, Guidant's ICDs typically have a VF detection time of approximately two seconds. The VF detection time of 2.4 ± 0.5 seconds in

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the RENEWAL study was statistically lower than 6 seconds⁵ ($p < 0.01$), demonstrating that there was no statistically significant prolongation of induced VF detection times with the independent sensing configuration. There were no adverse events reported in which a CONTAK RENEWAL device failed to detect a spontaneous ventricular tachyarrhythmia.

CONTAK RENEWAL Holter Study

Study Design

The CONTAK RENEWAL Holter Study was a prospective, multi-center, non-randomized evaluation conducted in Europe, in which 46 patients completed testing. The purpose of the study was to demonstrate continuous appropriate biventricular (BiV) pacing over a 24 hour period and during exercise using Holter monitor recordings. All patients had been implanted with a CONTAK RENEWAL for a minimum of one month at the time of the study initiation.

Inclusion/Exclusion Criteria

Patients who were enrolled in the study were required to meet the following inclusion criteria:

- Availability for 24 hours follow-up at an approved study center
- Willingness and ability to participate in all testing associated with this study
- Age 18 or above, or of legal age to give informed consent as specified by national law
- Implanted with the CONTAK RENEWAL system for at least 1 month
- Stable when programmed according to labeled recommendations for continuous BV pacing
- Sinus rhythm at follow-up
- Active atrial lead implanted

Patients were excluded from the investigation if they met any of the following criteria:

- Life expectancy of less than six months due to other medical conditions
 - Concurrent participation in any other clinical study, including drug study
 - In atrial fibrillation at follow-up
 - Inability or refusal to sign the Patient Informed Consent
5. Detection time at implant with legally marketed Guidant ICD devices is typically two seconds, and investigators have stated that an additional delay of 3 to 5 seconds would be a clinically significant event. The expected detection time is 2 seconds (95% CI: [0, 6 sec]).

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- Inability or refusal to comply with the follow-up schedule
- Known pregnancy

Baseline Demographics

The patient characteristics at study entry are summarized in Table 1-21.

Table 1-21. Preimplant Characteristics of Study Patients

Characteristics		Patient Data
N patients		46
Gender		Male: 40 (87%), Female: 6 (13%)
Age (years)		60.9 ± 9.0
NYHA at implant [N (%)]	I	0 (0%)
	II	5 (10.9%)
	III	34 (73.9%)
	IV	7 (15.2)%
NYHA current [N (%)]	I	9 (19.6%)
	II	25 (54.3%)
	III	11 (23.9%)
	IV	1 (2.2%)
Duration implanted (months)	Mean ± SD	8.3 ± 4.1
	Range	1.5 -- 15.0
	Median	9.0

Programming Parameters

Refer to Chapter 5 for information about programming to maintain CRT. Programming recommendations in this study were consistent with the recommendations in Chapter 5.

Endpoints

The study had two primary endpoints: 1) continuous appropriate BiV pacing during activities of daily living and 2) continuous appropriate BiV pacing during exercise. The mean percentage of sinus beats appropriately BiV paced was measured by a Holter monitor over a 24 hour period and during exercise. Exercise intensity was measured using the Borg rating of perceived exertion (RPE) 6-20 scale. Patients were asked to exercise to a Borg level of 15 (difficult). The exercise protocol used was left to the discretion of the physician based on the patients' functional status.

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The type of exercise performed, duration and intensity of exercise testing is listed in Table 1-22 and Table 1-23.

Table 1-22. Type of Exercise Testing Performed

Exercise Performed	Number of Patients
Bicycle Ergometry	24 (52.2%)
Hall Walk	8 (17.4%)
Stair Climbing	14 (30.4%)
Total	46

Table 1-23. Duration and Intensity of Exercise Testing

		Results (N=46)
Borg RPE Rating Obtained	Mean ± SD	15 ± 1
	Median	15
	Range	7 – 18
Duration of Exercise (minutes)	Mean ± SD	6.6 ± 3.3
	Median	6.0
	Range	1 – 17
Maximum HR Obtained (bpm)	Mean ± SD	103 ± 20
	Median	105
	Range	60 – 156

Study Results

Pacing during activities of daily living

The mean percentage of appropriately continuously paced beats during daily living was calculated as $99.6 \pm 1.3\%$ with a median of 100% and is summarized in Table 1-24. Continuous appropriate BiV pacing is defined as pacing provided between the lower rate limit and the MTR, excluding PVCs.

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Table 1-24. Activities of Daily Living: Continuous Appropriate BiV Pacing

	Statistic	P-value ^a
Mean ± SD	99.6 ± 1.3	--
Range	91.4 – 100	--
Median ^b	100	<0.01

- a. The p-value is based on the sign-rank test.
b. Due to the non-normality of the data a non-parametric test of the median was performed comparing the median to 90%.

Pacing During Exercise

The mean percentage of appropriately continuously paced beats during exercise was calculated as 98.3 ± 5.6% with a median of 100% and is summarized in Table 1-25. Continuous appropriate BiV pacing is defined as pacing provided between the lower rate limit and the MTR, excluding PVCs.

Table 1-25. Exercise: Continuous Appropriate BiV Pacing

	Statistic	P-value ^a
Mean ± SD	98.3 ± 5.6	--
Range	68.1 – 100	--
Median ^b	100	<0.01

- a. The p-value is based on the sign-rank test.
b. Due to the non-normality of the data a non-parametric test of the median was performed comparing the median to 90%.

Device Counters

Finally, during the study CONTAK RENEWAL device counters were found to correlate highly to the data collected on the independent Holter monitors.

Table 1-26. Correlation Between Holter and Device

	Mean ± SD	Correlation (P-value)
Holter	97,536 ± 13,307	0.97 (<0.01)
Device	100,143 ± 13,373	--

DEVICE FEATURES

By programming device parameters, the pulse generator provides ventricular tachyarrhythmia and cardiac resynchronization therapies. The device can detect and treat ventricular tachycardia and ventricular fibrillation with a combination of antitachycardia pacing and monophasic or biphasic cardioversion/defibrillation shocks. For the treatment of heart failure, the device uses biventricular electrical stimulation to synchronize ventricular contractions for the intent of providing mechanical synchronization. Left ventricular stimulation is delivered using a Guidant lead that is implanted in the coronary venous system. Detection of the atrial rate is available using an atrial lead. The pulse generator also detects and treats bradycardia conditions with pacing pulses in both the atrium and ventricles. Pulse generator memory provides a record of patient data, therapy delivery counts, and a therapy history consisting of arrhythmia episode data, conversion attempt data, stored electrograms (EGM), and annotated P-P and R-R intervals present during and following a tachyarrhythmic episode. The pulse generator automatically re-forms its capacitors and provides diagnostic data for evaluating battery status, lead integrity, and pacing thresholds.

The total system allows the physician to noninvasively interact with the pulse generator as listed below:

- Interrogate and program the pulse generator's tachycardia and bradycardia detection and therapy parameters and parameters for delivery of cardiac resynchronization therapy
- Test the leads (atrial, right ventricular, and left ventricular) and program stimulation voltages and pulse widths using independently programmable outputs
- Deliver a maximum-output STAT SHOCK with the STAT SHOCK command
- Deliver emergency VVI pacing with the STAT PACE command
- Divert therapy delivery
- Access the pulse generator memory to review patient clinical data, therapy history, and stored electrograms
- View real-time electrograms and event markers
- Induce, monitor, and terminate arrhythmias during electrophysiologic testing
- Program optional features such as magnet use and audible tones
- Review the pulse generator battery status
- Print reports and save patient information on disk

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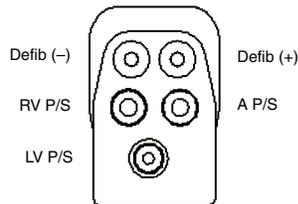
Mechanical Specifications

Table 1-27. Nominal Mechanical Specifications

	Dimensions H x W x D (cm)	Volume (cc)	Mass (g)	Connector Size	Case Electrode Surface Area (mm ²)
CONTAK RENEWAL 3 Models H170/H175	7.78 x 5.94 x 1.15	37	89	IS-1/LV-1, IS-1, DF-1	6950
CONTAK RENEWAL 3 HE Models H177/H179	8.26 x 6.30 x 1.15	40	89	IS-1/LV-1, IS-1, DF-1	7655

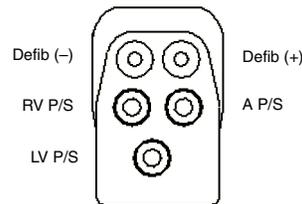
H170/H175/H177/H179	
Case Material	Hermetically sealed titanium
Header Material	Implantation-grade polymer
Power Supply (WGT)	Lithium-silver vanadium oxide cell

Lead Connections



Models H175, H179

DF-1 Defib ports
IS-1 Right Ventricular P/S port
IS-1 Atrial P/S port
LV-1 Left Ventricular P/S port



Models H170, H177

DF-1 Defib ports
IS-1 Right Ventricular P/S port
IS-1 Atrial P/S port
IS-1 Left Ventricular P/S port

- The device uses the pulse generator case as a defibrillating electrode.
- LV-1 refers to the Guidant LV[®] proprietary connector. IS-1 refers to the international standard ISO 5841.3:2000. DF-1 refers to the international standard ISO 11318:2002.

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Factory Nominal Parameter Settings

The pulse generator's parameters are preset at factory nominal values. Refer to the section "Factory Nominal Parameter Settings" on page 9-2. Appendix A provides a complete list of parameters and available programmable values.

MAINTAINING DEVICE EFFECTIVENESS

Perform follow-up testing to maintain continued verification of detection and therapy efficacy. Refer to the section "Follow-up Testing" on page 10-2.

X-RAY IDENTIFIER

Guidant pulse generators have an identifier that is visible on x-ray film or under fluoroscopy. This provides noninvasive confirmation of the device manufacturer. The identifier consists of the letters "GDT" to identify the manufacturer (Guidant), followed by 202, identifying the Model 2845 programmer software application needed to communicate with the pulse generator.

Refer to the Quick Start® section (page 2-5) for information on identifying the device via the programmer.

The model number of the pulse generator is stored in the device's memory and is available on the About screen selectable through the Utilities menu when the pulse generator is interrogated.

PULSE GENERATOR LONGEVITY

Based on simulated studies, it is anticipated that CONTAK RENEWAL 3 and CONTAK RENEWAL 3 HE pulse generators have average longevity to ERI as indicated below. The longevity expectations, accounting for the energy used during manufacture and storage (approximately six months), apply at the conditions shown below. Values apply whether Electrogram Storage options are programmed On or Off.

Table 1-28. Pulse Generator Life Expectancy Estimation (Implant to ERI)^{a b}

Atrial Pace/Sense%	DDD Mode (Years)	
	Standard Energy Models H170/H175	High Energy Models H177/H179
15%	6.0	5.0
100%	5.5	4.7

- a. 60 ppm LRL; 100% biventricular pacing; 3.0 V pacing pulse amplitude (atrium), 3.5 V pacing pulse amplitude (RV, LV); 0.4 ms pacing pulse width (atrium, RV, LV); and 700 Ω pacing impedance (atrium, LV), 900 Ω pacing impedance (RV).
- b. Projected longevity is calculated at 6 to 14 maximum energy charging cycles per year (depending on battery status) with automatic capacitor/battery management and maximum energy defibrillation therapy.

NOTE: The energy consumption in the longevity table is based upon theoretical electrical principles and verified via bench testing only.

The longevity of the pulse generator decreases with an increase in the pacing rate, pacing pulse amplitude, pacing pulse width, percentage of paced to sensed events, or charging frequency, or with a decrease in pacing impedance. Device longevity in CONTAK RENEWAL systems also is reduced if the Patient Triggered Monitor feature is programmed On (refer to “Patient Triggered Monitor” on page 7-18). A maximum-energy shock is equal to approximately 7 days (9 days for HE models) of monitoring.

Warranty Information

A limited warranty certificate for the pulse generator accompanies the pulse generator. For additional copies, please contact Guidant Corporation at the address and phone number on the back cover of this manual.

PATIENT COUNSELING INFORMATION

- The pulse generator is subject to random component failure. Such failure could cause inappropriate shocks, induction of arrhythmias or inability to treat arrhythmias, and could lead to the patient's death.
- Persons administering CPR may experience the presence of voltage on the patient's body surface (tingling) when the patient's cardiac resynchronization therapy (CRT) system delivers a shock.
- Advise patients to contact their physician immediately if they hear tones coming from their device.

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Patient Manual

Guidant recommends that the physician discuss the information in the patient manual with concerned individuals both before and after pulse generator implantation, so they are fully familiar with operation of the device. A copy of the patient manual is provided for the patient with the device. For additional copies of the patient manual, contact the nearest Guidant sales representative or contact Guidant at the phone number on the back cover of this manual.

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