SUMMARY OF SAFETY AND EFFECTIVENESS

General Information

Device Generic Name:	Dual Chamber Implantable Cardioverter Defibrillator; Leads
Device Trade Name:	InSync ICD Model 7272 Dual Chamber Implantable Cardioverter Defibrillator with Biventricular Pacing for Cardiac Resynchronization, Attain Models 2187, 2188, 4189 Leads
Applicant's Name and Address:	Medtronic, Inc. 710 Medtronic Parkway Minneapolis, MN 55432-5604
PMA Number:	P010031
Date of Panel Recommendation:	_____
Date of Notice of Approval to Applicant:	_____

Indications for Use

InSync ICD Model 7272 Device

The InSync ICD system is indicated for the reduction of the symptoms of moderate to severe heart failure (NYHA Functional Class III or IV) in those patients who remain symptomatic despite stable, optimal medical therapy (as defined in the clinical trials section), and have a left ventricular ejection fraction less than or equal to 35% and a QRS duration greater than or equal to 130 ms. The ICD is intended to provide ventricular antitachycardia pacing and ventricular defibrillation for automated treatment of life threatening ventricular arrhythmias.

Attain Leads

The Attain LV Model 2187 lead has application as part of a Medtronic biventricular pacing system.

The Attain CS Model 2188 lead has application where permanent atrial, or dual-chamber pacing systems are indicated.

OR

The lead has application as part of a Medtronic biventricular pacing system.

The Attain SD Model 4189 lead has application as part of a Medtronic biventricular pacing system.

System Description

Description of InSync ICD Model 7272

The InSync ICD Model 7272 Dual Chamber Implantable Cardioverter Defibrillator (ICD) System is a multi-programmable, implantable cardioverter defibrillator with biventricular pacing for cardiac resynchronization that monitors and regulates a patient's heart rate by providing ventricular arrhythmia therapy and single or dual chamber bradycardia pacing.

Description of Attain Leads

The Medtronic Attain LV Model 2187 transvenous, unipolar, left ventricular, cardiac vein pacing lead is designed for pacing and sensing via the cardiac vein. The lead features a platinum alloy electrode, nickel alloy conductors, polyurethane insulation, and an IS-1[1] unipolar (UNI) lead connector.

The Medtronic Attain CS Model 2188 transvenous, bipolar, coronary sinus/cardiac vein pacing lead is designed for pacing and sensing via the coronary sinus or cardiac vein. The lead features two platinum alloy electrodes, nickel alloy conductors, polyurethane insulation, and an IS-1[2] bipolar (BI) lead connector.

The Medtronic Attain SD Model 4189 steroid eluting, transvenous, unipolar, left ventricular, cardiac vein pacing lead is designed for pacing sensing via a cardiac vein. The lead features a platinum alloy electrode, nickel alloy conductors, polyurethane insulation, and an IS-1[1] unipolar (UNI) lead connector.

The Model 4189 lead's distal tip contains a maximum of 1.0mg dexamethasone acetate. Upon exposure to body fluids, the steroid elutes from the lead tip. The steroid is known to suppress the inflammatory response that is believed to cause threshold rises typically associated with implanted pacing electrodes.

[1] IS-UNI refers to an international Connector Standard (ISO 5841-3: (E)) whereby pulse generators and leads so designated are assured of a basic mechanical fit.
[2] IS-1 BI refers to an international Connector Standard (ISO 5841-3: (E)) whereby pulse generators and leads so designated are assured of a basic mechanical fit.

Note: To implant the Model 2187 and 4189 leads in a cardiac vein, a Medtronic delivery system is required.

Contraindications

InSync ICD Model 7272 Device

Do not use the InSync ICD system in:

- Patients whose ventricular tachyarrhythmias may have transient or reversible causes, such as:
  - Acute myocardial infarction
  - Digitalis intoxication
  - Drowning
  - Electrocution
  - Electrolyte imbalance
  - Hypoxia
  - Sepsis
- Patients with incessant VT or VF
- Patients who have a unipolar pacemaker
- Patients whose primary disorder is bradyarrhythmias or atrial arrhythmias.

Attain Leads

The leads are contraindicated for patients with coronary venous vasculature that is inadequate for lead placement, as indicated by venogram.

The Attain SD Model 4189 lead is contraindicated in patients for whom a single dose of 1.0mg of dexamethasone acetate may be contraindicated.

Warnings and Precautions

InSync ICD

Resuscitation Availability

Do not perform ICD testing unless an external defibrillator and medical personnel skilled in cardiopulmonary resuscitation (CPR) are readily available.

Lead System

Do not use another manufacturer's lead system without demonstrated compatibility as undersensing of cardiac activity and failure to deliver necessary therapy could result.

Electrical Isolation

Do not permit the patient to contact grounded equipment which could produce hazardous leakage current. Resulting arrhythmia induction could result in the patient's death.

Avoiding Shock during Handling

Program VF Detection to OFF during surgical implant and explant, or post-mortem procedures, because the ICD can deliver a serious shock if you touch the defibrillation terminals in certain situations if ICD detection is ON.

Sterilization, Storage, and Handling

Resterilization

Do not resterilize and re-implant an explanted ICD.

"Use Before" Date

Do not implant the ICD after the "Use Before" date, because the battery's longevity may be reduced.

If Package is Damaged

Do not used the ICD or accessories if the packaging is wet, punctured, opened, or damaged, because the integrity of the sterile packaging might be compromised. Return the ICD to Medtronic.

ICD Storage

Store the ICD in a clean area, away from magnets, kits containing magnets, and sources of electromagnetic interference to avoid ICD damage. Store and transport the ICD between -18 to 55°C (0 to 131°F), because temperatures outside this range could damage the ICD.

Equilibration

Allow the ICD to reach room temperature before programming or implanting the ICD, because rapid temperature changes could affect initial ICD function.

Implantation and ICD Programming

- **Atrial tracking modes.** Do not use atrial tracking modes in those 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 the following patients:
  - Patients with heart failure because such modes do not provide cardiac resynchronization.
  - Patients with impaired AV nodal conduction because ventricular capture cannot be assured.
- Infrequent charging of the high voltage capacitors could extend the ICD charge time. Program the ICD to condition the capacitors automatically, or perform a test charge to form the capacitors manually every six months (if the ICD has not charged to its maximum energy).

- Use only Medtronic programmers and application software to communicate with the ICD.
- Positioning a magnet or the programming head over the ICD suspends detection and treatment. The magnet does not alter bradycardia therapy.
- **End of Life (EOL).** Replace the ICD when the programmer displays an EOL message and a battery voltage of 4.57 volts or less. Immediate replacement is recommended if the programmer displays a Charge Circuit Timeout or Charge Circuit Inactive message.
- **Single chamber hysteresis.** For heart failure patients, the use of single chamber hysteresis will not provide cardiac resynchronization.
- Program ICD parameters such as sensitivity thresholds and VT and VF detection intervals according to the recommendations in the technical manual.
- **Pacemaker dependent patients –** Always program Ventricular Safety Pacing (VSP) ON for pacemaker dependent patients. Ventricular Safety Pacing prevents ventricular systole due to inappropriate inhibition of ventricular pacing caused by cross talk or ventricular asystole.
- If a pacemaker is used concurrently with the ICD:
  - Verify that the ICD will not sense the pacemaker output pulses and
  - Program the pacemaker so that pacing pulses are delivered at intervals longer than the ICD tachyarrhythmia detection intervals.

Lead Evaluation and Lead Connection

- For lead resterilization, use ethylene oxide only. Do not resterilize more than one time.
- Do not tie a ligature directly to the lead body, tie it too tightly, or otherwise create excessive strain at the insertion site as this can damage the lead.
- Do not immerse leads in mineral oil, silicone oil, or any other liquid.
- Do not grip the lead with surgical instruments.
- Do not use excessive force or surgical instruments to insert a stylet into a lead.
- Use the same polarity evaluated during testing when connecting the leads to the ICD to ensure defibrillation effectiveness.
- If a thoracotomy is required to place epicardial patches, it should be done during a separate procedure to reduce the risk of morbidity and mortality.
- Do not place the patch lead over nerve tissue as this can cause nerve damage.
- Place the patch lead with the conducting coil side facing the heart to ensure delivery of energy to the heart.
- Place the sutures well outside the coil of the patch lead or in the area between the coils to avoid possible coil fracture.
- If countershock is unsuccessful using external paddles, adjust the external paddle position (e.g., anterior-lateral to anterior-posterior) and be sure that the external paddle is not positioned over the patch.
- Do not fold, alter or remove any portion of the patch, because it could compromise electrode function or longevity.
- Do not use ventricular transvenous leads in patients with tricuspid valve disease or a mechanical prosthetic tricuspid valve. Use with caution in patients with a bioprosthetic valve.
- Use the correct suture sleeve (when needed) for each lead to immobilize the lead and protect it against damage from ligatures.

- Ensure that the defibrillation lead impedance is greater than 10 ohms. An impedance below 10 ohms could damage the ICD.
- Do not kink the leads. Kinking leads can cause additional stress on the leads, possibly resulting in lead fracture.
- Do not suture directly over the lead body as this may cause structural damage. Use the lead anchoring sleeve to secure the lead lateral to the venous entry site.
- Lead or Active Can® electrodes in electrical contact during a high voltage therapy could cause current to bypass the heart, possibly damaging the ICD and leads. While the ICD is connected to the leads, make sure than no therapeutic electrodes, stylets, or guidewires are touching or connected by an accessory low impedance conductive pathway. Move objects made from conductive materials (e.g., an implanted guidewire) well away from all electrodes before a high voltage shock is delivered.
- If a pacing lead is abandoned rather than removed, it must be capped to ensure that it is not a pathway for currents to or from the heart.
- If a header port is unused on the ICD, the port must be plugged to protect the ICD.
- If the high voltage path impedance value exceeds 200 ohms and the delivered energy is less than 0.6 joules, the ICD short circuit protection feature may have interrupted delivery of the shock into a short circuit. Perform a lead impedance test to assess high voltage circuit integrity.
- Refer to the lead technical manuals for specific instructions and precautions.

Follow-up Testing

- Ensure than an external defibrillator and medical personnel skilled in cardiopulmonary resuscitation (CPR) are present during post-implant ICD testing should be patient require external rescue.
- Be aware that changes in the patient's condition, drug regimen, and other factors may change the defibrillation threshold (DFT), which may result in nonconversion of the arrhythmia post-operatively. Successful conversion of ventricular fibrillation or ventricular tachycardia during testing is no assurance that conversion will occur post-operatively.

ICD Explant and Disposal

- Interrogate the ICD, and program the ICD to OFF and disable ICD functions prior to explanting, cleaning, or shipping to prevent unwanted shocks.
- Return all explanted ICDs and leads to Medtronic.
- Never incinerate the ICD due to the potential for explosion. The ICD must be explanted before cremation.

Environmental and Medical Therapy Hazards

Patients should be directed to avoid devices that generate strong electric or magnetic interference (EMI). EMI could cause malfunction or damage resulting in non-detection or delivery of unneeded therapy. Moving away from the interference source, or turning it off, usually allows the ICD to return to its normal mode of operation.

Hospital and Medical Environments

- **Electrosurgical cautery** could induce ventricular arrhythmias and/or fibrillation, or may cause device malfunction or damage. If use of electrocautery is necessary, the current path and ground plate should be kept as far away from the ICD and leads as possible (minimum of 15 cm [six inches]).
- **External defibrillation** may damage the ICD or may result in temporary and/or permanent myocardial damage at the electrode tissue interface as well as temporary or permanent elevated pacing thresholds. Minimize current flowing through the ICD and lead system by following these precautions when using external defibrillation on a patient with an ICD:
  - Position defibrillation paddles as far from the ICD as possible (minimum of 13 cm [five inches]). Minimize current flowing through the ICD and lead system by positioning the defibrillation paddles perpendicular to the implanted ICD-lead system.
  - Use the lowest clinically appropriate energy output (watt seconds).
  - Confirm ICD function following any defibrillation.
- **After direct or transthoracic defibrillation,** check lead and ICD integrity by performing lead impedance and pacing threshold tests as described in ICD System Reference Guide.
- **High radiation sources** such as cobalt 60 or gamma radiation should not be directed at the ICD. If a patient requires radiation therapy in the vicinity of the ICD, place lead shielding over the device to prevent radiation damage and confirm its function after treatment.
- **Lithotripsy** may permanently damage the ICD if it is at the focal point of the lithotripsy beam. If lithotripsy must be used, keep the ICD at least 2.5 to 5 cm (one to two inches) from the focal point of the lithotripsy beam.
- **Magnetic Resonance Imaging (MRI)** should not be used on patients who have an ICD because of the potential damage to the ICD.
- **Diathermy.** People with metal implants such as pacemakers, implantable cardioverter defibrillators (ICDs), and accompanying leads should not receive diathermy treatment. The interaction between the implant and diathermy can cause tissue damage, fibrillation, or damage to the device components, which could result in serious injury, loss of therapy, and/or the need to reprogram or replace the device.
- **Radio frequency ablation** procedure in a patient with an ICD could cause ICD malfunction or damage. RF ablation risks can be minimized by:
  - Programming the ICD to OFF.
  - Avoiding direct contact between the ablation catheter and the implanted lead or ICD.
  - Positioning the ground plate so that the current pathway does not pass through or near the ICD system; i.e., place the ground plate under the patient's buttocks or legs.
  - Having defibrillation equipment available.

Home and Occupational Environments

- **High voltage power transmission lines** could generate enough EMI to interfere with ICD operation if approached too closely.

- **Communication equipment** such as microwave transmitters, line power amplifiers, or high power amateur transmitters could generate enough EMI to interfere with ICD operation is approached too closely.
- **Commercial electrical equipment** such as arc welders, induction furnaces, or resistance welders could generate enough EMI to interfere with ICD operation if approached too closely.
- **Home appliances** which are in good working order and properly grounded do not usually produce enough EMI to interfere with ICD operation. There are reports of ICD disturbances caused by electrical hand tools or electric razors used directly over the ICD implant site.
- **Static magnetic fields.** Patients should avoid equipment or situations where they would be exposed to static magnetic fields (greater than 10 gauss or 1 millitesla) magnetic fields since it could suspend detection. Examples of magnetic sources that could interfere with normal ICD operation include stereo speakers, bingo wand, extractor wand, magnetic badges, or magnetic therapy products.

Electronic Article Surveillance (EAS)

- Electronic Article Surveillance (EAS) equipment such as retail theft prevention systems may interact with the ICD. Patients should be advised to walk directly through, and not to remain near an EAS system longer than necessary.

Cellular Phones

- Cellular phones may interact with the implanted ICD when placed in close proximity to the device. Patients should maintain separation of six inches (15 cm) between the phone and the implanted ICD, hold the phone in the ear opposite the side of the implanted ICD, and store the phone in a location opposite the side of the implanted device.
- The ICD has been tested to the frequency ranges used by the cellular phone included in Table 1, which represent most of the cellular phones in use worldwide. Based on this testing, the ICD should not be affected by the normal operation of such cellular phones when following the above placement guidelines. Patients can contact their local cellular phone service provider to confirm that the provider uses one of these technologies.

Table 1. Cellular Phone Transmission Technologies

Transmission Technology	Frequency Range
Analog	
FM (Frequency Modulation)	824 –849 MHz
Digital TDMA[a]	
North American Standards	
NADC[b] (TDMA-50Hz)	824 –849 MHz
USDC[c] 1800	825 MHz
International Standards	
GSM[d]	880 – 915 MHz
DCS[e]	1710 – 1785 MHz
Digital CDMA	
CDMA-DS[f]	824 – 849 MHz

[a] Time Division Multiple Access

[b] North American Digital Cellular

[c] United States Digital Cellular

[d] Global System for Mobile Communications

[e] Digital Cellular System

[f] Code Division Multiple Access – Direct Sequence

Attain Leads

Back-up pacing should be readily available during implant. Use of the delivery system and/or leads may cause heart block.

Inspecting the sterile package – Carefully inspect the package prior to opening:

- If the seal or package is damaged, contact your local Medtronic representative.
- Do not use the product after its expiration date.
- The lead has been sterilized with ethylene oxide prior to shipment. If the integrity has been compromised prior to the expiration date, resterilize using ethylene oxide.

Ethylene oxide Resterilization – If the sterile package seal is broken, resterilize the device using a validated ethylene oxide process. Avoid Resterilization techniques that could damage the lead:

- Refer to sterilizer instructions for operating instructions.
- Use an acceptable method for determining sterilizer effectiveness, such as biological indicators.

- Before Resterilization, place the device in an ethylene oxide permeable package.
- Do not exceed temperatures of 55°C (130°F).
- Do no resterilize more than one time.
- After Resterilization, allow the device to aerate ethylene oxide residues.

Handling the lead – Leads should be handled with great care at all times:

- If the lead is damaged, do not implant it. Return the lead to your local Medtronic representative.
- Protect the lead from materials shedding particles such as lint and dust. Lead insulators attract these particles.
- Handle the lead with sterile surgical gloves that have been rinsed in sterile water or a comparable substance.
- Do not severely bend, kink, or stretch the lead.
- Do not use surgical instruments to grasp the lead or connector pin.
- Do not immerse leads in mineral oil, silicone oil, or any other liquid, except blood at the time of implantation.
- Use and anchoring sleeve with all leads. Ensure that the anchoring sleeve is positioned close to the lead's connector pin, to prevent inadvertent passage of the sleeve into the vein. If wiping the lead is necessary prior to insertion, ensure that the anchoring sleeve remains in position.

Handling the stylets – Use care when handling stylets:

- Do not use excessive force or surgical instruments when inserting a lead.
- Avoid overbending, kinking, or blood contact.
- Use a new stylet when blood or other fluids accumulate on the stylet. Accumulated fluids may cause damage to the lead or difficulty in passing the stylet through the lead.
- Curve the stylet prior to insertion into the lead will achieve a curvature at the lead's distal end. Do not use a sharp object to impart a curve to the distal end of the stylet.

Necessary hospital equipment – Keep external defibrillation equipment nearby for immediate use during the acute lead system testing, implantation procedure, or whenever arrhythmias are possible or intentionally induced during post-implant testing.

Line-powered equipment – An implanted lead forms a direct current path to the myocardium. During lead implantation and testing, use only battery-powered equipment or line-powered equipment specifically designed for this purpose, to protect against fibrillation that may be caused by alternating currents. Line-powered equipment used in the vicinity of the patient must be properly grounded. Lead connector pins must be insulated from any leakage currents that may arise from line-powered equipment.

Concurrent devices – Output pulses, especially from unipolar devices, may adversely affect device-sensing capabilities. If a patient requires a separate stimulation device, either permanent or temporary, allow enough space between the leads of the separate systems to avoid interference in the sensing capabilities of the devices. Previously implanted pulse generators, implantable cardioverter defibrillators, and leads should generally be explanted.

Chronic repositioning or removal – Chronic repositioning or removal of leads may be difficult because of fibrotic tissue development. If a lead must be removed or repositioned, proceed with extreme caution. Return all removed or unused leads to Medtronic:

- Lead removal may result in avulsion of the endocardium, valve, or vein.
- Lead junctions may separate, leaving the lead tip and bare wire in the heart or vein.
- Cap abandoned leads to avoid transmitting electrical signals.
- For leads that have been severed, seal the remaining lead end and suture the lead to adjacent tissue.

Adverse Events and Deaths

The first successful implant of the Model 7272 InSync ICD cardiac resynchronization system was performed on October 4, 1999. 53 centers provided data for this clinical report (48 in USA, 5 in Canada). 636 patients had implant attempts. There were 567 successful implants (89.2% success) and 554 randomized patients. There were 282 patients randomized to the control arm (OFF), and 272 patients randomized to the treatment arm (ON).

Adverse events (complications and observations) are those reported as of the October 5, 2001 database closure date. There were 2830 adverse events reported. Of these, 823 were classified as complications and 2007 as observations. The following tables provide a summary of these events.

Summary of Complications

Table 1and **Table 2** provide a summary of all complications that occurred during the InSync ICD study as of the database closure of October 5, 2001 (554 randomized patients and 13 non-randomized patients).

Table 1. Summary of Complications, Part 1

	Number of Occurrences of Event Type:			Rate of Event Type for all 567 Implanted Patients (95% confidence interval)			Rate of Event Type at Six Months Post-implant		
Event Type	**Before Implant (n=659)**	**During Implant (n=651)**	**After Unsuccessful Implant (n=84)**	**6 months**	**12 months**	**18 months**	**Control (OFF)**	**Treatment (ON)**	**P-value**
Atrial flutter		1		1.1% (0.4-2.6%)	1.1% (0.4-2.6%)	1.1% (0.4- 2.6%)	1.6%	0.5%	0.19
Atrial fibrillation	1	3		1.3% (0.6-2.7%)	2.6% (1.3-5.1%)	2.6% (1.3-5.1%)	1.9%	0.7%	0.28
Atrial tachycardia	1			0.0%	0.0%	0.8% (0.1-5.5%)	0.0%	0.0%	---
Heart block		3		0.0%	0.0%	0.0%	0.0%	0.0%	---
Junctional rhythm	1			0.0%	0.0%	0.0%	0.0%	0.0%	---
Ventricular tachycardia	1	4	3	2.1% (1.2-3.9%)	3.0% (1.7-5.3%)	3.0% (1.7-5.3%)	2.0%	2.0%	0.95
Ventricular fibrillation	2	1		0.0%	0.0%	0.0%	0.0%	0.0%	---
Arm/hand swelling				0.2% (0.0-1.3%)	0.2% (0.0-1.3%)	0.2% (0.0-1.3%)	0.0%	0.4%	0.31
Back pain/discomfort		1		0.4% (0.1-1.5%)	0.8% (0.2-2.6%)	0.8% (0.2-2.6%)	0.0%	0.8%	0.15

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Cancer				0.6% (0.2-2.0%)	1.2% (0.4-3.5%)	1.2% (0.4-3.5%)	0.0%	1.3%	0.08
Cardiomyopathy	1		2	1.0% (0.4-2.5%)	1.0% (0.4-2.5%)	1.0% (0.4-2.5%)	0.4%	1.7%	0.16
Chest pain/Angina pectoris	2		1	1.9% (1.0-3.6%)	4.3% (2.3-8.0%	4.3% (2.3-8.0%	1.5%	1.8%	0.95
Chest pressure/tightness			1	0.7% (0.3-1.9%)	1.1% (0.4-2.7%)	2.4% (0.8-7.5%)	0.0%	1.5%	0.04
Chronic obstructive pulmo disease			1	0.4% (0.1-1.5%)	0.4% (0.1-1.5%)	0.4% (0.1-1.5%)	0.4%	0.4%	0.98
Depression				0.2% (0.0-1.3%)	0.2% (0.0-1.3%)	0.2% (0.0-1.3%)	0.0%	0.4%	0.31
Diabetes				0.5% (0.1-1.8%)	0.5% (0.1-1.8%)	0.5% (0.1-1.8%)	0.5%	0.0%	0.33
Dizziness	1		1	0.4% (0.1-1.4%)	0.4% (0.1-1.4%)	0.4% (0.1-1.4%)	0.7%	0.0%	0.16
Dyspnea/Shortness of breath	1			3.2% (2.0-5.4%)	4.0% (2.5-6.5%)	5.6% (2.9-10.7%)	4.7%	1.8%	0.08
Fatigue, tiredness	1			0.4% (0.1-1.5%)	0.8% (0.2-2.9%)	0.8% (0.2-2.9%)	0.4%	0.0%	0.33

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Heart failure decompensation	5	4	23	14.2% (11.4-17.7%)	19.6% (15.8-24.3%)	27.5% 20.3-36.5%)	14.7%	12.5%	0.26
Hypertension				0.2% (0.0-1.3%)	0.2% (0.0-1.3%)	0.2% (0.0-1.3%)	0.0%	0.4%	0.31
Hypokalemia				0.2% (0.0-1.2%)	0.5% (0.1-2.4%)	0.5% (0.1-2.4%)	0.0%	0.4%	0.31
Hypotension	1	4	1	2.3% (1.3-3.9%)	3.2% (1.9-5.6%)	3.2% (1.9-5.6%)	2.9%	1.5%	0.27
Inadequate cardiac output		1		0.5% (0.1-2.0%)	0.8% (0.3-2.6%)	1.7% (0.5-5.2%)	0.5%	0.5%	0.98
Ischemic heart disease			1	0.2% (0.0-1.4%)	0.6% (0.1-2.5%)	0.6% (0.1-2.5%)	0.0%	0.4%	0.30
Myocardial infarction				1.6% (0.8-3.3%)	1.6% (0.8-3.3%)	1.6% (0.8-3.3%)	2.2%	1.0%	0.28
Near (Pre) syncope				0.2% (0.0-1.4%)	0.2% (0.0-1.4%)	0.2% (0.0-1.4%)	0.4%	0.0%	0.33
Palpitations				0.2% (0.0-1.3%)	0.2% (0.0-1.3%)	0.2% (0.0-1.3%)	0.0%	0.4%	0.31
Pericardial effusion		1	1	0.4% (0.1-1.5%)	0.4% (0.1-1.5%)	0.4% (0.1-1.5%)	0.7%	0.0%	0.16

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Pericarditis				0.4% (0.1-1.5%)	0.4% (0.1-1.5%)	0.4% (0.1-1.5%)	0.4%	0.4%	0.98
Peripheral vascular disease			1	0.0%	0.0%	0.0%	0.0%	0.0%	---
Pleural effusion				1.1% (0.4-2.5%)	1.4% (0.6-3.2%)	1.4% (0.6-3.2%)	0.9%	1.3%	0.62
Pulmonary embolism				0.0%	0.5% (0.1-3.8%)	0.5% (0.1-3.8%)	0.0%	0.0%	---
Rash				0.4% (0.1-1.4%)	0.7% (0.2-2.1%)	0.7% (0.2-2.1%)	0.0%	0.7%	0.15
Shoulder pain/discomfort				1.3% (0.6-2.8%)	1.7% (0.8-3.5%)	1.7% (0.8-3.5%)	1.6%	1.1%	0.74
Sleep problems				0.2% (0.0-1.2%)	0.2% (0.0-1.2%)	0.2% (0.0-1.2%)	0.0%	0.4%	0.31
Stroke/CVA				0.4% (0.1-1.4%)	0.4% (0.1-1.4%)	0.4% (0.1-1.4%)	0.4%	0.4%	0.98
Syncope	1			0.7% (0.2-2.2%)	0.7% (0.2-2.2%)	3.7% (0.8-17.2%)	1.4%	0.0%	0.09
Thrombosis				1.2% (0.5-2.6%)	1.2% (0.5-2.6%)	1.2% (0.5-2.6%)	0.7%	1.7%	0.39

Table 1. Summary of Complications, Part 1									
	Number of Occurrences of Event Type:			Rate of Event Type for all 567 Implanted Patients (95% confidence interval)			Rate of Event Type at Six Months Post-implant		
Event Type	**Before Implant (n=659)**	**During Implant (n=651)**	**After Unsuccessful Implant (n=84)**	**6 months**	**12 months**	**18 months**	**Control (OFF)**	**Treatment (ON)**	**P-value**
Vascular heart disease			1	0.0%	0.0%	0.0%	0.0%	0.0%	---
Other (Patient Condition Code)	13	5	17	18.0% (14.9-21.7%)	27.4% (22.8-32.8%)	33.4% (26.9-40.9%)	19.3%	13.8%	0.08
Cardiac perforation		7		0.2% (0.0-1.3%)	0.2% (0.0-1.3%)	0.2% (0.0-1.3%)	0.4%	0.0%	0.32
Coronary Sinus dissection		12		0.0%	0.3% (0.0-2.4%)	0.3% (0.0-2.4%)	0.0%	0.0%	---
Hemo/Pneumothorax				0.7% (0.3-1.9%)	0.7% (0.3-1.9%)	0.7% (0.3-1.9%)	1.4%	0.0%	0.05
Other (Implant Code)		2	1	0.4% (0.1-1.4%)	0.4% (0.1-1.4%)	0.4% (0.1-1.4%)	0.0%	0.4%	0.31
Connector Block Problem				0.2% (0.0-1.2%)	0.2% (0.0-1.2%)	0.2% (0.0-1.2%)	0.0%	0.4%	0.31
Far-field R-wave sensing				0.2% (0.0-1.2%)	0.2% (0.0-1.2%)	0.2% (0.0-1.2%)	0.4%	0.0%	0.33
Muscle stimulation-pectoral				0.2% (0.0-1.2%)	0.2% (0.0-1.2%)	0.2% (0.0-1.2%)	0.4%	0.0%	0.33
Muscle stimulation - diaphragm		1		3.0% (1.9-4.9%)	4.5% (2.9-7.1%)	4.5% (2.9-7.1%)	1.6%	4.6%	0.03

Table 1. Summary of Complications, Part 1

	Number of Occurrences of Event Type:			Rate of Event Type for all 567 Implanted Patients (95% confidence interval)			Rate of Event Type at Six Months Post-implant		
Event Type	**Before Implant (n=659)**	**During Implant (n=651)**	**After Unsuccessful Implant (n=84)**	**6 months**	**12 months**	**18 months**	**Control (OFF)**	**Treatment (ON)**	**P-value**
Myopotential interference				0.0%	0.4% (0.1-2.6%)	0.4% (0.1-2.6%)	0.0%	0.0%	---
Oversensing			1	0.2% (0.0-1.2%)	0.2% (0.0-1.2%)	1.8% (0.3-10.0%)	0.0%	0.4%	0.31
Pacemaker mediated tachycardia				0.2% (0.0-1.7%)	0.2% (0.0-1.7%)	0.2% (0.0-1.7%)	0.0%	0.5%	0.31
Pain pocket site				2.4% (1.4-4.1%)	2.4% (1.4-4.1%)	2.4% (1.4-4.1%)	2.1%	2.2%	0.95
Pocket infection			1	2.0% (1.1-3.7%)	2.0% (1.1-3.7%)	2.0% (1.1-3.7%)	2.0%	2.0%	0.95
Pocket seroma/hematoma				0.9% (0.4-2.1%)	0.9% (0.4-2.1%)	0.9% (0.4-2.1%)	1.1%	0.7%	0.68
Suspected generator/ ICD failure				0.2% (0.0-1.4%)	0.2% (0.0-1.4%)	0.2% (0.0-1.4%)	0.4%	0.0%	0.33
Twiddler's syndrome				0.2% (0.0-1.6%)	0.2% (0.0-1.6%)	0.2% (0.0-1.6%)	0.4%	0.0%	0.34
Other (ICD Code)		1		0.6% (0.2-1.9%)	1.0% (0.4-2.8%)	1.0% (0.4-2.8%)	0.0%	1.2%	0.08
Elevated pacing thresholds			1	2.4% (1.4-4.1%)	2.4% (1.4-4.1%)	2.4% (1.4-4.1%)	2.6%	1.5%	0.40

Table 1. Summary of Complications, Part 1									
	Number of Occurrences of Event Type:			**Rate of Event Type for all 567 Implanted Patients (95% confidence interval)**			**Rate of Event Type at Six Months Post-implant**		
Event Type	**Before Implant (n=659)**	**During Implant (n=651)**	**After Unsuccessful Implant (n=84)**	**6 months**	**12 months**	**18 months**	**Control (OFF)**	**Treatment (ON)**	**P-value**
Failure to capture, loss of capture		1		2.1% (1.2-3.8%)	2.5% (1.4-4.5%)	2.5% (1.4-4.5%)	0.7%	2.5%	0.14
Lead dislodgment				9.9% (7.6-12.8%)	11.3% 8.8-14.6%)	11.3% (8.8-14.6%)	9.3%	9.4%	0.90
Other (Lead Code)				0.4% (0.1-1.4%)	0.4% (0.1-1.4%)	0.4% (0.1-1.4%)	0.0%	0.4%	0.31
Other (Other Code)		2	3	3.1% (1.9-5.1%)	5.4% (3.3-8.5%)	5.4% (3.3-8.5%)	2.0%	4.3%	0.17

Table 2. Summary of Complications, Part 2

Event Type	Control Group			Treatment Group			Not Randomized			Total		
	Pre-Implant	Implant	Post-Implant	Pre-Implant	Implant	Post-Implant	Pre-Implant	Implant	Post-Implant	Pre-Implant	Implant	Post-Implant
2187/2188 Related*		1	8		1	5			2		2	15
4189 Related*		1	34		1	37		6	8		8	79**
RA Lead Related*			7		1	8			1		1	16
RV Lead Related*			1		3	4			2		3	7**
Implant Tool Related		8			2			8			18	
7272 Related*			6			9						15
Heart Failure Decompensation	2		58			52	3		30	5		140
Not Device Related	7	1	140	10		151	5		53	22	1	344
Other	2	1	10		1	9			2	2	2	21
Possibly Device Related	1	1	11			2				1	1	13
Possibly Procedure Related	1	1	8		3	10		1	11	1	5	29
Procedure Related	1	8	22		4	19		3	6	1	15	47
Other System Related		1	2			5					1	7
Unknown						1						1
Total	**14**	**23**	**307**	**10**	**16**	**312**	**8**	**18**	**115**	**32**	**57**	**734**

*These events were considered to be system-related for the system-related complication primary safety objective analysis.
**One of each of these events occurred after an unsuccessful implant, so they are not reflected in the primary safety analysis.

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Summary of Observations

Table 3 and **Table 4** summarize all reported observations as of the database closure date of October 5, 2001.

Table 3. Summary of Observations, Part 1

Event Type	Control (Patients)	Treatment (Patients)	Not Randomized	Total Events (Patients)
Arrhythmias:				
A Fib/Flutter/AT	48	44	5	97
VT/VF/PVC	48	41	10	99
Heart Block	5	8	8	21
Junctional	2		1	3
Arm/Hand Numbness	4	2		6
Arm/hand swelling	8	4	1	13
Back Pain/discomfort	11	10	5	26
Cancer	1	2		3
Cardiomyopathy	2			2
Chest pain/Angina	21	14	1	36
Chest Pressure/tightness	13	6	3	22
Chronic Obstructive Pulm Disease	2	2		4
Cold/Flu	25	23	1	49
Depression	13	10	1	24
Diabetes	2	2		4
Diaphoresis/Sweating	3	1		4
Dizziness	30	29	2	61
Drug Change	12	6	1	19
Dyspnea/Shortness of Breath	24	27		51
Fatigue/Tiredness	23	15	2	40
Headache	4	10	2	16
Heart Failure Decompensation	39	34	5	78
Hypertension		7	1	8
Hypokalemia	3	9		12
Hypotension	17	16	2	35
Inadequate cardiac output		1	1	2

Table 3. Summary of Observations, Part 1				
Event Type	**Control (Patients)**	**Treatment (Patients)**	**Not Randomized**	**Total Events (Patients)**
Ischemic Heart Disease	2	1		3
Near (Pre) Syncope	2	6		8
Other patient code	289	311	76	676
Palpitations	4	14		18
Pericardial Effusion	4	1	2	7
Peripheral Edema	7	2	2	11
Peripheral Vascular Disease	1	2	2	5
Pleural Effusion	8	4	1	13
Rash	3	7	1	11
Shoulder Pain/Discomfort	30	33	3	66
Sleep Problems	12	16	3	31
Stroke/CVA	4	4		8
Syncope	8	4		12
Thrombosis		3		3
Coronary Sinus Dissection	6	3		9
Hemo/Pneumothorax	1	1	1	3
Other implant-related	4	2		6
Electromagnetic Interference		1		1
Far-field R wave sensing	2	2		4
Generator/ ICD migration		1		1
Inappropriate Programming	4			4
Muscle Stimulation-Diaphragm	14	24		38
Muscle Stimulation-Pectoral	3	5		8
Other ICD-related	18	16		34
Oversensing	3	5		8
PMT		1		1
Pacemaker Syndrome		1		1
Pain at Pocket Site	58	72	13	143
Pocket Infection	5	2		7

Table 3. Summary of Observations, Part 1				
Event Type	**Control (Patients)**	**Treatment (Patients)**	**Not Randomized**	**Total Events (Patients)**
Pocket Seroma/hematoma	18	9		27
Swelling at pocket site	2	3	1	6
Undersensing	2	1		3
Elevated Pacing Thresholds	6	9		15
Failure to Capture, loss of capture	2	1	2	5
Lead Dislodgement	3	2		5
Other lead-related	6	3	1	10
Programmer/Software anomaly		2		2
Other	24	32	3	59
Total	**915**	**929**	**163**	**2007**

Table 4. Summary of Observations, Part 2

Event Type	Control Group			Treatment Group			Not Randomized			Total		
	Pre-Implant	Implant	Post-Implant	Pre-Implant	Implant	Post-Implant	Pre-Implant	Implant	Post-Implant	Pre-Implant	Implant	Post-Implant
2187/2188 Related			4			4			2			10
4189 Related		7	17			33					7	50
RA Lead Related		2	5		1	5	1				3	10
RV Lead Related		1	6		2	8				1	3	14
Implant Tool Related		6			7			3			16	
7272 Related			46			40			4			90
Heart Failure Decompensation	1		62	1		53			12	2		127
Not Device Related	22	3	497	20		522	8		100	50	3	1119
Other			25	1	2	31			2	1	2	58
Possibly Device Related	1		40		1	25			4	1	1	69
Possibly Procedure Related	4	4	34	4		47	1	1	7	9	5	88
Procedure Related	4	2	114	2	4	103	1	3	14	7	9	231
Other System Related			6			11						17
Unknown			2	1		1				1		3
Total	**32**	**25**	**858**	**29**	**17**	**883**	**11**	**7**	**145**	**72**	**49**	**1886**

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Summary of Patient Deaths

A total of 75 deaths were reported in the 659 enrolled patients. Of these deaths, 3 occurred in 23 patients in whom an implant was not attempted; 13 occurred in 69 patients in whom an implant attempt was unsuccessful; 8 occurred in 13 patients who were implanted with an InSync ICD system but were not randomized; and 51 occurred in 554 patients who were implanted with an InSync ICD system and randomized to either the control or treatment group. **Table 5** below provides summary information on these deaths.

Table 5. Summary of Patient Deaths

	Patient ID	7272 Implant Date	Rand. Date	Death Date	Days Elapsed Post-Implant	NYHA Class	Rand. Mode	Mode at Death	Primary Cause of Death (PI)	Death Classification (PI)	Related to Procedure (PI)?	Related to System (PI)?	Events Committee Review Date	Events Committee Classification
1	100190002	8-Dec-99	16-Dec-99	8-Jul-01	570	III	ON	ON	End Stage CHF	Non-sudden cardiac	NO	NO	17-Oct-01	Medical, Progressive Heart Failure (end-stage failure), Cardiac, Non-Sudden, Witnessed; Not related to device or procedure
2	100190009	19-Jul-00	26-Jul-00	12-Feb-01	208	III	OFF	ON	Congestive Heart Failure	Non-sudden cardiac	NO	Unknown	9-Apr-01	Medical, progressive HF (end-stage failure), cardiac, non-sudden; not related to a device or procedure.
3	100190015	Not implanted with 7272	Not randomized	23-Aug-00	n/a	III	n/a	n/a	Cardiac Arrest	Sudden cardiac	NO	NO	5-Feb-01	Medical, arrhythmic (tachy), cardiac, sudden, witnessed death; not related to a device or procedure.
4	100190023	12-Oct-00	13-Oct-00	11-Feb-01	122	III	OFF	OFF	CHF/ Cardiomyopathy	Non-sudden cardiac	NO	NO	28-Aug-01	Pending
5	100190024	Not implanted with 7272	Not randomized	13-Oct-00	n/a	IV	n/a	n/a	Sudden death of unknown etiology	Sudden cardiac	NO	NO	5-Feb-01	Medical, arrhythmic (tachy), cardiac, sudden, witnessed death; not related to a device or procedure.
6	100190206	25-Oct-00	27-Oct-00	11-Jan-01	79	III	OFF	OFF	Cardiac Arrest	Non-sudden cardiac	NO	NO	9-Apr-01	Medical, Progressive HF (end-stage failure), Cardiac, Non Sudden, Witnessed: Not related to device or procedure
7	101540004	23-Mar-01	28-Mar-01	1-May-01	39	III	ON	ON	Unknown	Sudden cardiac	NO	NO	28-Aug-01	Pending

Table 5. Summary of Patient Deaths

	Patient ID	7272 Implant Date	Rand. Date	Death Date	Days Elapsed Post-Implant	NYHA Class	Rand. Mode	Mode at Death	Primary Cause of Death (PI)	Death Classification (PI)	Related to Procedure (PI)?	Related to System (PI)?	Events Committee Review Date	Events Committee Classification
8	102210001	6-Dec-99	Not randomized	3-Mar-00	88	III	n/a	OFF	Mitral Valve Disease	Non-sudden cardiac	NO	NO	5-Feb-01	Medical, progressive heart failure, cardiac, non-sudden death; not related to a device, related to procedure.
9	102210003	25-Feb-00	2-Mar-00	22-Sep-00	210	III	OFF	OFF	End Stage Cardiomyopathy	Non-sudden cardiac	NO	NO	5-Feb-01	Medical, progressive heart failure, cardiac, non-sudden death; not related to a device or procedure.
10	102210004	Not implanted with 7272	Not randomized	27-Jun-01	54	III	n/a	n/a	Chronic congestive heart failure	Non-sudden cardiac	NO	NO	17-Oct-01; 6-Nov-01	Pending
11	102210008	29-Sep-00	17-Nov-00	25-Apr-01	208	III	OFF	OFF	Cardiac Arrest	Non-sudden cardiac	NO	NO	17-Jul-01	Medical, progressive HF, cardiac, non-sudden; not related to device or procedure
12	102210016	23-Jan-01	30-Jan-01	20-Feb-01	28	IV	ON	ON	Congestive Heart Failure	Non-sudden cardiac	NO	NO	9-Apr-01	Medical, progressive HF (end-stage failure), cardiac, non-sudden; not related to a device or procedure.
13	102480001	1-Mar-01	6-Mar-01	1-Jun-01	92	IV	ON	ON	End stage ischemic cardiomyopathy	Non-sudden cardiac	NO	NO	17-Oct-01	Medical, Progressive HF (end-stage failure), Cardiac, Non-Sudden, Witnessed; Not related to device or procedure
14	105230001	1-May-00	8-May-00	5-Jul-00	65	IV	ON	ON	Coronary Artery Disease	Non-sudden cardiac	NO	NO	5-Feb-01	Medical, progressive heart failure, cardiac, non-sudden death; not related to a device or procedure.
15	107800001	7-Dec-99	Not Randomized	26-Dec.-00	384	III	n/a	n/a	Dilated Cardiomyopathy	Non-sudden cardiac	NO	NO	17-Jul-01	Medical, progressive HF, cardiac, non-sudden; not related to device or procedure

Table 5. Summary of Patient Deaths

	Patient ID	7272 Implant Date	Rand. Date	Death Date	Days Elapsed Post-Implant	NYHA Class	Rand. Mode	Mode at Death	Primary Cause of Death (PI)	Death Classification (PI)	Related to Procedure (PI)?	Related to System (PI)?	Events Committee Review Date	Events Committee Classification
16	107800002	26-May-00	Not randomized	26-Oct-00	153	III	n/a	ON	Dilated cardiomyopathy	Non-sudden cardiac	NO	NO	17-Jul-01	Medical, progressive HF, cardiac, non-sudden; not related to device or procedure
17	109620004	24-Mar-00	29-Mar-00	28-Apr-00	35	IV	OFF	OFF	Cardiac dysrhythmia, clinical	Sudden cardiac	NO	NO	5-Feb-01	Medical, arrhythmic (tachy), cardiac, sudden, witnessed death; not related to device or procedure.
18	109620005	27-Jun-00	1-Aug-00	25-Jul-01	393	III	ON	ON	Heart Failure (waiting for documentation)	Non-sudden cardiac	NO	NO	17-Oct-01; 6-Nov-01	Medical, Other-Respiratory Failure, Non-Cardiac, Non-Sudden, Witnessed; Not related to device or procedure
19	109620010	Not implanted with 7272	Not randomized	16-Dec-00	n/a	II	n/a	n/a	Myocardial infarction	Sudden cardiac	NO	NO	12-Mar-01	Medical, arrhythmic (tachy), cardiac, sudden, witnessed death; not related to a device, is related to procedure.
20	109620012	7-Mar-01	Not randomized	8-Mar-01	1	II	n/a	ON	Unknown	Unknown (pending autopsy)	NO	NO	9-April-01; 6-Nov-01	Medical, other-acute coronary syndrome, cardiac, sudden, non- witnessed death; not related to a device or procedure.
21	110950003	5-Nov-99	5-Nov-99	4-Apr-00	151	II	OFF	OFF	NonQ-wave myocardial Infarction, Cardiogenic Shock	Non-sudden cardiac	NO	NO	5-Feb-01	Medical, acute myocardial infarction, cardiac, non-sudden death; not related to a device or procedure.
22	110950004	15-Nov-99	16-Nov-99	7-Dec-99	22	II	ON	ON	Cardiopulmonary Arrest	Sudden cardiac	NO	Unknown	12-Feb-01; 5-Mar-01	Medical, arrhythmic (tachy), cardiac, sudden, witnessed death; not related to a device or procedure.

Table 5. Summary of Patient Deaths

	Patient ID	7272 Implant Date	Rand. Date	Death Date	Days Elapsed Post-Implant	NYHA Class	Rand. Mode	Mode at Death	Primary Cause of Death (PI)	Death Classification (PI)	Related to Procedure (PI)?	Related to System (PI)?	Events Committee Review Date	Events Committee Classification
23	110950007	4-Jan-00	5-Jan-00	8-Feb-00	35	II	ON	ON	Cardiopulmonary Arrest	Sudden cardiac	NO	Unknown	5-Feb-01	Medical, arrhythmic (tachy), cardiac, sudden, witnessed death; not related to a device or procedure.
24	110950010	12-Jan-00	18-Jan-00	31-Mar-01	444	II	OFF	ON	Malignant Neoplasm of Liver	Non-cardiac	NO	NO	17-Oct-01	Medical, Other-Hepatobiliary Carcinoma, Non-Cardiac, Non-Sudden, Witnessed; Not related to device or procedure
25	110950024	12-Jun-00	15-Jun-00	23-Jun-01	376	II	OFF	ON	Cardiomyopathy	Unknown	NO	NO	17-Oct-01; 6-Nov-01	Unknown, non-witnessed; Not related to device or procedure
26	110950026	24-Jul-00	3-Aug-00	29-Nov-00	128	IV	OFF	OFF	Cardiomyopathy	Non-sudden cardiac	NO	NO	9-Apr-01	Medical, progressive HF (end-stage failure), cardiac, non-sudden.
27	110950034	17-Jan-01	24-Jan-01	13-Apr-01	86	III	ON	ON	Cardiomyopathy	Non-sudden cardiac	NO	NO	28-Aug-01	Medical, Progressive HF (end-stage failure), Cardiac, Non-Sudden, Witnessed; Not related to device or procedure
28	110950036	16-Feb-01	20-Feb-01	18-Apr-01	61	III	ON	ON	Ventricular and atrial fibrillation	Unknown	NO	NO	17-Jul-01	Unknown cause of death.
29	112380002	4-Jan-00	7-Jan-00	1-Feb-00	28	IV	OFF	OFF	EMD due to end stage heart failure	Sudden cardiac	NO	NO	5-Feb-01; 9-Apr-01	Medical, progressive HF, cardiac, non-sudden; not related to device or procedure

Table 5. Summary of Patient Deaths

	Patient ID	7272 Implant Date	Rand. Date	Death Date	Days Elapsed Post-Implant	NYHA Class	Rand. Mode	Mode at Death	Primary Cause of Death (PI)	Death Classification (PI)	Related to Procedure (PI)?	Related to System (PI)?	Events Committee Review Date	Events Committee Classification
30	112380005	8-Sep-00	15-Sep-00	19-Sep-01	376	III	ON	ON	Progressive Heart Failure	Non-sudden cardiac	NO	NO	17-Oct-01	Medical, Progressive HF (end-stage failure), Cardiac, Non-Sudden, Witnessed; Not related to device or procedure
31	112620015	Not implanted with 7272	Not randomized	25-May-01	227	III	n/a	n/a	Unknown	Unknown	NO	NO	17-Jul-01	Medical, progressive Hf, cardiac, non-sudden; not related to device or procedure
32	113720005	Not implanted with 7272	Not randomized	7-Dec-00	n/a	III	n/a	n/a	Cardiac Arrest due to Heart Failure	Sudden cardiac	NO	NO	9-Apr-01	Medical, progressive HF (end-stage failure), cardiac, non-sudden.
33	113720007	19-Oct-00	24-Oct-00	25-Jul-01	279	III	ON	OFF	Lung Carcinoma	Non-cardiac	NO	NO	17-Oct-01: 6-Nov-01	Medical, Carcinoma of the Lung, Non-Cardiac, Non-Sudden, Witnessed; Not related to device or procedure
34	113720014	24-May-01	Not randomized	22-Sep-01	121	III	n/a	n/a	Heart Failure	Non-sudden cardiac	NO	NO	Pending	Pending
35	115390001	5/4/2000	8-May-00	27-Jan-01	268	II	ON	ON	Renal Failure/ Liver Failure	Non-sudden cardiac	NO	NO	9-Apr-01	Medical, Progressive HF, Cardiac, Non-Sudden, Not related to device or procedure
36	115390004	20-Jun-00	26-Jun-00	22-Feb-01	194	III	OFF	ON	Respiratory Arrest/Lung Cancer	Sudden cardiac	NO	NO	9-Apr-01	Medical, other-lung cancer, non-cardiac, non-sudden; not related to a device or procedure.

Table 5. Summary of Patient Deaths

	Patient ID	7272 Implant Date	Rand. Date	Death Date	Days Elapsed Post-Implant	NYHA Class	Rand. Mode	Mode at Death	Primary Cause of Death (PI)	Death Clas-sification (PI)	Related to Procedure (PI)?	Related to System (PI)?	Events Committee Review Date	Events Committee Classification
37	115390006	10-Aug-00	14-Aug-00	26-Dec-00	138	III	ON	ON	Sepsis	Non-sudden cardiac	NO	NO	12-Mar-01	Medical, other (cancer, sepsis), non-cardiac, non-sudden death; not related to a device or procedure.
38	115390008	24-Aug-00	28-Aug-00	18-Mar-01	206	III	OFF	ON	Rean Failure	Sudden cardiac	NO	NO	9-Apr-01	Medical, progressive HF (end-stage failure), cardiac, non-sudden; not related to a device or procedure.
39	115390009	31-Aug-00	6-Sep-00	27-Dec-00	118	III	OFF	ON	Cardiogenic Shock	Non-sudden cardiac	NO	NO	9-Apr-01	Medical, Progressive HF, Cardiac, Non-Sudden,Witnessed; Not related to device or procedure
40	115390011	5-Dec-00	Not randomized	13-Jan-01	39	III	n/a	OFF	Respiratory Arrest/CHF	Sudden cardiac	NO	NO	12-Mar-01	Unknown cause of death.
41	115390013	16-Jan-01	22-Jan-01	23-Aug-01	219	IV	ON	ON	Sepsis	Non-Cardiac	NO	NO	17-Oct-01; 6-Nov-01	Medical, Other-Malignancy, Sepsis, Non-Cardiac, Non-Sudden, Witnessed; Not related to device or procedure
42	117650001	4-Nov-99	Not Randomized	19-Jul-01	623	II	n/a	n/a	Electromechanical dissociation due to end stage heart failure	Non-sudden cardiac	NO	NO	17-Oct-01	Medical, Progressive HF (end- stage failure), Cardiac, Non-Sudden, Witnessed; Not related to device or procedure
43	118920020	17-Nov-00	28-Nov-00	10-May-01	174	III	OFF	OFF	Congestive Heart Failure	Non-sudden cardiac	NO	NO	17-Jul-01	Medical,other-pneumonia, non-cardiac, non-sudden: not related to device or procedure

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Table 5. Summary of Patient Deaths

	Patient ID	7272 Implant Date	Rand. Date	Death Date	Days Elapsed Post-Implant	NYHA Class	Rand. Mode	Mode at Death	Primary Cause of Death (PI)	Death Clas-sification (PI)	Related to Procedure (PI)?	Related to System (PI)?	Events Committee Review Date	Events Committee Classification
44	118920025	23-Apr-01	Not randomized	12-Jun-01	50	III	n/a	ON	End-stage cardiomyopathy with congestive heart failure	Non-sudden cardiac	NO	NO	28-Aug-01; 17-Oct-01	Medical, Progressive HF (end-stage failure), Cardiac, Non-Sudden, Witnessed; Not related to device or procedure
45	118920026	Not implanted with 7272	Not randomized	25-Apr-01	n/a	IV	n/a	n/a	Progressive Worsening of Heart Failure	Non-sudden cardiac	n/a	n/a	17-Jul-01	Medical, progressive HF, cardiac, non-sudden, witnessed: not related to device or procedure
46	119510003	2-Nov-00	8-Nov-00	12-Nov-00	10	III	ON	ON	Severe Cardiomyopathy	Sudden cardiac	NO	NO	5-Feb-01; 9-Apr-01	Medical, arrhythmic (tachy), cardiac, sudden, witnessed; not related to device or procedure
47	119510020	14-Jun-01	Not randomized	4-Jul-01	20	IV	n/a	n/a	Respiratory Failure	Non-Cardiac	NO	NO	28-Aug-01; 6-Nov-01	Medical, Other-renal failure, non-cardiac, non-sudden, witnessed: not related to device ; is related to procedure
48	120340001	13-Jan-00	Not randomized	4-Jun-01	507	III	n/a	n/a	Cardiac/respiratory failure	Non-sudden cardiac	NO	NO	17-Oct-01	Medical, Progressive HF (end-stage failure), Cardiac, Non-Sudden, Witnessed; Not related to device or procedure
49	120340008	10-Jan-01	11-Jan-01	25-Jan-01	15	II	OFF	OFF	Cardiopulmonary Arrest	Sudden cardiac	NO	NO	28-Aug-01	Medical, Arrhythmic Death (Tachy),Cardiac, Sudden, Witnessed; not related to device or procedure
50	123650003	9-Nov-00	17-Nov-00	14-Apr-01	156	III	ON	ON	Congestive Heart Failure	Non-sudden cardiac	NO	NO	17-Jul-01	Medical,progressive, cardiac, non-sudden, non-witnessed: not related to device or procedure

Table 5. Summary of Patient Deaths

	Patient ID	7272 Implant Date	Rand. Date	Death Date	Days Elapsed Post-Implant	NYHA Class	Rand. Mode	Mode at Death	Primary Cause of Death (PI)	Death Clas-sification (PI)	Related to Procedure (PI)?	Related to System (PI)?	Events Committee Review Date	Events Committee Classification
51	123850003	24-Feb-00	25-Feb-00	26-Jul-00	153	III	OFF	OFF	Acute Renal Failure	Non-cardiac	NO	NO	5-Feb-01; 12-Mar-01	Medical, progressive heart failure, cardiac, non-sudden death; not related to a device or procedure.
52	123850004	29-Mar-00	30-Mar-00	8-Aug-00	132	III	OFF	ON	Arrhythmia	Sudden cardiac	NO	NO	5-Feb-01	Medical, arrhythmic (tachy), cardiac, sudden, witnessed death; not related to a device or procedure.
53	127080002	28-Sep-00	29-Sep-00	8-Jul-01	283	III	ON	ON	Cardiomyopathy	Non-sudden cardiac	NO	Unknown	17-Oct-01	Medical, Progressive HF (end-stage failure), Cardiac, Non-Sudden, Witnessed; Not related to device or procedure
54	127080007	9-Mar-01	19-Mar-01	14-Jun-01	97	IV	OFF	OFF	Heart Failure	Non-sudden cardiac	NO	NO	28-Aug-01	Medical, Progressive HF (end-stage failure), Cardiac, Non-Sudden, Witnessed: Not device or procedure related
55	127670003	8-Mar-00	9-Mar-00	24-Mar-01	381	III	ON	ON	Congestive Heart Failure	Unknown	NO	NO	28-Aug-01	Pending
56	133260025	9-May-01	Not randomized	7-Jul-01	102	III	n/a	n/a	Septicemia with Cardio-Pulmonary Arrest	Non-sudden cardiac	NO	NO	17-Oct-01; 6-Nov-01	Medical, Other-septicemia, Non-Cardiac, Non-Sudden, Witnessed; Not related to device or procedure
57	135590007	Not implanted with 7272	Not randomized	19-Apr-01	139	III	n/a	n/a	Unknown	Unknown	NO	NO	28-Aug-01	Unknown cause of death.

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Table 5. Summary of Patient Deaths

	Patient ID	7272 Implant Date	Rand. Date	Death Date	Days Elapsed Post-Implant	NYHA Class	Rand. Mode	Mode at Death	Primary Cause of Death (PI)	Death Clas-sification (PI)	Related to Procedure (PI)?	Related to System (PI)?	Events Committee Review Date	Events Committee Classification
58	135640006	8-Jan-01	15-Jan-01	12-Jun-01	155	IV	ON	ON	Congestive Heart Failure	Non-sudden cardiac	NO	NO	28-Aug-01	Medical, Progressive HF (end-stage failure), Cardiac, Non-Sudden, Witnessed,:Not related to device or procedure.
59	142270001	11-Feb-00	1-Mar-00	5-Jan-01	328	III	ON	ON	Primary Cardiomyopathy (secondary CHF)	Non-sudden cardiac	NO	NO	17-Jul-01	Medical, progressive HF, cardiac, non-sudden; not related to device or procedure
60	142270003	5-May-00	8-May-00	24-Dec-00	233	II	OFF	ON	Pump Failure	Non-sudden cardiac	NO	NO	5-Feb-01	Medical, progressive heart failure, cardiac, non-sudden death; not related to a device or procedure.
61	147870011	8-May-00	11-May-00	24-Jan-01	261	II	ON	ON	Hyperkalemia	Non-sudden cardiac	NO	NO	9-Apr-01	Medical, progressive HF (end-stage failure), cardiac, non-sudden; not related to a device or procedure.
62	147870013	14-Jun-00	20-Jun-00	23-Jul-01	404	III	OFF	ON	Heart Failure	Non-sudden cardiac	NO	NO	17-Oct-01	Medical, Progressive HF (end-stage failure), Cardiac, Non-Sudden, Witnessed; Not related to device or procedure
63	147870018	1-Sep-00	8-Sep-00	22-May-01	263	III	OFF	ON	Dilated Cardiomyopathy	Non-sudden cardiac	NO	NO	17-Jul-01	Medical, progressive HF, cardiac, non-sudden; not related to device or procedure
64	147870034	16-Apr-01	18-Apr-01	22-Jun-01	67	III	ON	ON	Congestive Heart Failure	Non-Sudden cardiac	NO	NO	17-Oct-01; 6-Nov-01	Medical, Progressive HF (end-stage failure), Cardiac, Non-Sudden, Witnessed; Not device or procedure
65	236670006	Not implanted with 7272	Not randomized	4-Feb-01	n/a	III	n/a	n/a	End Stage Cardiomyopathy	Non-sudden cardiac	NO	NO	12-Mar-01	Medical, progressive heart failure, cardiac, non-sudden death; not related to a device or procedure.

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Table 5. Summary of Patient Deaths

	Patient ID	7272 Implant Date	Rand. Date	Death Date	Days Elapsed Post-Implant	NYHA Class	Rand. Mode	Mode at Death	Primary Cause of Death (PI)	Death Clas-sification (PI)	Related to Procedure (PI)?	Related to System (PI)?	Events Committee Review Date	Events Committee Classification
66	236670013	22-Feb-01	27-Feb-01	15-Apr-01	52	IV	OFF	OFF	End Stage Cardiomyopathy	Non-sudden cardiac	NO	NO	17-Jul-01	Medical, progressive HF, cardiac, non-sudden; not related to device or procedure
67	377150001	11-May-00	15-May-00	30-Jun-01	415	III	OFF	OFF	Bilateral brain hemorrhage led to cardiac arrest	Non-sudden cardiac	NO	NO	28-Aug-01	Pending
68	381480006	21-Jul-00	Not randomized	2-Jul-01	346	III	n/a	n/a	Heart Failure	Non-sudden cardiac	NO	NO	17-Oct-01; 6-Nov-01	Pending
69	381480008	13-Sep-00	18-Sep-00	19-Dec-00	97	III	OFF	OFF	Sepsis/Cardiogenic Shock	Non-sudden cardiac	NO	NO	5-Feb-01	Medical, progressive heart failure, cardiac, non-sudden death; not related to a device or procedure.
70	381480010	2-Nov-00	Not randomized	5-Feb-01	95	II	n/a	n/a	Heart Failure	Non-sudden cardiac	NO	NO	17-Oct-01; 6-Nov-01	Medical, Progressive HF (end-stage failure), Cardiac, Non-Sudden; Not related to device or procedure
71	387050002	Not implanted with 7272	Not randomized	23-Nov-00	n/a	III	n/a	n/a	Cardiopulmonay Arrest	Non-sudden cardiac	NO	NO	5-Feb-01	Unknown cause of death.
72	408490005	22-Feb-01	1-Mar-01	4/4/2001	41	III	OFF	ON	Multi-organ failure	Non-cardiac	NO	NO	17-Jul-01	Medical, progressive, Cardiac, non-sudden: not related to device or procedure
73	451320007	19-Apr-01	23-Apr-01	11-Jul-01	83	III	OFF	ON	Cardiopulmonary Arrest	Non-sudden cardiac	NO	NO	17-Oct-01	Medical, Progressive HF (end-stage failure), Cardiac, Non-Sudden, Witnessed; Not related to device or procedure

Table 5. Summary of Patient Deaths

	Patient ID	7272 Implant Date	Rand. Date	Death Date	Days Elapsed Post-Implant	NYHA Class	Rand. Mode	Mode at Death	Primary Cause of Death (PI)	Death Classification (PI)	Related to Procedure (PI)?	Related to System (PI)?	Events Committee Review Date	Events Committee Classification
74	465570001	25-Jan-00	26-Jan-00	10-Jul-00	167	III	ON	ON	Ventricullar Fibrillation: Sudden Death	Sudden cardiac	NO	NO	5-Feb-01	Medical, arrhythmic (tachy), cardiac, sudden, witnessed death; not related to a device or procedure.
75	465570003	Not implanted with 7272	Not randomized	21-Jun-01	415	IV	n/a	n/a	Renal Failure	Non-cardiac	NO	NO	28-Aug-01	Medical, Progressive HF (end-stage failure), non-cardiac, Non-Sudden; not related to a device or procedure

Potential adverse events associated with ICD systems include (in alphabetical order): Acceleration of arrhythmias (caused by ICD); air embolism; bleeding; chronic nerve damage; erosion; excessive fibrotic tissue growth; extrusion; fluid accumulation; formation of hematomas or cysts; inappropriate shocks; infection; keloid formation; lead abrasion and discontinuity; lead migration / dislodgment; myocardial damage; pneumothorax; potential mortality due to inability to defibrillate or pace; shunting current or insulating myocardium during defibrillation; thromboemboli; venous occlusion; venous or cardiac perforation.

The adverse events related to the use of transvenous leads include, but are not limited to, the follow patient-related conditions when the lead is being inserted and/or repositioned: cardiac dissection, cardiac perforation, cardiac tamponade, coronary sinus dissection, endocarditis, fibrillation or other arrhythmias, heart block, heart wall or vein wall rupture, infection, muscle or nerve stimulation, myocardial irritability, pericardial effusion, pericardial rub, pneumothorax, thrombolytic and air embolism, thrombosis, and valve damage (particularly in fragile hearts).

Alternative Practices and Procedures

The present established therapies for the treatment of heart failure and sudden cardiac death and the associated signs and symptoms include pharmacological therapy, heart transplantation, or other surgical procedures.

Marketing History

The InSync ICD device and Attain Models 2187 / 2188 /4189 leads are currently distributed commercially outside the United States. Specifically, these devices are approved for sale in the European Community, Australia, Canada, and Latin America (Argentina, Uruguay). The Model 2187 and 2188 leads were approved by FDA on August 28, 2001 (P010015).

As of October 31, 2001, approximately 1,600 InSync ICD Model 7272 devices, 5,200 Attain Model 2187 leads, 1,200 Attain Model 2188, and 1,450 Attain Model 4189 leads have been distributed commercially outside the United States.

In the United States, there have been approximately 1,300 Attain Model 2187, and 120 Attain Model 2188 leads commercially distributed since approval in August, 2001.

Neither the device nor leads have been withdrawn from the market in any country for any reason related to the safety and effectiveness of the device.

Summary of Pre-clinical Studies

Non-clinical Laboratory Studies – InSync ICD Model 7272

IC / Hybrid

The InSync ICD Model 7272 is a derivation of the GEM DR Model 7271 and GEM II DR Model 7273 systems with biventricular pacing capability added for cardiac resynchronization. The InSync ICD Model 7272 components are identical or similar to those used in the GEM DR Model 7271.

Major Components of the InSync ICD Model 7272

Component	Comparison to Model 7271 GEM DR	Qualification
Connector Module	• Polyurethane module that contains lead ports. The module is bonded to device can • Similar to Model 7271 GEM DR. LV lead port added to the connector module	• InSync ICD Model 7272 Connector Qualification Testing
Battery (2)	• Same lithium-silver vanadium oxide cells (Li/SVO) developed by the Promeon Division of Medtronic	• By similarity – same component as Model 7271 GEM DR
High Voltage Capacitors (2)	• Two HV output capacitors provide energy for cardioversion and defibrillation therapies	• By similarity – same component as Model 7271 GEM DR
Antenna	• The antenna sends/receives device communications through bi-directional telemetry • Same component used in Model 7271 GEM DR	• By similarity – same component as Model 7271 GEM DR
Transformer	• The transformer converts low voltage from the battery to high voltage for the HV capacitors • Same component used in Model 7271 GEM DR	• By similarity – same component as Model 7271 GEM DR
Reedswitch	• The reedswitch is a magnetically controlled mechanical switch that, once closed, signals the device that telemetry communications with the external programmer can occur • Same component used in Model 7271 GEM DR	• By similarity – same component as Model 7271 GEM DR

Qualification activities performed on the InSync ICD Model 7272 tested the electrical and physical integrity of the connector module, adhesive interfaces, and block / MBC-to-feedthrough welds (qualified by similarity to GEM Model 7227Cx). The connector design met all connector-specific requirements specified in the InSync ICD product specification and the IS-1 and DF-1 international standards for connectors (ISO 5841-3 and ISO 11318, respectively). Qualification demonstrated that the connector module met these requirements with 90% reliability at a 90% confidence level.

Connector Test	**Result**
1. Insertion / Withdrawal (Go Gauge & Lead Connector)	Passed
2. IS-1 Electrical Leakage Impedance	Passed
3. DF-1 Electrical Isolation	Passed
4. DF-1 Current Carrying	Qualified by Similarity
5. Suture Hole Pull Force	Passed

Device qualification testing was performed to ensure that the InSync ICD Model 7272 performs acceptably in typical shipping, handling and operating environments. The device qualification testing is summarized below. The results demonstrated that the InSync ICD Model 7272 will perform acceptably in typical shipping, handling, and operating environments and is qualified for its intended use.

Test	Sample Size	Acceptance Criteria	Results
Environmental	10	**Temperature Storage:** Meets Section 26.2 of European Standard prEN45502-2-2 **Mechanical Vibration:** Meets Section 23.2 of European Standard prEN45502-2-2. **Mechanical Shock:** Show no visible signs of damage which affects function of device after a shock having a change in velocity (dV) or 118 inches per second and a duration of 1ms in each of six axes. Simulates a drop of 45cm (18") to a hard surface.	Meets Acceptance Criteria
Electromagnetic Compatibility	22	**Electromagnetic Interference:** Meets requirements of the 1975 AAMI Pacemaker Standard. Also meets performance standards at additional frequencies, including radiated continuous wave and pulsed electromagnetic fields and conducted continuous wave sinusoidal currents.	Meets Acceptance Criteria
	3	**Cellular Phone:** Not susceptible to interference from analog or digital cellular telephones, including the following systems: AMPS, TDMA-50 (NADC), GSM, DCS, and CDMA.	
	22	**X-ray:** Testing waived based on similarity to GEM DR Model 7271.	
	22	**Electrosurgical Cautery:** Must withstand spark cutting, spark coagulating, and sine cutting modes and energies.	
	22	**Transthoracic Defibrillation:** 1000V and 1500V.	
Design Verification Testing	3	Because of hardware similarity between InSync ICD and GEM DR, verification testing was conducted only on hardware components which may be affected by the biventricular pacing modifications.	Meets Acceptance Criteria

Battery

The InSync ICD device utilizes the same Promeon Sigma lithium-silver vanadium oxide (Li/SVO) cells that are used by the previously approved GEM DR Model 7271.

Biocompatibility Testing

The materials used in the InSync ICD device are identical to those used in the Medtronic GEM DR Model 7271. These materials include: titanium, silicone adhesive, silicone rubber, and polyurethane). No new materials or processes were introduced with the InSync ICD Model 7272 that would introduce new issues of biocompatibility.

Performance Standards

Performance standards for implantable cardioverter-defibrillators have not been promulgated per Section 514 of the Federal Food, Drug and Cosmetic Act; therefore no action is required.

Non-clinical Laboratory Testing – Software Validation

System testing of the InSync ICD system (InSync ICD Model 7272, Model 9969 Software, Model 9790C programmer, and accessories) was performed to ensure that all system components work together appropriately under simulated clinical situations. The InSync ICD Model 7272 performed appropriately during system testing.

The Model 9969 Software is based on the GEM DR software (Model 9964), with the addition of the following features:

- **Biventricular Pacing.** Allows for bradycardia pacing in both the right and left ventricle. The clinician has the option of selecting which ventricle (right, left, or both) the pacing pulses will be delivered in.
- **Biventricular Anti-Tachy Pacing (ATP).** Allows for ATP in both the right and left ventricle. The clinician has the option of selecting which ventricle (right, left, or both) the anti-tachy pacing pulses will be delivered in.
- **Left-Sided EGM Sources.** Allows for the display and recording of EGM traces from both the right and left ventricles.

The design qualification, verification, and validation activities performed on the Model 9969 software demonstrated that the Model 9969 software met the design inputs and product specifications.

The InSync ICD system was analyzed to verify that hazard-mitigating actions were implemented for all components of the InSync ICD system. The system hazard analysis verified that all mitigating actions were implemented.

Non-clinical Laboratory Testing – Attain Leads

Environmental Conditioning

Thirty Attain Model 2187, 30 Attain Model 2188, and 30 Attain Model 4189 leads were subjected to four cycles of ethylene oxide (EtO) sterilization and five cycles of thermal shock (-45°C to +70°C) prior to undergoing mechanical and electrical testing. No damage or degradation to the test leads was noted following sterilization and thermal shock.

Mechanical Testing

Thirty Attain Model 2187, 30 Attain Model 2188, and 30 Attain Model 4189 leads were subjected to the following mechanical tests: connector mating insertion / withdrawal, leak testing, lead composite pull testing (minimum 1.0 lb tensile strength), conductor joint testing (minimum 3.0 lb distal, 2.5 lb proximal), anchoring sleeve suture test and stylet insertion / withdrawal testing. All leads met all test requirements. Twenty-two Attain Model 2188 and 22 Attain Model 4189 leads were subjected to the lead body flex test (B_{50} flex life > 2.0×10^5 cycles at bend radius of 0.236"); all leads exceeded the requirements. Eighteen samples of each model were subjected to the composite distal fatigue test (no failures of metallic joints up to 400,000,000 cycles); all of the samples passed.

Electrical Testing

Thirty Attain Model 2187 and 30 Attain Model 2188 leads were subjected to DC resistance, IS-1 connector impedance (>50K ohms) and Medtronic AC impedance of multipolar leads (>50k ohms); all test requirements were met.

For the Attain Model 4189 lead, 22 leads were subjected to DC resistance, IS-1 connector impedance (>50K ohms) and Medtronic AC impedance testing. All tests requirements were met.

Biocompatibility Testing

All blood-contacting materials used in the Attain Models 2187, 2188 and 4189 leads are identical to those used in PMA-approved Medtronic pacing leads. These currently marketed leads have previously been subject to standard biocompatibility evaluations and their materials of construction have been shown to be safe for human implant. All testing that was performed on previous lead models is applicable to the Attain Models 2187 and 2188.

Medtronic conducted all biocompatibility testing in compliance with Good Laboratory Practices (GLP).

Sterilization Information

The 100% ethylene oxide (EtO) sterilization process used to sterilize all implantable pulse generators and bradycardia pacing leads has been previously approved. This process is considered an overkill sterilization cycle with 12 logs of

reduction. This method is accepted by all major guidelines, including: AAMI, ANSI, DHSS, and ISO/CEN.

All processes used to sterilize a product are validated and qualified according to the major guidelines and standards. Validation consists of determining a maximum allowable bioburden, microbial lethality characteristics, and minimum sterilization process specifications. All Medtronic products intended to contact tissue are specified to have a sterility assurance level (SAL) of at least 10^{-6} (probability of non-sterility).

The procedures used to establish the maintenance and calibration practices for sterilization and aeration equipment are the same as used for other manufacturing equipment. As part of this process qualification, determination of lethality (D-value testing), bioburden, and EtO residual levels were completed.

Package qualification testing was performed on both the device and leads to ensure suitability for their intended purpose. These tests included temperature storage; mechanical shock, vibration and stacking; package leak test; and peel (seal) strength testing. All testing was successfully completed.

Animal Studies

GLP studies were conducted in canines with the InSync ICD Model 7272, Attain Model 2187 cardiac vein lead, Attain Model 2188 coronary sinus lead, and Attain Model 4189 cardiac vein lead. The purpose of the Model 7272 InSync ICD study was to determine that the device provided acceptable performance for sensing and detection of cardiac rhythms, appropriate rejection of sinus arrhythmias, and correct delivery of appropriate programmed therapy. In each of the LV lead canine studies, appropriate pacing, sensing, and thresholds were documented.

Conclusion Concerning Non-clinical Laboratory Testing

Medtronic conducted a hazard analysis on all new features and critical components and then conducted testing to evaluate these and other device features. All test results were found to be acceptable.

Summary of Clinical Studies

Study Design

The Multicenter InSync Randomized Clinical Evaluation (MIRACLE)-ICD is a prospective, multi-center, randomized, double-blind, parallel arm, controlled clinical trial to assess the safety and efficacy of transvenous atrial-based synchronous biventricular resynchronization for heart failure therapy in patients who are indicated for an ICD. The products being evaluated include the Model 7272 InSync ICD and Models 4189, 2187 and 2188 Attain LV leads.

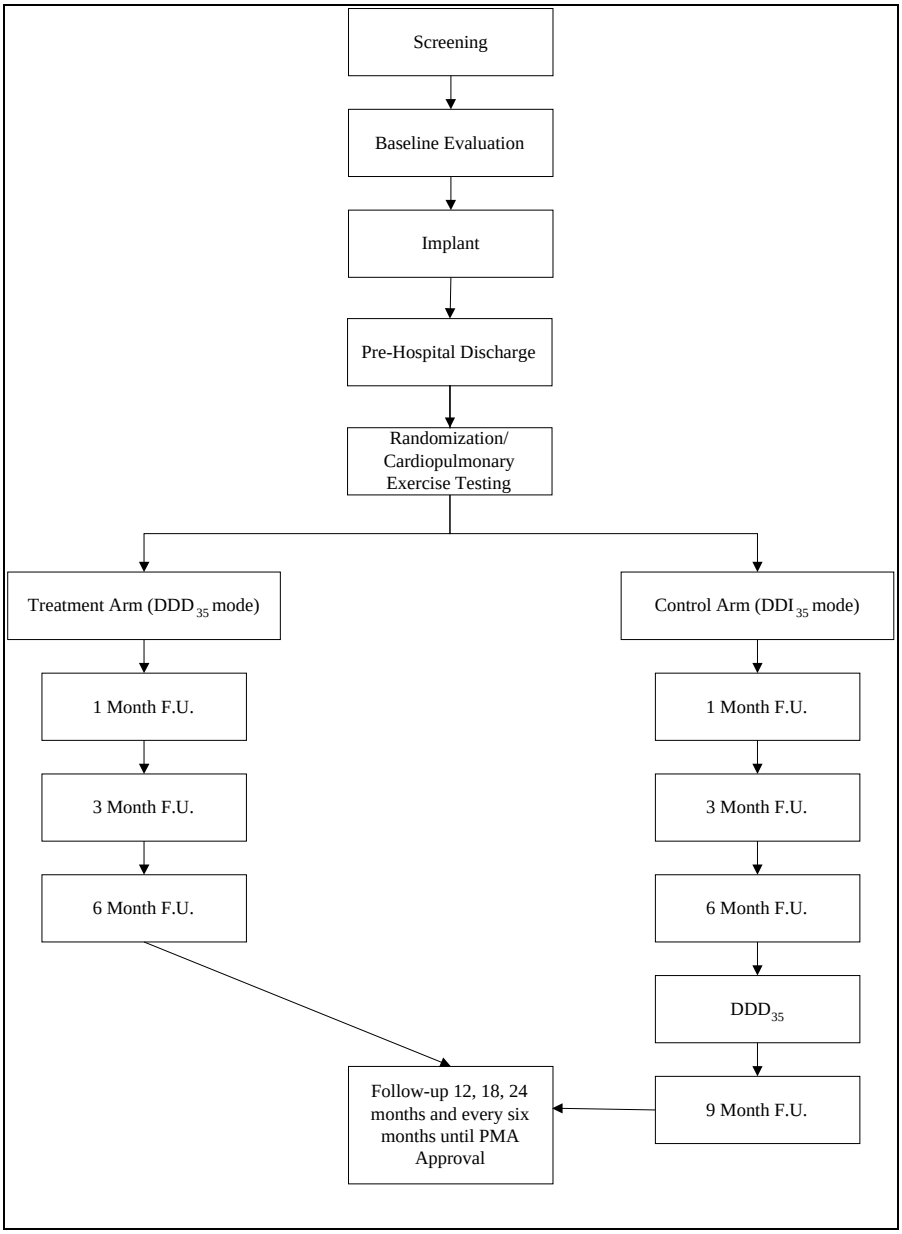

Figure 1. MIRACLE ICD Study Design

Patient Selection

Inclusion Criteria

- Signed study Informed Consent document.
- 18 years of age or older.
- Patients who have had a least one episode of cardiac arrest (manifested by loss of consciousness) due to ventricular tachyarrhythmia;

or

- Patients having recurrent, poorly tolerated, sustained VT that occurs spontaneously or can be induced;

or

- ***Canada Only:*** Patients who have had a prior myocardial infarction, left ventricular ejection fraction less than or equal to 35%, a documented episode of non-sustained VT and inducible ventricular tachyarrhythmia.
- Patients having symptomatic congestive heart failure (NYHA Class II, III, IV) with evidence of ventricular dysynchrony demonstrated by:
- QRS duration ≥ 130 ms,
- LV Ejection Fraction ≤ 35%,
- LV End Diastolic Diameter ≥ 55 mm.
- Stable medical regimen for at least 1 month prior to enrollment (to include at least ACE inhibitors, or ACE inhibitor substitute) patients currently on stable beta blockade regimes for at least 3 months prior to enrollment were allowed in the study. Patients may not be started on beta blockers during the 6-month randomization period.

Exclusion Criteria

- Baseline Six Minute Hall Walk distance greater than 450 meters (Class III and IV only).
- Unstable angina, or acute MI, CABG, or PTCA within the past 3 months.
- Recent CVA or TIA (within the previous 3 months).
- Intermittent positive inotropic drug therapy (intermittent is defined as more than two infusions per week).
- Patients having indications or contraindications for standard cardiac pacing.
- Systolic blood pressure of less than 80 mm or greater than 170 mm.
- Resting Heart rate greater than 140 bpm.
- Serum Creatinine greater than 3 mg/dl.
- Hepatic function (serum) greater than 3 times the upper limit of normal.
- Primary valvular disease.

- Severe primary pulmonary disease.
- Chronic atrial arrhythmias (or cardioversion for afib within the past month) or paroxysmal atrial fib event within the previous month.
- Post heart transplant (patients who are waiting for a heart transplant are allowed entry into the study).
- Enrolled in any concurrent study that may confound the results of this study.
- Patients who are not expected to survive for 6 months of study participation.
- Women who are pregnant or with child bearing potential and who are not on a reliable form of birth control.
- Patients with mechanical right heart valves.
- Patients with VT associated with reversible causes.

Primary Objectives

Primary Safety Objectives

Below are the primary safety objectives defined for this study. Please refer to the appropriate Statistical Methods sections for details on the hypotheses and sample size calculations.

- The InSync ICD Model 7272 implantable cardioverter defibrillator will be considered safe if the freedom from ICD related complications at three months has a 95% lower confidence bound of at least 89%.
- The InSync ICD system, including ICD, left ventricular leads, right ventricular leads, right atrial leads, and software, will be considered safe if the system survival at six months has a 95% lower confidence bound of at least 67%.
- The Attain Model 4189 LV lead will be considered safe if the freedom from lead-related complications at six months has a 95% lower confidence bound of at least 75%.
- The Attain Model 2187 and 2188 LV leads will be considered safe if the freedom from lead-related complications at six months has a 95% lower confidence bound of at least 75%.

Primary Efficacy Objectives

Below are the primary efficacy objectives defined for this study. Please refer to the appropriate Statistical Methods sections for details on the hypotheses and sample size calculations.

NYHA Class III and IV Patients

The InSync ICD system will be considered effective for NYHA Class III and IV patients if the treatment arm shows statistically significant improvement at 6 months over baseline when compared to the control arm in patient functional status.

Improvement in patient functional status will be demonstrated if Quality of Life (QOL), New York Heart Association (NYHA) classification, and/or Six Minute Hall Walk are significantly better in the treatment arm than in the control arm.

Primary LV Lead Effectiveness Objectives

Below are the LV lead efficacy objectives defined for this study. Please refer to the appropriate Statistical Methods sections for details on the hypotheses and sample size calculations.

- The implant success of LV lead Models 4189, 2187, 2188 will be considered adequate if the mean LV implant success rate has a 95% lower confidence bound of greater than or equal to 83%.
- The electrical performance of LV lead Model 4189 will be considered adequate if the mean left ventricular threshold at 6 months has a 95% upper confidence bound of less than or equal to 3.0 V.
- The electrical performance of LV lead Models 2187 and 2188 will be considered adequate if the mean left ventricular threshold at 6 months has a 95% upper confidence bound of less than or equal to 3.0 V.

Secondary Objectives

Below are the secondary objectives defined for this study. Data from all MIRACLE ICD patients will be included. Secondary objectives are intended to provide additional information on patient response and the InSync ICD cardiac resynchronization system performance.

- Change in QRS duration
- Changes in functional capacity for all patients as assessed by cardiopulmonary testing (including peak VO_2 as assessed using a modified Naughton protocol)
- Echocardiographic indices of cardiac function and dimensions (e.g. end diastolic and end systolic volumes, EF, CI, MR, LV mass and filling times, and IV mechanical delay)
- Changes in plasma neurohormone levels
- Patient survival
- Characterization of the electrical performance of the left ventricular leads in a biventricular pacing system
- Summary of all adverse events in this study
- Spontaneous VT/VF therapy efficacy
- CHF composite response of either “worsened”, “improved”, or “unchanged”
- Implant ventricular defibrillation criterion
- Comparison of VT/VF event rates in the control and treatment arms
- ATP therapy efficacy with biventricular pacing
- Healthcare utilization

Demographic Data

Table 6. Comparison of Control and Treatment Patients at Baseline – NYHA Class II, III and IV Patients

InSync ICD Clinical Study – NYHA Class II, III and IV Patients Comparison of Demographics by Treatment Assignment All Randomized Patients				
	Control (OFF) (n=282)	**Treatment (ON) (n=272)**	**All Patients (n=554)**	**P-value**
Gender (n,%)				
Male	231 (81.9%)	217 (79.8%)	448 (80.9%)	0.59
Female	51 (18.1%)	55 (20.2%)	106 (19.1%)	
Age (years)				
Mean ± Standard Deviation	66.0 ± 10.6	65.5 ± 11.9	65.8 ± 11.2	0.95
Median	68.2	68.5	68.4	
Range	25.6 - 87.9	23.0 - 89.0	23.0 - 89.0	
n recorded	282 (100.0%)	272 (100.0%)	554 (100.0%)	
New York Heart Classification (n,%)	106 (37.6%)	86 (31.6%)	192 (34.7%)	0.34
II	156 (55.3%)	164 (60.3%)	320 (57.8%)	
III	20 (7.1%)	22 (8.1%)	42 (7.6%)	
IV				
QRS Width (ms)				
Mean ± Standard Deviation	163 ± 22	166 ± 23	165 ± 23	0.27
Median	160	160	160	
Range	130 - 230	130 - 250	130 - 250	
n recorded	281 (99.6%)	272 (100.0%)	553 (99.8%)	
Ejection Fraction (%)				
Mean ± Standard Deviation	21.3 ± 6.6	20.7 ± 6.9	21.0 ± 6.7	0.22
Median	20.0	20.0	20.0	
Range	6.0 - 36.0	10.0 - 40.0	6.0 - 40.0	
n recorded	281 (99.6%)	272 (100.0%)	553 (99.8%)	
LVEDD (mm)				
Mean ± Standard Deviation	70.0 ± 9.4	70.6 ± 9.2	70.3 ± 9.3	0.46
Median	68.0	70.0	70.0	
Range	50.0 - 98.0	55.0 - 103.0	50.0 - 103.0	
n recorded	279 (98.9%)	272 (100.0%)	551 (99.5%)	
MN Living with HF Score				
Mean ± Standard Deviation	49.6 ± 23.3	52.1 ± 24.4	50.8 ± 23.9	0.19
Median	49.0	53.5	52.0	
Range	0.0 - 100.0	0.0 - 105.0	0.0 - 105.0	
n recorded	277 (98.2%)	270 (99.3%)	547 (98.7%)	
6 -Minute Hall Walk (meters)				
Mean ± Standard Deviation	295 ± 132	281 ± 139	288 ± 136	0.29
Median	305	290	298	
Range	0 - 615	0 - 625	0 - 625	
n recorded	277 (98.2%)	266 (97.8%)	543 (98.0%)	

InSync ICD Clinical Study – NYHA Class II, III and IV Patients Comparison of Demographics by Treatment Assignment All Randomized Patients				
	Control (OFF) (n=282)	**Treatment (ON) (n=272)**	**All Patients (n=554)**	**P-value**
Peak VO_2/kg (ml/kg/min.)				
Mean ± Standard Deviation	14.5 ± 4.5	14.5 ± 4.2	14.5 ± 4.4	0.87
Median	14.1	14.8	14.3	
Range	5.4 - 29.3	5.8 - 31.1	5.4 - 31.1	
n recorded	200 (70.9%)	196 (72.1%)	396 (71.5%)	
Exercise Time (seconds)				
Mean ± Standard Deviation	544 ± 238	527 ± 239	536 ± 238	0.52
Median	534	525	529	
Range	35 - 1353	65 - 1215	35 - 1353	
n recorded	203 (72.0%)	196 (72.1%)	399 (72.0%)	
Supine Heart Rate (bpm)				
Mean ± Standard Deviation	70.6 ± 13.1	70.6 ± 12.1	70.6 ± 12.6	0.59
Median	69.0	70.0	70.0	
Range	40.0 - 127.0	40.0 - 117.0	40.0 - 127.0	
n recorded	275 (97.5%)	269 (98.9%)	544 (98.2%)	
Standing BP Systolic (mmHg)				
Mean ± Standard Deviation	113.3 ± 17.1	113.0 ± 18.6	113.1 ± 17.8	0.64
Median	110.5	110.0	110.0	
Range	75.0 - 173.0	76.0 - 205.0	75.0 - 205.0	
n recorded	268 (95.0%)	251 (92.3%)	519 (93.7%)	
Standing BP Diastolic (mmHg)				
Mean ± Standard Deviation	68.2 ± 11.9	66.9 ± 10.7	67.6 ± 11.4	0.29
Median	68.0	66.0	67.0	
Range	44.0 - 166.0	42.0 - 112.0	42.0 - 166.0	
n recorded	268 (95.0%)	251 (92.3%)	519 (93.7%)	
Standing Heart Rate (bpm)				
Mean ± Standard Deviation	73.4 ± 12.9	72.5 ± 12.7	73.0 ± 12.8	0.57
Median	72.0	72.0	72.0	
Range	44.0 - 114.0	40.0 - 125.0	40.0 - 125.0	
n recorded	268 (95.0%)	251 (92.3%)	519 (93.7%)	

InSync ICD Clinical Study – NYHA Class II, III and IV Patients **Comparison of Demographics by Treatment Assignment** **All Randomized Patients**				
	Control (OFF) (n=282)	**Treatment (ON) (n=272)**	**All Patients (n=554)**	**P-value**
Baseline CV Medical History (n, %)				
(non-exclusive)	281	271	552	.
n recorded	201 (71.5%)	177 (65.3%)	378 (68.5%)	0.12
Coronary Artery Disease	2 (0.7%)	4 (1.5%)	6 (1.1%)	0.44
Congenital Heart Disease	193 (68.7%)	165 (60.9%)	358 (64.9%)	0.06
HF etiology: ischemic	90 (32.0%)	103 (38.0%)	193 (35.0%)	0.15
HF etiology: non-ischemic	24 (8.5%)	21 (7.7%)	45 (8.2%)	0.76
Hypertension	49 (17.4%)	65 (24.0%)	114 (20.7%)	0.06
Idiopathic	8 (2.8%)	9 (3.3%)	17 (3.1%)	0.81
Valvular	17 (6.0%)	15 (5.5%)	32 (5.8%)	0.86
Other	167 (59.4%)	142 (52.4%)	309 (56.0%)	0.10
Myocardial Infarction	74 (26.3%)	66 (24.4%)	140 (25.4%)	0.63
Anterior	20 (7.1%)	20 (7.4%)	40 (7.2%)	1.00
Lateral	3 (1.1%)	6 (2.2%)	9 (1.6%)	0.33
Posterior	43 (15.3%)	43 (15.9%)	86 (15.6%)	0.91
Inferior	18 (6.4%)	8 (3.0%)	26 (4.7%)	0.07
Non Q-wave	261 (92.9%)	255 (94.1%)	516 (93.5%)	0.61
Cardiomyopathy	6 (2.1%)	8 (3.0%)	14 (2.5%)	0.60
Primary electrical disease	0 (0%)	0 (0%)	0 (0%)	0.60
Valvular Disease	134 (47.5%)	117 (43.2%)	251 (45.4%)	0.31
Hypertension	2 (0.7%)	1 (0.4%)	3 (0.5%)	1.00
Chronotropic incompetence	68 (24.2%)	73 (26.9%)	141 (25.5%)	0.49
Syncope/presyncope	39 (13.9%)	35 (12.9%)	74 (13.4%)	0.80
Other				
Prior Cardiac Intervention (n, %)				
(non-exclusive)	273	265	538	.
n recorded	118 (43.2%)	112 (42.3%)	230 (42.8%)	0.86
CABG	14 (5.1%)	21 (7.9%)	35 (6.5%)	0.22
Valve replacement	11 (4.0%)	11 (4.2%)	22 (4.1%)	1.00
Ablation	75 (27.5%)	60 (22.6%)	135 (25.1%)	0.23
Coronary Artery Intervention	2 (0.7%)	3 (1.1%)	5 (0.9%)	0.68
Repair/Correction of Cong. Abn	82 (30.0%)	79 (29.8%)	161 (29.9%)	1.00
ICD currently implanted	83 (30.4%)	83 (31.3%)	166 (30.9%)	0.85
None				

InSync ICD Clinical Study – NYHA Class II, III and IV Patients Comparison of Demographics by Treatment Assignment All Randomized Patients				
	Control (OFF) (n=282)	**Treatment (ON) (n=272)**	**All Patients (n=554)**	**P-value**
Spontaneous Arrhythmia History (non-exclusive)	282	271	553	.
n recorded	43 (15.2%)	60 (22.1%)	103 (18.6%)	0.04
Paroxysmal Atrial Fibrillation	6 (2.1%)	3 (1.1%)	9 (1.6%)	0.51
Chronic Atrial Fibrillation	12 (4.3%)	16 (5.9%)	28 (5.1%)	0.44
Atrial Flutter	1 (0.4%)	0 (0%)	1 (0.2%)	1.00
AV Nodal Reentrant Tachycardia	104 (36.9%)	100 (36.9%)	204 (36.9%)	1.00
Sustained Monomorphic VT	13 (4.6%)	10 (3.7%)	23 (4.2%)	0.67
Sustained Polymorphic VT	93 (33.0%)	109 (40.2%)	202 (36.5%)	0.08
Nonsustained VT	4 (1.4%)	1 (0.4%)	5 (0.9%)	0.37
Ventricular Flutter	41 (14.5%)	38 (14.0%)	79 (14.3%)	0.90
Ventricular Fibrillation	1 (0.4%)	1 (0.4%)	2 (0.4%)	1.00
Torsades de Pointes	0 (0%)	0 (0%)	0 (0%)	1.00
Long QT Syndrome	46 (16.3%)	43 (15.9%)	89 (16.1%)	0.91
Sinus Bradycardia	3 (1.1%)	5 (1.8%)	8 (1.4%)	0.50
Sick Sinus Syndrome	139 (49.3%)	119 (43.9%)	258 (46.7%)	0.23
1º AV Block	4 (1.4%)	3 (1.1%)	7 (1.3%)	1.00
2º AV Block	4 (1.4%)	2 (0.7%)	6 (1.1%)	0.69
Type 1 (Wenckebach)	1 (0.4%)	0 (0%)	1 (0.2%)	1.00
Type 2	3 (1.1%)	1 (0.4%)	4 (0.7%)	0.62
3º AV Block	43 (15.2%)	34 (12.5%)	77 (13.9%)	0.39
Right Bundle Branch Block	188 (66.7%)	194 (71.6%)	382 (69.1%)	0.23
Left Bundle Branch Block	0 (0%)	2 (0.7%)	2 (0.4%)	0.24
Bradycardia-Tachycardia Syndrome	55 (19.5%)	52 (19.2%)	107 (19.3%)	1.00
Others				
Other Medical History (n, %) (non-exclusive)				
n recorded	280	272	552	.
Dermatologic	7 (2.5%)	6 (2.2%)	13 (2.4%)	1.00
Endocrine (includes diabetes)	45 (16.1%)	30 (11.0%)	75 (13.6%)	0.11
Gastrointestinal	130 (46.4%)	123 (45.2%)	253 (45.8%)	0.80
Genitourinary	108 (38.6%)	109 (40.1%)	217 (39.3%)	0.73
Hematologic	84 (30.0%)	69 (25.4%)	153 (27.7%)	0.25
Infectious Disease	46 (16.4%)	46 (16.9%)	92 (16.7%)	0.91
Neurological	15 (5.4%)	17 (6.3%)	32 (5.8%)	0.72
Pulmonary (includes COPD)	50 (17.9%)	67 (24.6%)	117 (21.2%)	0.06
Psychological/Emotional	105 (37.5%)	102 (37.5%)	207 (37.5%)	1.00
Renal	46 (16.4%)	41 (15.1%)	87 (15.8%)	0.73
Skeletal/Orthopedic	50 (17.9%)	61 (22.4%)	111 (20.1%)	0.20
Others	106 (37.9%)	112 (41.2%)	218 (39.5%)	0.43

InSync ICD Clinical Study – NYHA Class II, III and IV Patients **Comparison of Demographics by Treatment Assignment** **All Randomized Patients**				
	Control (OFF) (n=282)	**Treatment (ON) (n=272)**	**All Patients (n=554)**	**P-value**
Medications (n, %) (non-exclusive)				
n recorded	281	272	553	.
ACE Inhibitor	254 (90.4%)	253 (93.0%)	507 (91.7%)	0.28
Anti-Arrhythmic	92 (32.7%)	110 (40.4%)	202 (36.5%)	0.06
Anti-Depressant	47 (16.7%)	44 (16.2%)	91 (16.5%)	0.91
Anti-Coagulant	222 (79.0%)	209 (76.8%)	431 (77.9%)	0.61
Beta-Blocker	165 (58.7%)	170 (62.5%)	335 (60.6%)	0.38
Calcium Channel Blocker	18 (6.4%)	15 (5.5%)	33 (6.0%)	0.72
Diuretic	252 (89.7%)	248 (91.2%)	500 (90.4%)	0.57
Positive Inotrope	201 (71.5%)	192 (70.6%)	393 (71.1%)	0.85
Nitrate	84 (29.9%)	85 (31.3%)	169 (30.6%)	0.78
Other Medication	157 (55.9%)	151 (55.5%)	308 (55.7%)	1.00

Table 7. Comparison of Control and Treatment Patients at Baseline – NYHA Class III and IV Patients

InSync ICD Clinical Study – NYHA Class III and IV Patients **Comparison of Demographics by Treatment Assignment** **All Randomized NYHA Class III/IV Patients**				
	Control (OFF) (n=176)	**Treatment (ON) (n=186)**	**All Patients (n=362)**	**P-value**
Gender (n,%)				
Male	136 (77.3%)	142 (76.3%)	278 (76.8%)	0.90
Female	40 (22.7%)	44 (23.7%)	84 (23.2%)	
Age (years)				
Mean ± Standard Deviation	67.6 ± 9.2	66.6 ± 11.3	67.1 ± 10.4	0.68
Median	69.1	69.4	69.1	
Range	32.7 - 85.3	28.1 - 89.0	28.1 - 89.0	
n recorded	176 (100.0%)	186 (100.0%)	362 (100.0%)	
New York Heart Classification (n,%)				1.00
II	156 (88.6%)	164 (88.2%)	320 (88.4%)	
III	20 (11.4%)	22 (11.8%)	42 (11.6%)	
IV				
QRS Width (ms)				
Mean ± Standard Deviation	162 ± 22	165 ± 22	164 ± 22	0.20
Median	160	160	160	
Range	130 - 230	130 - 237	130 - 237	
n recorded	175 (99.4%)	186 (100.0%)	361 (99.7%)	
Ejection Fraction (%)				
Mean ± Standard Deviation	20.2 ± 6.2	20.6 ± 7.0	20.4 ± 6.6	0.73
Median	20.0	20.0	20.0	
Range	6.0 - 36.0	10.0 - 40.0	6.0 - 40.0	
n recorded	175 (99.4%)	186 (100.0%)	361 (99.7%)	
LVEDD (mm)				
Mean ± Standard Deviation	70.8 ± 9.1	70.3 ± 8.9	70.5 ± 9.0	0.54
Median	70.0	70.0	70.0	
Range	50.0 - 97.0	55.0 - 98.0	50.0 - 98.0	
n recorded	173 (98.3%)	186 (100.0%)	359 (99.2%)	
MN Living with HF Score				
Mean ± Standard Deviation	55.2 ± 22.6	56.7 ± 22.8	56.0 ± 22.7	0.47
Median	57.0	59.0	57.0	
Range	0.0 - 100.0	3.0 - 105.0	0.0 - 105.0	
n recorded	173 (98.3%)	184 (98.9%)	357 (98.6%)	
6 -Minute Hall Walk (meters)				
Mean ± Standard Deviation	247 ± 118	245 ± 127	246 ± 123	0.88
Median	268	250	256	
Range	0 - 512	0 - 550	0 - 550	
n recorded	174 (98.9%)	182 (97.8%)	356 (98.3%)	

InSync ICD Clinical Study – NYHA Class III and IV Patients **Comparison of Demographics by Treatment Assignment** **All Randomized NYHA Class III/IV Patients**				
	Control (OFF) (n=176)	**Treatment (ON) (n=186)**	**All Patients (n=362)**	**P-value**
Peak VO_2/kg (ml/kg/min.)				
Mean ± Standard Deviation	13.5 ± 4.1	13.5 ± 3.7	13.5 ± 3.9	0.63
Median	12.9	13.6	13.1	
Range	5.4 - 26.6	5.8 - 23.3	5.4 - 26.6	
n recorded	117 (66.5%)	123 (66.1%)	240 (66.3%)	
Exercise Time (seconds)				
Mean ± Standard Deviation	479 ± 213	475 ± 213	477 ± 213	0.97
Median	459	460	460	
Range	35 - 1129	65 - 1142	35 - 1142	
n recorded	120 (68.2%)	123 (66.1%)	243 (67.1%)	
Supine Heart Rate (bpm)				
Mean ± Standard Deviation	71.6 ± 13.0	70.8 ± 12.4	71.2 ± 12.6	0.78
Median	70.5	70.0	70.0	
Range	40.0 - 109.0	40.0 - 117.0	40.0 - 117.0	
n recorded	170 (96.6%)	185 (99.5%)	355 (98.1%)	
Standing BP Systolic (mmHg)				
Mean ± Standard Deviation	110.7 ± 16.6	111.6 ± 19.6	111.1 ± 18.1	0.93
Median	110.0	110.0	110.0	
Range	75.0 - 173.0	76.0 - 205.0	75.0 - 205.0	
n recorded	170 (96.6%)	171 (91.9%)	341 (94.2%)	
Standing BP Diastolic (mmHg)				
Mean ± Standard Deviation	67.3 ± 12.7	65.5 ± 10.6	66.4 ± 11.7	0.26
Median	66.0	64.0	65.0	
Range	44.0 - 166.0	42.0 - 112.0	42.0 - 166.0	
n recorded	170 (96.6%)	171 (91.9%)	341 (94.2%)	
Standing Heart Rate (bpm)				
Mean ± Standard Deviation	74.0 ± 12.9	72.8 ± 13.2	73.4 ± 13.0	0.47
Median	72.0	71.0	72.0	
Range	44.0 - 114.0	40.0 - 125.0	40.0 - 125.0	
n recorded	170 (96.6%)	171 (91.9%)	341 (94.2%)	

InSync ICD Clinical Study – NYHA Class III and IV Patients **Comparison of Demographics by Treatment Assignment** **All Randomized NYHA Class III/IV Patients**				
	Control (OFF) (n=176)	**Treatment (ON) (n=186)**	**All Patients (n=362)**	**P-value**
Baseline CV Medical History (n, %)				
(non-exclusive)	176	185	361	.
n recorded	133 (75.6%)	122 (65.9%)	255 (70.6%)	0.05
Coronary Artery Disease	0 (0%)	2 (1.1%)	2 (0.6%)	0.50
Congenital Heart Disease	131 (74.4%)	117 (63.2%)	248 (68.7%)	0.02
HF etiology: ischemic	49 (27.8%)	67 (36.2%)	116 (32.1%)	0.09
HF etiology: non-ischemic	14 (8.0%)	13 (7.0%)	27 (7.5%)	0.84
Hypertension	24 (13.6%)	41 (22.2%)	65 (18.0%)	0.04
Idiopathic	3 (1.7%)	5 (2.7%)	8 (2.2%)	0.72
Valvular	10 (5.7%)	10 (5.4%)	20 (5.5%)	1.00
Other	111 (63.1%)	97 (52.4%)	208 (57.6%)	0.04
Myocardial Infarction	44 (25.0%)	47 (25.4%)	91 (25.2%)	1.00
Anterior	12 (6.8%)	16 (8.6%)	28 (7.8%)	0.56
Lateral	3 (1.7%)	5 (2.7%)	8 (2.2%)	0.72
Posterior	29 (16.5%)	30 (16.2%)	59 (16.3%)	1.00
Inferior	15 (8.5%)	5 (2.7%)	20 (5.5%)	0.02
Non Q-wave	165 (93.8%)	173 (93.5%)	338 (93.6%)	1.00
Cardiomyopathy	5 (2.8%)	6 (3.2%)	11 (3.0%)	1.00
Primary electrical disease	0 (0%)	0 (0%)	0 (0%)	1.00
Valvular Disease	88 (50.0%)	83 (44.9%)	171 (47.4%)	0.34
Hypertension	2 (1.1%)	0 (0%)	2 (0.6%)	0.24
Chronotropic incompetence	45 (25.6%)	47 (25.4%)	92 (25.5%)	1.00
Syncope/presyncope	29 (16.5%)	31 (16.8%)	60 (16.6%)	1.00
Other				
Prior Cardiac Intervention (n, %)				
(non-exclusive)	172	180	352	.
n recorded	86 (50.0%)	82 (45.6%)	168 (47.7%)	0.46
CABG	9 (5.2%)	13 (7.2%)	22 (6.3%)	0.51
Valve replacement	6 (3.5%)	6 (3.3%)	12 (3.4%)	1.00
Ablation	48 (27.9%)	44 (24.4%)	92 (26.1%)	0.47
Coronary Artery Intervention	0 (0%)	2 (1.1%)	2 (0.6%)	0.50
Repair/Correction of Cong. Abn	51 (29.7%)	54 (30.0%)	105 (29.8%)	1.00
ICD currently implanted	49 (28.5%)	53 (29.4%)	102 (29.0%)	0.91
None				

InSync ICD Clinical Study – NYHA Class III and IV Patients **Comparison of Demographics by Treatment Assignment** **All Randomized NYHA Class III/IV Patients**				
	Control (OFF) (n=176)	**Treatment (ON) (n=186)**	**All Patients (n=362)**	**P-value**
Spontaneous Arrhythmia History (non-exclusive)	176	186	362	.
n recorded	25 (14.2%)	45 (24.2%)	70 (19.3%)	0.02
Paroxysmal Atrial Fibrillation	5 (2.8%)	3 (1.6%)	8 (2.2%)	0.49
Chronic Atrial Fibrillation	7 (4.0%)	10 (5.4%)	17 (4.7%)	0.62
Atrial Flutter	0 (0%)	0 (0%)	0 (0%)	0.62
AV Nodal Reentrant Tachycardia	67 (38.1%)	64 (34.4%)	131 (36.2%)	0.51
Sustained Monomorphic VT	10 (5.7%)	7 (3.8%)	17 (4.7%)	0.46
Sustained Polymorphic VT	53 (30.1%)	72 (38.7%)	125 (34.5%)	0.10
Nonsustained VT	1 (0.6%)	0 (0%)	1 (0.3%)	0.49
Ventricular Flutter	27 (15.3%)	25 (13.4%)	52 (14.4%)	0.65
Ventricular Fibrillation	1 (0.6%)	1 (0.5%)	2 (0.6%)	1.00
Torsades de Pointes	0 (0%)	0 (0%)	0 (0%)	1.00
Long QT Syndrome	26 (14.8%)	27 (14.5%)	53 (14.6%)	1.00
Sinus Bradycardia	2 (1.1%)	5 (2.7%)	7 (1.9%)	0.45
Sick Sinus Syndrome	90 (51.1%)	82 (44.1%)	172 (47.5%)	0.21
1º AV Block	3 (1.7%)	1 (0.5%)	4 (1.1%)	0.36
2º AV Block	3 (1.7%)	1 (0.5%)	4 (1.1%)	0.36
Type 1 (Wenckebach)	1 (0.6%)	0 (0%)	1 (0.3%)	0.49
Type 2	2 (1.1%)	0 (0%)	2 (0.6%)	0.24
3º AV Block	23 (13.1%)	24 (12.9%)	47 (13.0%)	1.00
Right Bundle Branch Block	122 (69.3%)	134 (72.0%)	256 (70.7%)	0.64
Left Bundle Branch Block	0 (0%)	1 (0.5%)	1 (0.3%)	1.00
Bradycardia-Tachycardia Syndrome	31 (17.6%)	36 (19.4%)	67 (18.5%)	0.69
Others				
Other Medical History (n, %) (non-exclusive)				
n recorded	176	186	362	.
Dermatologic	3 (1.7%)	2 (1.1%)	5 (1.4%)	0.68
Endocrine (includes diabetes)	31 (17.6%)	24 (12.9%)	55 (15.2%)	0.24
Gastrointestinal	86 (48.9%)	88 (47.3%)	174 (48.1%)	0.83
Genitourinary	73 (41.5%)	75 (40.3%)	148 (40.9%)	0.83
Hematologic	51 (29.0%)	50 (26.9%)	101 (27.9%)	0.73
Infectious Disease	36 (20.5%)	34 (18.3%)	70 (19.3%)	0.69
Neurological	9 (5.1%)	14 (7.5%)	23 (6.4%)	0.39
Pulmonary (includes COPD)	35 (19.9%)	48 (25.8%)	83 (22.9%)	0.21
Psychological/Emotional	80 (45.5%)	73 (39.2%)	153 (42.3%)	0.24
Renal	32 (18.2%)	29 (15.6%)	61 (16.9%)	0.57
Skeletal/Orthopedic	41 (23.3%)	47 (25.3%)	88 (24.3%)	0.71
Others	69 (39.2%)	84 (45.2%)	153 (42.3%)	0.29

InSync ICD Clinical Study – NYHA Class III and IV Patients **Comparison of Demographics by Treatment Assignment** **All Randomized NYHA Class III/IV Patients**				
	Control (OFF) (n=176)	**Treatment (ON) (n=186)**	**All Patients (n=362)**	**P-value**
Medications (n, %) (non-exclusive)				
n recorded	176	186	362	.
ACE Inhibitor	155 (88.1%)	170 (91.4%)	325 (89.8%)	0.30
Anti-Arrhythmic	57 (32.4%)	78 (41.9%)	135 (37.3%)	0.07
Anti-Depressant	34 (19.3%)	35 (18.8%)	69 (19.1%)	1.00
Anti-Coagulant	142 (80.7%)	144 (77.4%)	286 (79.0%)	0.52
Beta-Blocker	100 (56.8%)	117 (62.9%)	217 (59.9%)	0.24
Calcium Channel Blocker	11 (6.3%)	13 (7.0%)	24 (6.6%)	0.83
Diuretic	166 (94.3%)	172 (92.5%)	338 (93.4%)	0.53
Positive Inotrope	129 (73.3%)	140 (75.3%)	269 (74.3%)	0.72
Nitrate	57 (32.4%)	68 (36.6%)	125 (34.5%)	0.44
Other Medication	104 (59.1%)	105 (56.5%)	209 (57.7%)	0.67

Statistical Methods

Primary Safety Objectives

To demonstrate the safety of the Model 7272 InSync ICD and Models 4189, 2187 and 2188 left ventricular cardiac vein pacing leads, the following hypotheses were evaluated. Per the investigational plan, NYHA II, III, and IV patients were included in the following safety objectives.

ICD-Related Complications

To demonstrate the safety of the InSync ICD Model 7272 the following hypothesis was evaluated:

Hypothesis

The freedom from Model 7272 complications at 3 months will be greater than or equal to 89% (i.e. the 95% lower confidence bound must be at least 89%):

H_0: p(Survival from Model 7272 complications) < 89%

H_A: p(Survival from Model 7272 complications) ≥ 89%

(*Complication* is defined as an adverse event that is resolved invasively or that directly results in the death or serious injury to the patient, the explant or repositioning of the ICD, or the termination of significant device function regardless of other treatments.)

Performance Requirement

The freedom from device-related complications at 3 months will have a 95% lower confidence bound of at least 89%:

$$p(\text{survival from Model 7272 complications}) - 1.645\ \sqrt{V(\text{survival})} \geq 89\%.$$

Analysis Methods

A survival analysis was conducted on all ICD related complications to three months. A patient's data is included from the time of implant (skin closure) to their last follow-up at the time of the data cutoff. The survival rate and 95% lower confidence bound on the rate is presented for the three-month time point.

A table summarizing all adverse events is provided. Specifically, events related to the atrial lead, right and left ventricular leads, the implant procedure and the heart failure status are summarized, but are not defined as ICD-related complications.

Determination of Subjects for Analysis

All patients implanted with the InSync ICD Model 7272 are included in this analysis.

System-Related Complications

To demonstrate the safety of the InSync ICD system, which include the ICD, left ventricular leads, right ventricular leads, right atrial leads and programmer software, the following hypothesis was evaluated.

Hypothesis

The InSync ICD system survival at 6 months will be greater than or equal to 67% (i.e. the 95% lower confidence bound must be at least 67%).

$$H_0: p_{(\text{Survival from system-related complications})} < 67\%$$

$$H_A: p_{(\text{Survival from Lead-related complications})} \geq 67\%$$

System survival is defined as a functioning three-lead ICD system comprised of the initially placed system components including the InSync ICD, an Attain Model 4189, 2187 or 2188 left ventricular pacing lead, and right atrial and ventricular leads. If an event requires an invasive treatment or invasive means of resolution or directly results in the death or serious injury to the patient or requires the termination of a significant device function, the system would be considered as a failed system at that point.

Performance Requirements

The freedom from system-related complications at 6 months must have a 95% lower confidence bound of at least 67%.

$$p_{(\text{survival from system-related complications})} - 1.645\ \sqrt{V}_{(\text{survival})} \geq 67\%.$$

Analysis Methods

A survival analysis was conducted on the system survival rate to 6 months. Patient data were included from the time of randomization to their last follow-up at the time of the data cutoff. The 95% lower confidence bound on the rate is presented for the six-month time point. In addition, system related complications are listed separately for NYHA Class II and Class III/IV patients.

Determination of Subjects for Analysis

All successfully implanted patients are included in the analysis.

Primary Efficacy Objectives (NYHA Class III and IV Patients)

For NYHA Class III and IV patients, the primary efficacy objectives of this study are to demonstrate the response to biventricular pacing on patient functional status as follows:

- The Quality of Life scores for patients in the treatment arm will show significant improvement over baseline when compared to patients in the control arm.
- The NYHA class for patients in the treatment arm will show significant improvement over baseline when compared to patients in the control arm.
- The Six Minute Hall Walk distance for patients in the treatment arm will show significant improvement over baseline when compared to patients in the control arm.

LV Lead Effectiveness Objectives

Attain Model 4189 LV Lead-Related Complications

Hypothesis

The freedom from Model 4189 LV lead-related complications at 6 months will be greater than or equal to 75% (i.e. the 95% lower confidence bound must be at least 75%).

H_O: p(Survival from lead-related complications) < 75%

H_A: p(Survival from lead-related complications) ≥ 75%

A *lead-related complication* is defined as a lead related adverse event that is resolved invasively or that directly results in the death of or serious injury to the patient, the repositioning or explant of the lead, or the termination of significant lead function regardless of other treatments. Unsuccessful implants will not be considered complications unless patient injury occurs (e.g. myocardial perforation).

Performance Requirement

The freedom from lead-related complications at 6 months must have a 95% lower confidence bound of at least 75%.

$$p(\text{survival from lead-related complications}) - 1.645\ \sqrt{V}(\text{survival}) \geq 75\%.$$

Analysis Methods

A survival analysis was conducted on the lead-related complications to six months. Patient data were included from the time of implant to their last follow-up at the time of the data cutoff.

Determination of Subjects for Analysis

- All patients implanted with the Attain Model 4189 LV lead are included in this analysis.

Attain Model 2187 and 2188 LV Lead-Related Complications

Hypothesis

The freedom from Models 2187 and 2188 LV lead-related complications at 6 months will be greater than or equal to 75% (i.e. the 95% lower confidence bound must be at least 75%).

H_O: p(Survival from lead-related complications) < 75%

H_A: p(Survival from lead-related complications) ≥ 75%

A *lead-related complication* is defined as a lead related adverse event that is resolved invasively or that directly results in the death of or serious injury to the patient, the repositioning or explant of the lead, or the termination of significant lead function regardless of other treatments. Unsuccessful implants will not be considered complications unless patient injury occurs (e.g. myocardial perforation).

Performance Requirement

The freedom from lead-related complications at 6 months must have a 95% lower confidence bound of at least 75%.

$$p(\text{survival from lead-related complications}) - 1.645\ \sqrt{V(\text{survival})} \geq 75\%.$$

Analysis Methods

A survival analysis was conducted on the lead-related complications to six months. Patient data are included from the time of implant to their last follow-up at the time of the data cutoff. In addition, lead related complications are listed separately for NYHA Class II and Class III/IV patients. A table summarizing all Model 2187 and 2188 lead-related adverse events is provided.

Determination of Subjects for Analysis

All patients implanted with the Attain Models 2187 and 2188 LV leads are included in this analysis.

Results

Primary Safety Results

Table 8 summarizes the primary safety results. All primary safety objectives have been met.

Table 8. Summary of Primary Safety Results

Objective *(Performance criterion)*	**Results**
Freedom from InSync ICD-related complications at 3 months *(Lower 95% confidence limit ≥ 89%)*	11 complications in 9 patients. Survival at 3 months is 98.4%. The lower 95% confidence limit on the freedom from ICD-related complications at 3 months is **97.5%**
Freedom from InSync ICD System-related complications at 6 months *(Lower 95% confidence limit ≥ 67%)*	124 complications in 107 patients. Survival at 6 months is 79.7%. The lower 95% confidence limit on the freedom from system-related complications at 6 months is **76.7%**
Freedom from Model 4189 lead complications at 6 months (Lower 95% confidence limit ≥ 75%)	71 complications in 65 patients. Survival at 6 months is 85.3%. The lower 95% confidence limit on the freedom from Model 4189 lead-related complications at 6 months is **82.5%**
Freedom from Model 2187 and 2188 lead complications at 6 months *(Lower 95% confidence limit ≥ 75%)*	12 complications in 12 patients. Survival at 6 months is 86.1%. The lower 95% confidence limit on the freedom from Model 2187/88 lead-related complications at 6 months is **79.9%**

Primary Efficacy Results

Table 9. Summary of Primary Efficacy Results– NYHA Class III and IV Patients

Endpoint	Results		
	Control Group *(OFF)*	**Treatment Group** *(ON)*	**P- value**
6-month change in QOL score	112 patients with paired data **Baseline:** median 57.0 mean 56.1 ± 21.7 **6-month:** median 44.5 mean 43.1 ± 22.5 **Median Paired Difference: –10.0**	120 patients with paired data **Baseline:** median 58.5 mean 55.2 ± 23.0 **6-month:** median 34.0 mean 34.5 ± 22.0 **Median Paired Difference: –20.0**	0.0044
6-month change in NYHA Classification	115 patients with paired data **Baseline:** median 3.0 mean 3.09 ± 0.28 **6-month:** median 3.0 mean 2.55 ± 0.68 **Median Paired Difference: 0**	123 patients with paired data **Baseline:** median 3.0 mean 3.11 ± 0.31 **6-month:** median 2.0 mean 2.34 ± 0.71 **Median Paired Difference: –1**	0.0145
6-month change in 6 minute hall walk (meters)	111 patients with paired data **Baseline:** median 275 mean 251 ± 117 **6-month:** median 335 mean 320 ± 115 **Median Paired Difference: 54**	115 patients with paired data **Baseline:** median 261 mean 260 ± 129 **6-month:** median 343 mean 345 ± 112 **Median Paired Difference: 55**	0.4993

Primary LV Lead Effectiveness Results

Table 10. Summary of Primary LV Lead Effectiveness Results

Objective *(Performance criterion)*	**Results**
Demonstrate the implantability of the Model 4189, 2187, and 2188 leads *(Lower 95% confidence limit ≥ 83%)*	567 patients successfully implanted out of 636 patients attempted (89.2%) The lower 95% confidence limit on the implant success rate is **86.9%.**
Demonstrate the electrical performance of the Model 2187 and Model 2188 leads *(Upper 95% confidence limit ≤ 3.0V)*	The mean 6-month voltage pacing threshold measured at 0.5 ms was 1.9 V. The upper 95% confidence limit was **2.2V.**
Demonstrate the electrical performance of the Model 4189 lead *(Upper 95% confidence limit ≤ 3.0V)*	The mean 6-month voltage pacing threshold measured at 0.5 ms was 1.5 V. The upper 95% confidence limit was **1.7V**.

Secondary Objective Results

Table 11. Summary of Secondary Objective Results – NYHA Class II, III and IV Patients

Secondary Objectives	**Results for NYHA Class II, III and IV Patients**		
(no pre-specified performance criteria)	**Control Group *(OFF)***	**Treatment Group *(ON)***	**P-value**
Change in QRS duration from baseline through 6-months (ms)	179 patients with paired data **Baseline:** median 160 mean 163 ± 22 **6-month:** median 150 mean 153 ± 36 **Median Paired Difference: –12**	176 patients with paired data **Baseline:** median 160 mean 166 ± 22 **6-month:** median 145 mean 145 ± 28 **Median Paired Difference: –20**	0.008
Health Care Utilization (all cause hospitalization) from baseline through 6-months			
Number of patients hospitalized	**All-cause:** n=282, 107 (37.9%) **CHF related:** n=282, 58 (20.6%)	**All-cause:** n=272, 102 (37.5%) **CHF related:** n=272, 47 (17.3%)	0.93 0.33
Length of Stay (days)	**All-cause:** 181 hospitalizations median; 6 days mean: 8.6 ± 8.0 **CHF related:** 85 hospitalizations median; 6 days mean: 7.6 ± 6.5	**All-cause:** 172 hospitalizations median; 5 days mean: 8.3 ± 9.7 **CHF related:** 66 hospitalizations median; 4 days mean: 7.5 ± 8.3	 0.16 0.16
Change in Echo indices from baseline through 6-months			
LV Ejection Fraction (%)	136 patients with paired data **Baseline:** median 21.9 mean 23.7 ± 6.6 **6-month:** median 24.3 mean 25.0 ± 7.6 **Median Paired Difference 1.3**	134 patients with paired data **Baseline**: median 23.4 mean 24.1 ± 6.5 **6-month:** median 26.0 mean 27.7 ± 8.4 **Median Paired Difference 3.1**	0.008

Secondary Objectives	**Results for NYHA Class II, III and IV Patients**		
(no pre-specified performance criteria)	**Control Group *(OFF)***	**Treatment Group *(ON)***	**P-value**
Mitral Regurgitation (cm^2, jet area)	91 patients with paired data **Baseline:** median 6.9 mean 8.2 ± 7.4 **6-month:** median 5.9 mean 7.1 ± 6.8 **Median Paired Difference –0.5**	90 patients with paired data **Baseline:** median 7.0 mean 7.9 ± 6.5 **6-month:** median 4.3 mean 6.0 ± 5.6 **Median Paired Difference -1.6**	0.25
Cardiac Index (four chamber view)	86 patients with paired data **Baseline:** median 2.35 mean 2.42 ± 0.75 **6-month:** median 2.36 mean 2.52 ± 0.76 **Median Paired Difference 0.02**	96 patients with paired data **Baseline:** median 2.36 mean 2.47 ± 0.73 **6-month:** median 2.40 mean 2.48 ± 0.75 **Median Paired Difference 0.01**	0.37
LV Systolic Volume (cm^3)	131 patients with paired data **Baseline:** median 232 mean 247 ± 90 **6-month:** median 224.0 mean 244 ± 96 **Median Paired Difference –7**	133 patients with paired data **Baseline:** median 232 mean 250 ± 101 **6-month:** median 209 mean 223 ± 103 **Median Paired Difference –28**	0.0004
LV Diastolic Volume (cm^3)	131 patients with paired data **Baseline:** median 299 mean 319 ± 100 **6-month:** median 298 mean 319 ± 101 **Median Paired Difference -5**	134 patients with paired data **Baseline:** median 302 mean 323 ± 109 **6-month:** median 282 mean 299 ± 112 **Median Paired Difference –29**	0.0005
LV mass (g)	76 patients with paired data **Baseline:** median 354 mean 362 ± 79 **6-month:** median 356 mean 363 ± 93 **Median Paired Difference – 6**	84 patients with paired data **Baseline:** median 335 mean 359 ± 93 **6-month:** median 348 mean 359 ± 106 **Median Paired Difference – 7**	0.85

Secondary Objectives	**Results for NYHA Class II, III and IV Patients**		
(no pre-specified performance criteria)	**Control Group *(OFF)***	**Treatment Group *(ON)***	**P-value**
Interventricular mechanical delay (IVMD) (ms)	88 patients with paired data **Baseline**: median 26.0 mean 24.0 ± 41.5 **6-month:** median 26.5 mean 20.5 ± 35.9 **Median Paired Difference 0.0**	101 patients with paired data **Baseline:** median 41.0 mean 32.7 ± 40.0 **6-month:** median 24.0 mean 19.1 ± 33.1 **Median Paired Difference –17.0**	0.049
Left Ventricular Inflow E Wave Max Velocity (cm/s)	101 patients with paired data **Baseline:** median 68.0 mean 69.2 ± 24.6 **6-month:** median 66.0 mean 70.7 ± 26.2 **Median Paired Difference 1.0**	118 patients with paired data **Baseline:** median 75.0 mean 78.7 ± 29.7 **6-month:** median 64.5 mean 70.9 ± 28.5 **Median Paired Difference –10.5**	0.001
Left Ventricular Inflow A Wave Max Velocity (cm/s)	120 patients with paired data **Baseline:** median 64.0 mean 64.4 ± 27.3 **6-month:** median 69.0 mean 68.7 ± 28.2 **Median Paired Difference 6.5**	128 patients with paired data **Baseline:** median 68.0 mean 69.8 ± 32.4 **6-month:** median 65.0 mean 65.5 ± 28.4 **Median Paired Difference –1.0**	0.02
E Wave /A Wave ratio	100 patients with paired data **Baseline:** median 1.13 mean 1.50 ± 1.23 **6-month:** median 1.00 mean 1.40 ± 1.06 **Median Paired Difference -0.04**	117 patients with paired data **Baseline:** median 1.14 mean 1.47 ± 1.03 **6-month:** median 0.98 mean 1.40 ± 1.01 **Median Paired Difference -0.11**	0.82
Normalized LV Filling Time	122 patients with paired data **Baseline:** median 0.44 mean 0.43 ± 0.09 **6-month:** median 0.44 mean 0.43 ± 0.11 **Median Paired Difference 0.00**	129 patients with paired data Baseline: median 0.44 mean 0.43 ± 0.09 6-month: median 0.49 mean 0.48 ± 0.09 **Median Paired Difference 0.04**	<0.0001

Secondary Objectives	**Results for NYHA Class II, III and IV Patients**		
(no pre-specified performance criteria)	**Control Group *(OFF)***	**Treatment Group *(ON)***	**P-value**
LV Diameter in Systole	63 patients with paired data **Baseline:** median 6.7 mean 6.9 ± 1.1 **6-month:** median 6.8 mean 6.7 ± 1.0 **Median Paired Difference -0.2**	75 patients with paired data **Baseline:** median 6.4 mean 6.5 ± 1.1 **6-month:** median 6.3 mean 6.3 ± 1.3 **Median Paired Difference -0.1**	0.99
LV Diameter in Diastole	67 patients with paired data **Baseline:** median 7.6 mean 10.2 ± 11.7 **6-month:** median 7.6 mean 7.6 ± 0.9 **Median Paired Difference 0.0**	76 patients with paired data **Baseline:** median 7.5 mean 8.3 ± 6.8 **6-month:** median 7.3 mean 7.4 ± 1.1 **Median Paired Difference 0.0**	0.93
Composite Response Improved Unchanged Worsened	n = 217 39% 27% 34%	n = 213 56% 19% 25%	0.002
Comparison of VT/VF Event Rates	N=282 # patients: 58 (20.6%) Total episodes: 392 Episodes per month: 0.30	N=272 # patients: 53 (19.5%) Total episodes: 415 Episodes per month: 0.33	0.12
Patient Survival at 6 months (95% confidence interval)	93.3% (89.2% - 95.8%)	94.1% (90.3% - 96.5%)	0.65
Plasma Neurohormone Levels Plasma neurohormone levels including brain natriuretic peptide (BNP), big endothelin (Big ET) and catecholamines (epinephrine, norepinephrine and dopamine) were evaluated at baseline and 6 months for both the control and treatment groups. No statistically significant changes were observed.			

Sensing Performance of the Left Ventricular Leads

	Visit	N	Mean ± SD
Model 2187/2188 R-wave Amplitude	**Implant**	88	12.7 ± 4.9
	6 Months	63	13.5 ± 5.7
Model 4189 R-wave Amplitude	**Implant**	444	12.5 ± 4.6
	6 Months	317	13.7 ± 5.4

Spontaneous VT/VF Therapy Efficacy

Episode Detection Zone	Percent Successfully Terminated
FVT	97.6%
VF	99.4%
VT	99.0%
OVERALL	98.9%

ATP Therapy Efficacy With Biventricular Pacing

ATP Site	Rhythm	ATP Success rate	P-value
RV	Induced VT	19/33 (58%)	1.00
RV+LV	Induced VT	20/33 (61%)	
RV	Spontaneous VT	297/348 (85%)	<0.0001
RV+LV	Spontaneous VT	619/658 (94%)	
RV	Spontaneous FVT	89/98 (91%)	0.002
RV+LV	Spontaneous FVT	19/30 (63%)	

Implant Ventricular Defibrillation Criterion

Implant Criteria Used	N	Percent (%)
2 at ≤ 24 Joules	445	78.5%
Binary Search	87	15.3%
Not Successful	35	6.2%

Device Explants

Table 12 summarizes information related to InSync ICD Model 7272 devices that were explanted during the clinical study.

Table 12. Explanted Devices – ICDs

Patient ID	Date of implant	Date of explant	Model 7272 Serial #	Reason for Explant	Returned to Medtronic	Returned Product Analysis
100190002	8-Dec-99	08-Jul-01		Patient death	Yes	Device within specification
100190206	25-Oct-00	11-Jan-01		Patient death	Yes	Device within specification
100190207	26-Jan-01	04-Apr-01		Heart transplant	Yes	Analysis pending
100190210	19-Apr-01	04/19/01		Improper function during DFT testing; device not implanted	Yes	Electrical reset parameters
101540004	23-Mar-01	01-May-01		Patient death	Yes	Device within specification
102210001	6-Dec-99	3-Mar-00		Patient death	Yes	Device within specification
102210008	29-Sep-00	27-Apr-01		Patient death	Yes	Device within specification
102210016	23-Jan-01	20-Feb-01		Patient death	Yes	Device within specification
102480001	1-Mar-01	04-Jun-01		Patient death	Yes	Device within specification
102820001	16-Mar-01	31-May-01		Heart transplant	No	N/A
105230001	1-May-00	5-Jul-00		Patient death	No	N/A
107800002	26-May-00	26-Oct-00		Patient death	Yes	Device within specification
109620004	24-Mar-00	28-Apr-00		Patient death	Yes	Device within specification
109620005	27-Jun-00	25-Jul-01		Patient death	Yes	Device within specification
109620005	27-Jun-00	28-Jun-01		Patient death	Yes	Device within specification
109620012	7-Mar-01	8-Mar-01		Patient death	Yes	Device within specification
110950003	5-Nov-99	4-Apr-00		Patient death	Yes	Device within specification
110950004	15-Nov-99	7-Dec-99		Patient death	Yes	Apparent explant damage to diode
110950006	2-Dec-99	30-Mar-00		Inappropriate patient alerts	Yes	Device within specification
112620022	25-Apr-01	15-Aug-01		Infection	Yes	Analysis pending
113720007	19-Oct-00	25-Jun-01		Patient death	Yes	Device within specification
115390004	20-Jun-00	22-Feb-01		Patient death	No	N/A
115390006	10-Aug-00	26-Dec-00		Patient death	Yes	Device within specification
117650001	4-Nov-99	07/20/01		Patient death	Yes	Device within specification
118920020	17-Nov-00	11-May-01		Patient death	Yes	Device within specification
118920025	23-Apr-01	13-Jul-01		Patient death	Yes	Device within specification
119510003	2-Nov-00	12-Nov-00		Patient death	Yes	Device within specification
119510020	14-Jun-01	4-Jul-01		Patient death	Yes	Device within specification
119510020	14-Jun-01	06-Jul-01		Patient death	Yes	Device within specification

Patient ID	Date of implant	Date of explant	Model 7272 Serial #	Reason for Explant	Returned to Medtronic	Returned Product Analysis
123850003	24-Feb-00	26-Jul-00		Patient death	Yes	Device within specification
123850017	27-Apr-01	30-Apr-01		Abnormal impedance measurement	Yes	Analysis pending
127080002	28-Sep-00	07/08/01		Patient death	Yes	Device within specification
127670003	8-Mar-00	3/24/2001		Patient death	Yes	Device within specification
127670015	30-Oct-00	2-Nov-00		Unable to place CS lead; physician decision to not implant system	Yes	Analysis pending
131240001	8-Jan-01	7-Feb-01		ICD contaminated during repositioning of lead	Yes	Device within specification
132320010	16-May-01	17-May-01		Heart transplant	Yes	Device within specification
133260007	11-Aug-00	1-Nov-00		Heart transplant	Yes	Device within specification
133260014	6-Dec-00	23-Feb-01		Electrical reset parameters	Yes	Device within specification
133260022	22-Mar-01	11-Apr-01		Infection	Yes	Analysis pending
135640006	8-Jan-01	20-Jun-01		Patient death	Yes	Device within specification
142270001	11-Feb-00	8-Jan-01		Patient death	Yes	Short output transistor in high voltage output circuit (appears due lead being cut during explant procedure).
142270003	5-May-00	24-Dec-00		Patient death	Yes	Device within specification
147870008	13-Apr-00	14-Nov-00		Myopotential interference	No	N/A
147870011	8-May-00	24-Jan-01		Patient death	Yes	Device within specification
147870016	7-Aug-00	22-Jul-01		Heart transplant	Yes	Analysis pending
147870034	16-Apr-01	24-Jun-01		Patient death	Yes	Device within specification
377150006	27-Apr-01	08-Aug-01		Heart transplant	No	N/A
381480008	13-Sep-00	19-Dec-00		Patient death	Yes	Device within specification
408490005	22-Feb-01	04-Apr-01		Patient death	Yes	Device within specification
417480009	25-Apr-01	14-May-01		Infection/sepsis	Yes	Analysis pending
465570001	25-Jan-00	13-Jul-00		Patient death	Yes	Device within specification
706943007	20-Apr-00	04-Apr-01		Heart transplant	Yes	Device within specification
706943015	28-Aug-00	05-Sep-01		Heart transplant	No	N/A
706943026	26-Feb-01	27-Apr-01		Heart transplant	No	N/A
706943029	8-Mar-01	06-Apr-01		Infection	Yes	Analysis pending

Table 13 summarizes information related to Attain LV leads that were explanted during the clinical study.

Table 13. Explanted Devices – LV Leads

LV Lead Explants								
Patient ID	**Date of Implant**	**Date of Explant**	**Device Explanted**	**Device Serial Number**	**Reason for Explant**	**Device Reimplanted**	**Returned Product Analysis Lead Finding**	**Lead Analysis Result**
100190-002	08-Dec-99	08-Jul-01	4189		Death	N/A	Device within specification	No anomalies found
100190-018	26-Sep-00	7-Nov-00	4189		Lead dislodgement	2187	Outer insulation melted / Distal conductor blood (not obstructed)	Melted / Blood in coil (not obstructed)
100190-029	19-Jan-01	03-Oct-01	2187		Lead dislodgement	4189	Not returned to Medtronic	N/A
100190-033	23-Feb-01	04-Apr-01	4189		Loss of capture / lead dislodgement	2187	Device within specification	No anomalies found
100190-205	04-Oct-00	02-Mar-01	4189		Loss of capture / lead dislodgement	4189	Returned to Medtronic	Analysis pending
100190-206	25-Oct-00	11-Jan-01	4189		Death	N/A	Device within specification	No anomalies found
100190-207	26-Jan-01	04-Apr-01	4189		Heart transplant	N/A	Device within specification	No anomalies found
101540-002	09-Mar-01	15-May-01	4189		System explanted due to infection	4189	Not returned to Medtronic	N/A
101540-004	23-Mar-01	01-May-01	4189		Death	N/A	Device within specification	No anomalies found
102210-001	06-Dec-99	03-Mar-00	4189		Death	N/A	Device within specification	No anomalies found
102210-008	29-Sep-00	30-Apr-01	4189		Death	N/A	Device within specification	No anomalies found
102210-016	23-Jan-01	20-Feb-01	4189		Death	N/A	Device within specification	No anomalies found
102210-020	06-Mar-01	21-May-01	4189		Lead dislodgement	2187	Device within specification	No anomalies found
102650-002	10-Jul-00	18-Jul-00	4189		Phrenic Nerve Stimulation	2187	Not returned to Medtronic	N/A
107800-002	26-May-00	26-Oct-00	2187		Death	N/A	Not returned to Medtronic	N/A
109620-004	24-Mar-00	28-Apr-00	2187		Death	N/A	Device within specification	No anomalies found
109620-005	27-Jun-00	25-Jul-01	4189		Death	N/A	Device within specification	No anomalies found
109620-012	07-Mar-01	08-Mar-01	4189		Death	N/A	Device within specification	No anomalies found
110930-002	05-Nov-99	8-Feb-00	2187		Lead dislodgement	4189	Not returned to Medtronic	N/A
110930-003	03-Nov-00	04-Apr-00	2187		Death	N/A	Device within specification	No anomalies found
110930-004	15-Nov-99	07-Dec-99	2188		Death	N/A	Not returned to Medtronic	N/A
110930-008	14-Jan-00	13-Jan-00	4189		Lead dislodgement at implant between defib testing & pace/sense testing	2187	Not returned to Medtronic	N/A

LV Lead Explants

Patient ID	Date of Implant	Date of Explant	Device Explanted	Device Serial Number	Reason for Explant	Device Reimplanted	Returned Product Analysis Lead Finding	Lead Analysis Result
110950-011	19-Jan-00	15-Feb-00	4189		Lead dislodgement	2187	Outer insulation melted / Distal conductor blood (not obstructed)	Melted / Blood in coil (not obstruction)
110950-023	26-May-00	13-Oct-00	2187		Lead dislodgement	2187	Device within specification	No anomalies found
110950-024	12-Jun-00	02-Nov-00	4189		Loss of capture / lead dislodgement	2187	Not returned to Medtronic	N/A
112620-022	25-Apr-01	15-Aug-01	4189		System explanted due to infection	N/A	Device within specification	No anomalies found
113720-007	19-Oct-00	25-Jul-01	4189		Death	N/A	Device within specification	No anomalies found
115390-006	10-Aug-00	26-Dec-00	4189		Death	N/A	Device within specification	No anomalies found
116263-004	24-Sep-01	27-Sep-01	4193		Lead dislodgement	2187	Not returned to Medtronic	N/A
116263-010	13-Jun-01	21-Jun-01	4189		Elevated pacing thresholds	2187	Device within specification	No anomalies found
118920-020	17-Nov-00	10-May-01	2187		Death	N/A	Device within specification	No anomalies found
118920-025	23-Apr-01	12-Jun-01	4189		Death	N/A	Device within specification	No anomalies found
119310-003	02-Nov-00	12-Nov-00	4189		Death	N/A	Device within specification	No anomalies found
119310-020	14-Jan-01	04-Jul-01	4189		Death	N/A	Device within specification	No anomalies found
120340-002	19-Jun-00	26-Jun-00	4189		Chest wall stim / dislodgement	4189	Device within specification	No anomalies found
120340-003	18-Sep-00	22-Sep-00	4189		Phrenic Nerve Stimulation	2188	Device within specification	No anomalies found
120340-007	15-Dec-00	15-Dec-00	4189		Diaphragmatic stim post pocket closure	2188	Device within specification	No anomalies found
123850-002	26-Jan-00	28-Jan-00	2187		Lead dislodgement	4189	Not returned to Medtronic	N/A
123850-003	24-Feb-00	25-Jul-00	4189		Death	N/A	Device within specification	No anomalies found
123850-012	5-Dec-00	14-Dec-00	2187		Diaphragmatic stim	4189	Not returned to Medtronic	N/A
127080-002	28-Sep-00	08-Jul-01	4189		Death	N/A	Device within specification	No anomalies found
127080-003	26-Oct-00	8-Feb-01	4189		Twiddler's syndrome / unable to reposition	N/A (capped)	Not returned to Medtronic	N/A
127080-007	09-Mar-01	06-Jun-01	4189		Lead dislodgement	N/A (Pt expired on 14-Jun-01)	Device within specification	No anomalies found
127670-003	08-Mar-00	24-Mar-01	4189		Death	N/A	Device within specification	No anomalies found
127670-015	30-Oct-00	2-Nov-00	4189		Lead dislodgment	Couldn't reposition – explanted device	Not returned to Medtronic	N/A

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LV Lead Explants								
Patient ID	**Date of Implant**	**Date of Explant**	**Device Explanted**	**Device Serial Number**	**Reason for Explant**	**Device Reimplanted**	**Returned Product Analysis Lead Finding**	**Lead Analysis Result**
						and CS lead		
132320-004	14-Feb-01	17-Apr-01	2187		Loss of capture / lead dislodgement	2187	Device within specification	No anomalies found
132320-010	16-May-01	17-May-01	4189		Heart transplant	N/A	Device within specification	No anomalies found
132320-013	02-Jun-01	05-Jun-01	4189		Failure to capture / lead dislodgement	2187	Device within specification	No anomalies found
133260-007	11-Aug-00	1-Nov-00	2187		Heart transplant	N/A	Device within specification	No anomalies found
133260-015	15-Jan-01	23-Feb-01	2187		Loss of capture / lead dislodgement	2188	Not returned to Medtronic	N/A
133260-017	17-Jan-01	15-Feb-01	4189		High capture threshold w/pectoral & diaphragmatic stim	2187	Device within specification	No anomalies found
133260-022	22-Mar-01	01-May-01	4189		System explanted due to infection	2187	Not returned to Medtronic	N/A
133260-025	09-May-01	12-Jun-01	4189		Lead dislodgement	4698 (Epicardial lead)	Not returned to Medtronic	N/A
135640-006	08-Jan-01	12-Jun-01	4189		Death	N/A	Device within specification	No anomalies found
142270-001	11-Feb-00	05-Jan-01	4189		Death	N/A	Device within specification	No anomalies found
142270-003	05-May-00	24-Dec-00	2187		Death	N/A	Device within specification	No anomalies found
142270-012	21-May-01	15-Jun-01	4189		Lead dislodgement	4189	Not returned to Medtronic	N/A
147870-011	08-May-00	24-Jan-01	4189		Death	N/A	Device within specification	No anomalies found
147870-016	07-Aug-00	22-Jul-01	4189		Placement of LVAD 7/01 & Heart transplant 9/01	N/A	Device within specification	No anomalies found
147870-024	14-Nov-00	5-Dec-00	4189-85		LV lead fell back into CS annulus	2187	Not returned to Medtronic	N/A
147870-034	16-Apr-01	22-Jun-01	4189		Death	N/A	Device within specification	No anomalies found
183340-001	30-Aug-00	13-Mar-01	4189		Diaphragmatic stimulation	N/A Unable to reposition (4193 implanted 04-Sep-01)	Device within specification	No anomalies found
183340-010	13-Dec-00	01-Jun-01	4189		Elevated pacing thresholds / lead dislodgement	4189	Not returned to Medtronic	N/A
183340-015	28-Mar-01	30-Mar-01	4189		Loss of capture / lead dislodgement	2187	Device within specification	No anomalies found

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LV Lead Explants

Patient ID	Date of Implant	Date of Explant	Device Explanted	Device Serial Number	Reason for Explant	Device Reimplanted	Returned Product Analysis Lead Finding	Lead Analysis Result
236670-009	3-Jan-01	9-Jan-01	4189		Lead dislodgment / increased ectopy	4189	Not returned to Medtronic	N/A
287240-003	16-Oct-00	24-Nov-00	4189		Lead dislodgement	2187	Not returned to Medtronic	N/A
377150-001	11-May-00	14-Nov-00	2187		Lead dislodgement into CS	4189	Not returned to Medtronic (Lead was destroyed during explantation and discarded)	N/A
381480-008	13-Sep-00	19-Dec-00	4189		Death	N/A	Device within specification	No anomalies found
408490-005	22-Feb-01	04-Apr-01	4189		Death	N/A	Device within specification (not obstructed)	No anomalies found (not obstructed)
417480-005	20-Nov-00	8-Dec-00	2188		Lead dislodgement	4189	Device within specification	No anomalies found
417480-009	25-Apr-01	14-May-01	2188		Pocket infection post implant (fever / chills / diaphoresis)	N/A	Device within specification	No anomalies found
451320-005	29-Jan-01	05-Apr-01	4189		Lead dislodgement	2187	Device within specification	No anomalies found
465570-001	25-Jan-00	10-Jul-00	4189		Death	N/A	Device within specification	No anomalies found
706943-002	24-Feb-00	17-Mar-00	4189		Lead dislodgement	2187	Not returned to Medtronic	N/A
706943-017	21-Sep-00	12-Oct-00	4189		Diaphragmatic stimulation upon standing	4189	Device within specification	No anomalies found
706943-026	26-Feb-01	09-Apr-01	4189		Persistent diaphragmatic stimulation	N/A - lead could not be repositioned (Pt received a heart transplant 27-Apr-01)	Not returned to Medtronic	N/A
706943-029	08-Mar-01	06-Apr-01	4189		Diagnosed with hemophilia / Pocket hematoma	4189 (13-Apr-01)	Device within specification	No anomalies found
706943-034	01-Jun-01	16-Jun-01	2187		System explanted due to possible infection	N/A	Not returned to Medtronic	N/A