Medtronic

JEWEL® AF 7250

Dual Chamber Implantable Cardioverter Defibrillator

Prescriber's Package Insert

Caution: Federal law (USA) restricts this device to sale by or on the order of a physician.

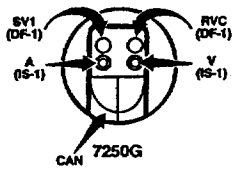
Nominal Specifications

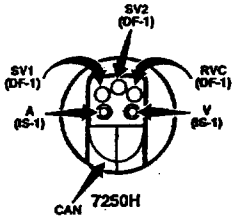
Model #	Maximum Shock Energy	Defibrillating Lead[a,b,c,d] Connection	Pacing Lead[b,d] Connection	Dimensions W x H x D	Volume	Mass
7250G	27 J	Two DF-1 (3.2 mm)	Two IS-1 bipolar (3.2 mm)	76 x 55 x 16 mm	56 cc	95 g
7250H	27 J	Three DF-1 (3.2 mm)	Two IS-1 bipolar (3.2 mm)	79 x 55 x 16 mm	57 cc	96 g

Case Material	Titanium
Header Materials	Polyurethane, silicone rubber
Power Supply	Lithium silver vanadium oxide (6.4 V nominal)

[a] The ICD case serves as a defibrillation electrode.
[b] For lead compatibility information, refer to the next page and the warning "Lead System" on page 5.
[c] The DF-1 ports will not accept a 3.2 mm in-line bipolar lead.
[d] DF-1 refers to the international standard ISO 11318:1993.
IS-1 refers to ISO 5841-3:1992(E).

Lead Connections





Lead Compatibility
The ICD is designed to accept DF-1 and IS-1 bipolar lead connectors.[1] The Medtronic leads listed below are directly compatible with the Jewel® AF ICD.

Model	Placement	Fixation
Multipolar Pacing / Sensing / High Voltage Leads		
Sprint 6932	RV	Tines
Sprint 6942	RV and SVC coils	Tines
Sprint 6943	RV or RA	Extendable Screw
Sprint 6945	RV and SVC coils	Extendable Screw
Transvene RV 6934S	RV	Tines
Transvene RV 6936	RV	Extendable Screw
IS-1 Bipolar Pacing / Sensing Leads		
SureFix 5072	Atrium	Fixed Screw
CapSure Fix 6940	Atrium	Extendable Screw
CapSure Fix 4568 / 5568	Atrium (J-curved)	Extendable Screw
CapSure Fix 4068 / 5068	Atrium or Ventricle	Extendable Screw
CapSure SP 5024M	Ventricle	Tines
DF-1 Unipolar Cardioversion / Defibrillation Leads		
Transvene 6933	SVC or CS	Passive
Transvene 6937	SVC	Passive
Transvene 6937A	SVC or CS	Passive
Transvene 6939	SQ patch	Suture
Model 6721	Epicardial Patch	Suture

1. DF-1 refers to the international standard ISO 11318:1993.
IS-1 refers to ISO 5841-3:1992(E).

1 DEVICE DESCRIPTION

The Model 7250 Jewel® AF Implantable Cardioverter Defibrillator (ICD) System is a multiprogrammable, implantable cardioverter defibrillator that monitors and regulates a patient's heart rate by providing atrial and ventricular arrhythmia therapy, and single or dual chamber bradycardia pacing.

Therapies: The Jewel® AF is an implantable medical device that automatically detects and treats episodes of atrial fibrillation (AF), atrial tachycardia (AT), ventricular fibrillation (VF), ventricular tachycardia (VTs), and bradycardia. When an arrhythmia is detected, the implantable device delivers defibrillation, cardioversion, antitachycardia pacing, or bradycardia pacing therapy.

Leads: The Model 7250 Jewel® AF ICD, along with the Medtronic® Transvene® CS/SVC Model 6937A Lead, and other commercially available pace/sense leads and cardioversion/ defibrillation leads, constitutes the implantable portion of the ICD system. The lead systems for the Jewel® AF system are implanted using standard transvenous placement techniques.

Patient Assistant: By means of a hand-held communicator (Patient Assistant), the patient can request delivery of atrial cardioversion therapy as programmed by the physician.

1.1 Programming Options

1.1.1 Tiered Therapy for AT

Up to six automatic AT therapies are available for device-detected AT:

AT Therapies 1 – 2	Programmable to Antitachycardia Pacing (or Skip)
AT Therapy 3	Programmable to 50 Hz Burst Pacing (or Skip)
AT Therapies 4 – 6	Programmable to A-Defib (or Skip)

1.1.2 AT Therapy Programming Sequence Options:

Antitachycardia Pacing only

Antitachycardia Pacing → 50 Hz Burst Pacing

Antitachycardia Pacing → 50 Hz Burst Pacing → A-Defib

50 Hz Burst Pacing only

50 Hz Burst Pacing → A-Defib

A-Defib only

1.1.3 Tiered Therapy for AF

Up to six automatic AF therapies are available for device-detected AF:

AF Therapy 1	Programmable to 50 Hz Burst Pacing (or Skip)
AT Therapies 2-6	Programmable to A-Defib (or Skip)

1.1.4 AF Therapy Programming Sequence Options:

50 Hz Burst Pacing only

50 Hz Burst Pacing → A-Defib

A-Defib only

1.2 Model 6937A Transvene® CS/SVC Lead

The Medtronic Transvene® CS/SVC Model 6937A Lead is a modified Model 6937 SVC lead. The modifications include a shorter defibrillation coil and the addition of urethane tubing overlay to increase lead body stiffness. These modifications allow placement in the coronary sinus (CS) in addition to the superior vena cava (SVC).

2 INDICATIONS AND USAGE

The Model 7250 Jewel® AF system is intended to provide pacing, cardioversion, and defibrillation for treatment of patients with:

- symptomatic, drug-refractory, atrial fibrillation, and/or
- life-threatening ventricular tachyarrhythmias.

Notes: Associated with atrial tachyarrhythmia treatment.

1. Use of the ICD system has not been demonstrated to decrease the morbidity related to atrial tachyarrhythmias.
2. The effectiveness of High Frequency Burst pacing (A-50 Hz Burst therapy) in terminating device classified atrial tachycardia (AT) was found to be 11.7%, and in terminating device classified atrial fibrillation (AF) was found to be 18.2%, in the patient population studied.

3 CONTRAINDICATIONS

Do not use the Jewel® AF system in:

- Patients whose tachyarrhythmias may have transient or reversible causes, such as:
  - acute myocardial infarction,
  - digitalis intoxication,
  - drowning,
  - electrocution,
  - electrolyte imbalance,
  - hypoxia,
  - sepsis.
- Patients with incessant VF, VT, or chronic atrial tachyarrhythmia.
- Patients who have a unipolar pacemaker.
- Patients whose primary disorder is bradyarrhythmias.

4 WARNINGS AND PRECAUTIONS

- **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 during implantation.** Do not permit the patient to contact grounded equipment which could produce hazardous leakage current during implantation. Resulting arrhythmia induction could result in the patient's death.
- **Avoiding shock during handling.** Program the ICD 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 while the ICD is charged.
- **Anti-coagulation.** Use of the ICD system should not change the application of established anti-coagulation protocols.
- **Suspension of ventricular pacing.** There is no backup bradycardia pacing in the ventricle during atrial antitachycardia pacing (ATP).
- **Occurrence of stroke.** Following an ischemic or cerebrovascular accident, disable atrial defibrillation therapies until the patient has stabilized.

4.1 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 could be reduced.
- **If package is damaged.** Do not use 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.

4.2 Implantation and ICD Programming

- 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, application software, and accessories 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 4.50 volts or less. Immediate replacement is recommended if the programmer displays a Charge Circuit Timeout or Charge Circuit Inactive message.
- Program ICD parameters such as sensitivity thresholds and detection intervals according to the recommendations in the technical manual.
- Program the first atrial defibrillation therapy to two times the atrial defibrillation threshold, or the maximum output.

  Note: Limit the number of automatic atrial defibrillation therapies in patients who experience frequent episodes of atrial tachyarrhythmias.
- **Suspension of ventricular pacing.** There is no backup bradycardia pacing in the ventricle during atrial antitachycardia pacing (ATP). The "Initial # Pulses" parameter should not be set to large values for ventricular pace dependent patients.

4.3 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.
- 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 that 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.
- Refer to the lead technical manuals for specific instructions and precautions.

4.4 Follow-up Testing

- Ensure that an external defibrillator and medical personnel skilled in cardiopulmonary resuscitation (CPR) are present during post-implant ICD testing should the 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.

4.5 ICD Explant and Disposal

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

4.6 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.

4.6.1 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 bipolar configuration is recommended whenever practical. Also, the current path and (if monopolar electrocautery is used) the 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.

- **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.
- **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.

4.6.2 **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 if 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 is necessary.

Cellular Phones – Cellular phones may interact with the implanted ICD when placed in close proximity to the device. Patients should maintain a minimum separation of 15 centimeters [six inches] between the phone and the implanted ICD, hold the phone to 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 phones included in Table 1. Based on this testing, the ICD should not be affected by the normal operation of such cellular phones.
- The ICD contains circuitry that allows usage without interaction (when programmed to nominal sensitivity) of all cellular phones having one of the transmission technologies listed in Table 1. These transmission technologies represent most of the cellular phones in use worldwide. 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 - 50 Hz)	824 - 849 MHz
PCS[c] 1800	1850 - 1910 MHz
International Standards	
GSM[d] [minimum of 2.5 cm from ICD recommended]	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] Personal Communication System
[d] Global System for Mobile Communications
[e] Digital Cellular System
[f] Code Division Multiple Access - Direct Sequence

5 ADVERSE EVENTS (AF-Only Patients)

The clinical study of the Model 7250 Jewel® AF system for AF-only patients is summarized below.

Table 2. Patient Enrollment, Device Implantations, and Follow-Up, AF-Only Study

Patient enrollment (worldwide)	146 patients
Patients implanted with Jewel® AF	144 patients
Cumulative patient follow-up	1838 months
Average individual patient follow-up	12.6 ± 6.2 months

There were 8 deaths (5.5%) in the 146-patient clinical study. Causes of death as classified by the investigator and the independent clinical events committee were as follows: one death attributed to ventricular fibrillation arrest (37 days post-implant); one death attributed to congestive heart failure (89 days post-implant); one death attributed to pneumonia (251 days post-implant); one death attributed to post-heart transplant complications (390 days post-implant); one death attributed to refractory heart failure and respiratory failure (444 days post-implant); one death attributed to cardiogenic shock/respiratory failure (454 days post-implant); one death attributed to unknown cause (466 days post-implant); one death attributed to hyperkalemia (476 days post-implant).

The following table indicates incidence of three types of adverse outcomes (cardiovascular accident, death, and new onset ventricular tachyarrhythmias) among patients in the 7250 AF-Only PMA Clinical Report Update population (N=146). This table has been stratified by patients' ejection fraction (EF) as measured within six months prior to enrollment. Results of a statistical analysis of the above numbers indicate a significant difference in rate of adverse outcomes among the three groups (Pearson chi-square test, p=0.002), with patients in the low EF group (EF =40%) suffering significantly more adverse outcomes than those in the other two groups (p<0.001). The high EF group (EF>40%) and the unknown EF group did not differ significantly (p=0.26).

Table 3. Patients Experiencing Adverse Outcomes by Ejection Fraction, AF-Only Study (N=146)

EF Group	CVA	Death	New VT/VF	Total[a]
EF = 40% (n=28)	1 (3.6 %)	4 (14.3 %)	6 (21.4 %)	10 (35.7 %)
EF > 40% (n=67)	3 (4.5 %)	1 (1.5 %)	1 (1.5 %)	5 (7.6 %)
EF unknown (n=51)	0 (0.0 %)	3 (5.9 %)	4 (7.8 %)	7 (13.7 %)
Total (N=146)	4 (2.7 %)	8 (5.5 %)	11 (7.5 %)	22 (15.1 %)

[a] One patient who experienced new onset VT/VF subsequently died, so row totals do not all add up.

Table 4 summarizes adverse events experienced during the clinical investigation.

Table 4. Adverse Event Summary, AF-Only Study

Adverse Event Summary (N=146)[a]	Number of events	Number of patients	Percent of patients
Adverse Events at Implant	11	11	7.5 %
Complications	26	23	15.8 %
Observations	221	97	66.4 %
Non System-Related Adverse Events	322	95	65.1 %
Total Adverse Events	**580**	**131**	**89.7 %**

[a] Over a cumulative follow-up of 1838 months.

Table 5 reports system-related adverse events at implant. Table 6 reports system-related complications post-implant. Table 7 reports system-related observations. Each adverse event was reviewed by an independent clinical events committee to determine whether it was related to the ICD system.

Table 5. Adverse Events Related to ICD System at Implant, AF-Only Study (N=146)

	# of Events	# of Patients	% of Patients
Early recurrence of AF (ERAF)	4	4	2.7 %
Shoulder pain	2	2	1.4 %
Congestive heart failure	1	1	0.7 %
Inappropriate detection	1	1	0.7 %
No device implanted (atrial myopathy)	1	1	0.7 %
No device implanted (high ventricular DFT)	1	1	0.7 %
Oversensing	1	1	0.7 %
Total	**11**	**11**	**7.5 %**

Table 6. Complications[a] Related to ICD System Post-Implant (N=146)

	# of Events	# of Patients	% of Patients
Lead dislodgement	11	10	6.8 %
Atrial fibrillation	3	3	2.1 %
Hematoma	2	2	1.4 %
Infection	2	2	1.4 %
Allergic reaction	1	1	0.7 %
Anxiety	1	1	0.7 %
Inappropriate detection	1	1	0.7 %
Lead failure	1	1	0.7 %
Pacemaker syndrome	1	1	0.7 %
Patient unable to tolerate therapy	1	1	0.7 %
Skin irritation	1	1	0.7 %
Total	26	23	15.8 %

[a] Complications are adverse events that required invasive intervention.

Table 7. Observations[a] Related to ICD System, AF-Only Study (N= 146)

Adverse Event	# of Events	# of Patients	% of Patients
Inappropriate detection	41	27	18.5 %
Failure to cardiovert / defibrillate	26	19	13.0 %
Incisional pain	23	22	15.1 %
Atrial fibrillation	17	15	10.3 %
Oversensing	16	16	11.0 %
Patient activator	12	11	7.5 %
Anxiety	10	7	4.8 %
Shoulder pain	9	9	6.2 %
Hematoma	8	8	5.5 %
Undersensing	6	4	2.7 %
Bleeding/hemorrhage	4	4	2.7 %
Defibrillation therapy	4	4	2.7 %
Nausea	4	4	2.7 %

Table 7. Observations[a] Related to ICD System, AF-Only Study (N= 146)

Adverse Event	# of Events	# of Patients	% of Patients
Failure to capture	3	3	2.1 %
Pacing therapy	3	3	2.1 %
Other (Fewer than three events)	35	30	20.5 %
Total Observations[b] (including single observations)	**221**	**97**	**66.4 %**

[a] Observations are adverse events that did not require invasive intervention.
[b] Observations that occurred in only one patient are listed following the table. Some patients had more than one type of adverse event.

Single Observations in the AF-Only Study – Each of the following was observed once in one patient:

- Atrial rate stabilization (ARS) Off
- Atrial rate stabilization (ARS) On
- Cerebrovascular accident
- Chest wall pain
- Depression
- Development of VT / Disease progression
- Diaphragmatic stimulation
- Dizziness
- Early recurrence of AF (ERAF)
- Ecchymosis
- Edema
- Infection
- Neuritis
- Pacing threshold
- Pleural effusion
- Pneumothorax
- Thrombus

5.1 Potential Adverse Events

Adverse events associated with ICD systems, in addition to those reported in the tables above, include: Cardiac perforation; Cardiac tamponade; Coronary sinus perforation; Erosion through the skin; Extrusion; False sensing; Fibrotic tissue growth; Fluid accumulation; Formation of hematomas or cysts; Inappropriate pulsing or inhibition of normal electrical conduction; Infection; Keloid formation; Lead dislodgement; Loss of sensing; Muscle and nerve stimulation; Myocardial irritability at implant; Pericarditis; Psychological effects, including psychological intolerance to the ICD, imagined therapies, dependency, fear of inappropriate therapies, and fear that therapeutic capability may be lost; Rejection phenomena (local tissue reaction and fibrotic tissue formation); and Venous perforation.

6 CLINICAL STUDIES (AF-Only Patients)

6.1 Jewel® AF Clinical Study Design (AF-Only Patients)

A global (USA, Europe, and Canada), multicenter, prospective non-randomized clinical study was performed to evaluate the safety (incidence of system-related complications) and effectiveness (treatment of atrial tachyarrhythmias) of the Model 7250 Jewel® AF System in 146 patients.

6.1.1 Patient Population

The study specified that patients eligible for enrollment included those who evidenced symptomatic, drug-refractory atrial tachyarrhythmias. Specifically, the inclusion criteria were as follows:

The patient must have had at least two episodes of atrial fibrillation (AF) and/or atrial flutter (AT) within the three months prior to implant; and

One episode must have had electrocardiographic documentation; and

The episodes must have been symptomatic; and

The patient must have been drug-refractory or intolerant (defined as failure of one or more anti-arrhythmic drug(s) because the drug was deemed ineffective by the investigator or not tolerated by the patient); and

The patient must have been in sinus rhythm at the time of implant, or it must have been possible to cardiovert an atrial arrhythmia to sinus rhythm. Post-cardioversion, the patient must be in sinus rhythm for one hour or longer.

6.1.2 Crossover Study

The Jewel® AF AF-Only clinical trial included a two-period, two-arm, cross-over design to have atrial prevention therapies programmed ON vs. OFF during the first three months of follow-up, then reversed during the second three months of follow-up (with patients acting as their own controls). This design was intended to assess the ability of the prevention therapies to reduce the frequency of atrial arrhythmias. From the sixth month onward, these therapies were programmed at the discretion of the investigator.

6.1.3 Primary Objectives

- **System-Related Complications (complication-free survival):** assess the relative risk of system-related complications following the implant of the Model 7250 Jewel® AF ICD system compared to the Model 7219D system.
- **AF Therapy:** estimate the efficacy of the atrial treatment therapies of the Model 7250 Jewel® AF ICD system in terminating spontaneous atrial tachyarrhythmia episodes.

6.1.4 Secondary Objectives

- Determine the impact of the Model 7250 system on patients' quality of life.
- Estimate the relative risk of death of patients enrolled in the Model 7250 study compared to those enrolled in the Model 7219D study.
- Estimate the positive predictive value of the Model 7250's AT/AF detection algorithm.
- Estimate the efficacy of atrial shock treament therapy in terminating spontaneous AF episodes.
- Estimate the efficacy of antitachycardia pacing (ATP) and high-frequency burst (HFB) in terminating spontaneous atrial tachycardias.
- Estimate the effect of atrial prevention therapies on the frequency of atrial tachyarrhythmia episodes.
- Estimate the mean atrial defibrillation threshold at implants and 3 months post-implant.
- Estimate the incidence of documented atrial shock induced ventricular arrhythmia.

6.1.5 Control Devices

The Model 7219D was prospectively identified as the control device for comparisons involving the primary objectives.

6.1.6 Follow-up

The study specified that patients were to be followed-up with an office visit at one, three, and six months post-implant, and every six months thereafter until completion of the study.

6.2 Clinical Results (AF-Only Patients)

Demographic	Patient Population (N = 146)	
Gender	104 (71%) Male; 42 (29%) Female	
Age	62.1 years (22 - 83 years)	
LV Ejection Fraction	51.1% (15% - 91%)	
Left Atrial Diameter	46.1 mm (11.0 - 60.0 mm)	
History of AT/AF	146 (100%)	
NYHA Classification	Class I	54%
	Class II	34%
	Class III	12%
Primary Indication	History of symptomatic atrial fibrillation	74%
	History of symptomatic atrial fibrillation and flutter	23%
	History of symptomatic atrial flutter	3%
Primary Cardiovascular History (non-exclusive)	Hypertension	45%
	Mitral valve disease/disorder	34%
	Coronary artery disease	32%
	Cardiomyopathy	30%

Table 8. Implant Experience, AF-Only Study

ICD and Lead Implant Success (N=146)	Patients
Patients in whom Model 7250 was implanted	99%
Patients who received a two-lead system	39%
Reason Not Implanted (2 patients, 1.4%)	**Patients**
High ventricular defibrillation threshold	1
Atrial myopathy	1

6.2.1 Lead Configurations

The table below indicates the lead configurations used in the clinical study, and identifies the percentage of the 144 patients receiving the Model 7250 Jewel® AF who were implanted with each lead system.

Table 9. Implanted Lead Configurations, AF-Only Study (N = 144)

Final lead system configurations (ventricular / atrial / coronary sinus)		# of Patients	% of Patients
6940 Atrial Lead			
6945 / 6940		24	16.7 %
6942 / 6940		19	13.2 %
6942 / 6940 / 6937A		10	6.9 %
6945 / 6940 / 6937A		7	4.9 %
6945 / 6940 / 6937		1	0.7 %
	Subtotal	61	42.4 %
6943 Atrial Lead			
6943 / 6943		6	4.2 %
6932 / 6943		3	2.1 %
6945 / 6943		1	0.7 %
6943 / 6943 / 6937A		49	34.0 %
6932 / 6943 / 6937A		6	4.2 %
6932 / 6943 / 6937		3	2.1 %
6943 / 6943 / 6937		2	1.4 %
6943 / 6943 / 6933		1	0.7 %
6943 / 6943 / 6940		1	0.7 %
	Subtotal	72	50.0 %
Other Lead Configurations			
6945 / 4558		2	1.4 %
6942 / 5554		1	0.7 %
6942 / 5554 / 6937A		3	2.1 %
6942 / 1388T / 6937A		1	0.7 %
6942 / 4269 / 6937A		1	0.7 %
6942 / 4592 / 6937A		1	0.7 %
6945 / 4068 / 6937A		1	0.7 %
6721L / 5071 / 438 / 6721M		1	0.7 %
	Subtotal	11	7.6 %

6.2.2 Tiered Therapy Programming Sequences

Programmed settings for atrial therapy parameters that occurred in the PMA patients at baseline, three months, and the six month follow-up (database cutoff of May 31, 2000) are presented in the following table.

Table 10. Device Programming at Baseline, Three Months and Six Months, AF-Only Study

	Baseline (n=144)	Three Months (n=130)	Six Months (n=124)
AT Therapies			
None			
ATP only	64 (44.4%)	49 (37.7%)	44 (35.5%)
HFB only	- 0 -	3 (2.3%)	2 (1.6%)
Shock only	3 (2.1%)	3 (2.3%)	2 (1.6%)
ATP+HFB	27 (18.8%)	40 (30.8%)	48 (38.7%)
ATP+Atrial Shock	14 (9.7%)	9 (6.9%)	9 (7.3%)
HFB+Atrial Shock	2 (1.4%)	2 (1.5%)	2 (1.6%)
ATP+HFB+Atrial Shock	16 (11.1%)	16 (12.3%)	14 (11.3%)
AF Therapies			
None	44 (30.6%)	34 (26.2%)	30 (24.2%)
HFB only	30 (20.8%)	49 (37.7%)	53 (42.7%)
Atrial Shock only	32 (22.2%)	26 (20.0%)	21 (16.9%)
HFB+Atrial Shock	38 (26.4%)	21 (16.2%)	20 (16.1%)
Atrial Shock Therapies			
None	21 (14.6%)	15 (11.5%)	12 (9.7%)
AF shock only	27 (18.8%)	10 (7.7%)	10 (8.1%)
Patient Activated shock only	52 (36.1%)	68 (52.3%)	70 (56.5%)
AT+AF shocks	19 (13.2%)	13 (10.0%)	11 (8.9%)
AT+Patient Activated shocks	1 (0.7%)	- 0 -	1 (0.8%)
AF+Patient Activated shocks	9 (6.3%)	7 (5.4%)	5 (4.0%)
AT+AF+Patient Activated shocks	15 (10.4%)	17 (13.1%)	15 (2.1%)

6.3 Primary Objectives (AF-Only Study)

6.3.1 System Related Complications

Hypothesis – The objective is met when the ratio of the upper one-sided 95 percent confidence bound for the relative risk of system-related complications, comparing the Model 7250 Jewel® AF to the Model 7219D, is less than or equal to three.

Results – The primary objective of complication-free survival was met. The results included the following:

System Related Complications	Relative Risk	Upper Bound
Model 7250 Jewel® AF vs. Model 7219D	1.31	2.25

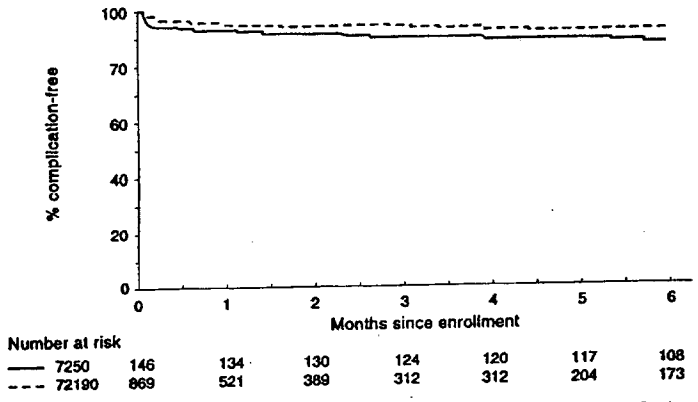


Figure 1. Complication-Free Survival (Kaplan-Meier Plot) For the Model 7250 AF-Only Study

6.3.2 Termination of Spontaneous Atrial Arrhythmias

Hypothesis – The objective is met when the lower one-sided 95% confidence bound on the effectiveness of therapies in terminating spontaneous atrial episodes does not go below 75%. For this high a rate of effectiveness, the sequence of therapies delivered for the episode must include at least one atrial shock.

Results – Among 4859 total spontaneous, appropriately detected atrial episodes, one hundred and seven (107) patients experienced a total of 1200 spontaneous atrial episodes which were treated with a sequence of therapies which included at least one atrial shock. Of these episodes, 1092 (91.0%) were successfully terminated. Based on the results from a generalized estimating equations (GEE) analysis of therapy effectiveness, the estimate of therapy effectiveness is 85.9% with a lower one-sided 95% confidence bound of 81.7%. Thus, this primary objective was met.

Table 11. Atrial Shock Efficacy for AT and AF Episodes

# Episodes Terminated / # Episodes Treated	GEE Estimate	Lower Confidence Bound
1092/1200 (91.0%)	85.9%	81.7%

Table 12 provides a detailed breakdown of the 4859 appropriately detected AT/AF episodes by the sequence of therapies delivered.

Table 12. Breakdown of Spontaneous AF/AT Episodes by Therapy Sequence, AF-Only Study

		AT		AF	
	Therapy Sequences	Episodes	Successes	Episodes	Successes
1	*aATP, 50 Hz, aATP, A-Defib, aATP, A-Defib	1	1	0	0
2	*aATP, 50 Hz, A-Defib, 50 Hz, A-Defib, 50 Hz, A-Defib	1	1	0	0
3	*aATP, 50 Hz, aATP, 50 Hz, A-Defib, 50 Hz, A-Defib	1	1	0	0
4	*aATP, 50 Hz, aATP, A-Defib, aATP, 50 Hz	1	0	0	0
5	aATP	1406	1043	0	0
6	aATP, 50 Hz	872	136	0	0
7	aATP, 50 Hz, aATP	24	4	0	0
8	aATP, 50 Hz, aATP, 50 Hz	78	3	0	0
9	aATP, 50 Hz, aATP, 50 Hz, aATP	2	1	0	0
10	aATP, 50 Hz, aATP, 50 Hz, aATP, 50 Hz	4	0	0	0
11	*aATP, 50 Hz, aATP, 50 Hz, A-Defib	18	17	0	0
12	*aATP, 50 Hz, aATP, A-Defib	5	3	0	0
13	*aATP, 50 Hz, aATP, A-Defib, aATP, 50 Hz, A-Defib	2	1	0	0
14	*aATP, 50 Hz, A-Defib	206	185	0	0
15	*aATP, 50 Hz, A-Defib, aATP, 50 Hz, A-Defib	2	2	0	0
16	*aATP, A-Defib	94	77	0	0
17	*aATP, A-Defib, aATP	1	1	0	0
18	*aATP, A-Defib, aATP, 50 Hz	1	0	0	0
19	50 Hz	128	24	409	227
20	50 Hz, aATP	0	0	265	61
21	50 Hz, aATP, 50 Hz	0	0	437	56
22	50 Hz, aATP, 50 Hz, aATP	0	0	7	1
23	50 Hz, aATP, 50 Hz, aATP, 50 Hz	0	0	26	1
24	50 Hz, aATP, 50 Hz, aATP, 50 Hz, aATP, 50 Hz	0	0	1	0
25	*50 Hz, aATP, 50 Hz, aATP, 50 Hz, A-Defib	0	0	5	5

Table 12. Breakdown of Spontaneous AF/AT Episodes by Therapy Sequence, AF-Only Study

		AT		AF	
	Therapy Sequences	Episodes	Successes	Episodes	Successes
26	*50 Hz, aATP, 50 Hz, aATP, A-Defib	0	0	3	3
27	*50 Hz, aATP, 50 Hz, A-Defib	0	0	160	145
28	*50 Hz, aATP, 50 Hz, A-Defib, aATP	0	0	1	0
29	*50 Hz, aATP, A-Defib	0	0	33	31
30	*50 Hz, aATP, A-Defib, aATP, 50 Hz, A-Defib	0	0	2	2
31	*50 Hz, aATP, A-Defib, aATP, A-Defib	0	0	2	1
32	*50 Hz, A-Defib	48	48	212	202
33	*50 Hz, A-Defib, aATP	0	0	1	0
34	*50 Hz, A-Defib, 50 Hz, A-Defib	0	0	1	0
35	*A-Defib	95	88	298	278
36	*A-Defib, aATP	1	0	0	0
37	*A-Defib, 50 Hz, A-Defib, 50 Hz	0	0	1	1
38	*50 Hz, aATP, A-Defib, aATP, A-Defib, aATP, 50 Hz	0	0	1	1
39	*50 Hz, A-Defib, aATP, 50 Hz, A-Defib	0	0	1	1
40	*50 Hz, aATP, 50 Hz, A-Defib, 50 Hz	0	0	1	0
41	*50 Hz, aATP, A-Defib, 50 Hz	0	0	1	0
	Total	2991	1636	1868	1016

6.4 Secondary Objectives (AF-Only Study)

6.4.1 Impact on Patients' Quality of Life

Hypothesis – Two quality of life instruments were used to assess the impact of the Model 7250 Jewel® AF system on patients' quality of life. The first, the Health Status Questionnaire Short Form (SF-36), is a standardized generic health survey instrument. The second quality of life instrument used was the Symptom Checklist (SCL) developed by Bublen and Kay.

Results – Using repeated-measures analyses, a majority of the eight basic SF-36 scales showed significant improvement over time. The Role-Physical scale, which shows the greatest raw increase from baseline to 3 and 6 months among all the scales, has a significant MANOVA test of differences ($p<0.001$). Both contrasts, baseline to 3 months and baseline to 6 months, are significant ($p<0.001$ and $p<0.001$, respectively) as well. Also showing significant improvement over time are physical functioning (overall $p<0.001$, 3 and 6 month contrast p-values<0.001); vitality (overall $p<0.001$, 3-month $p<0.001$, 6-month $p=0.002$); social functioning (overall $p=0.024$, 3-month $p=0.010$, 6-month $p=0.022$); and mental health (overall $p=0.039$, 3-month $p=0.012$).

Looking at the Symptom Checklist, the frequency of symptoms at 3 and 6 months decreases significantly from baseline. The overall test is significant ($p<0.001$) with the tests comparing baseline to 3 months and baseline to 6 months also significant ($p<0.001$ and $p<0.001$, respectively). Similarly, severity of symptoms decreases over time, with an overall $p=0.002$ and 3- and 6-month p-values less than 0.001 and equal to 0.006, respectively.

Table 13. Results of Repeated Measures MANOVA for SF-36 and SCL Scales

Scale	Repeated Measures MANOVA p-value	Baseline to 3 months p-value	Baseline to 6 months p-value
General Health	0.16	n/a	n/a
Physical Functioning	<0.001[a]	<0.001[a]	<0.001[a]
Role Physical	<0.001[a]	<0.001[a]	<0.001[a]
Role Emotional	0.16	n/a	n/a
Social Functioning	0.024[b]	0.010[b]	0.022[b]
Mental Health	0.039[b]	0.012[b]	0.11
Bodily Pain	0.14	n/a	n/a
Vitality	<0.001[a]	<0.00[a]	0.002[a]
Frequency of symptoms	<0.001[a]	<0.001[a]	<0.001[a]
Severity of Symptoms	0.002[a]	<0.001[a]	0.006[a]

[a] Indicates a highly significant result, without Bonferroni corrections.
[b] Indicates a significant result, without Bonferroni corrections.
n/a refers to not applicable since the overall test is not significant.

6.4.2 Relative risk of death compared to the Model 7219D

Hypothesis – Using a Cox proportional-hazards model, the risk of death for patients implanted with the Model 7250 system was compared to the risk of death reported in Medtronic's clinical study of its Model 7219D system.

Results – The estimated relative risk of death for the Model 7250 compared to the Model 7219D was 0.51 in a covariate adjusted Cox proportional hazards regression model. The upper one-sided 95% confidence bound on the relative risk was 2.17.

6.4.3 Positive predictive value of the AT/AF detection algorithm

Methods – The positive predictive value (PPV) measures the accuracy of the dual chamber detection algorithm. It is the ratio of true positive AT/AF detections to the sum of true positive and false positive AT/AF detections.

Results – Using a Generalized Estimating Equations model, the estimate of the PPV is 98.6% with a two-sided 95% confidence interval of (96.0%, 99.5%).

Table 14. Detection of Spontaneous AT/AF Episodes, AF-Only Study

Parameter	Result
Spontaneous Episodes	4913
Number of Episodes Appropriately Detected	4859
Number of Episodes Inappropriately Detected	54
PPV (4859/4913)	98.6%

6.4.4 Efficacy of atrial shock therapy for AF episodes

Methods – Atrial shock was applied to terminate AF, and the efficacy of the treatment assessed.

Results – Of 1868 AF episodes, 723 were treated with atrial shock. These 723 episodes occurred in 85 patients. Of these episodes, 668 (92.4%) were successfully terminated. The mean number of shocks per episode was 1.18 and 629 (87.0%) were treated with a single shock. The GEE estimate of therapy efficacy is 88.4%, with a lower one-sided 95% confidence bound of 84.2%.

Table 15. Atrial Shock Efficacy for AF Episodes Only

# Episodes Terminated / # Episodes Treated	GEE Estimate	Lower Confidence Bound
668/723 (92.4%)	88.4%	84.2%

6.4.5 Efficacy of ATP and HFB in terminating atrial tachyarrhythmias

Methods – The Model 7250 Jewel® AF atrial pacing therapies include antitachycardia pacing and high-frequency burst, the latter of which is employed to terminate both AT and AF episodes.

Results – Of 4859 spontaneous, appropriately detected atrial episodes, ATP and/or HFB were used in 4466 cases among 109 patients, of which pacing therapy successfully terminated 1560 episodes (34.9%). The GEE estimate of pacing therapy efficacy for all atrial episodes was 28.0%, with a lower one-sided 95% confidence bound of 24.0%. Of 2991 AT episodes, 2696, occurring in 92 patients, were treated with at least one pacing therapy. Pacing therapy successfully terminated 1212 AT episodes (41.9%). The GEE estimate for AT was 35.5%, with a lower one-sided 95% confidence bound of 30.9%. Considering the two therapies separately, ATP successfully terminated 1049 of 2720 AT episodes (38.6%) in 89 patients, with a GEE estimate of 32.1%. HFB was used to terminate both AT and AF; for AT, 74 patients experienced 1394 episodes treated with HFB, of which 163 (11.7%) were successfully terminated, for a GEE estimate of 10.6% efficacy. Among 1570 AF episodes in 86 patients treated with HFB, the therapy successfully terminated 286 episodes (18.2%), with a GEE estimate of 14.1%.

Table 16. ATP and HFB (Pacing) Efficacy for Atrial Episodes

Therapy Delivered / Type of Episodes	# Episodes Terminated / # Episodes Treated	GEE Estimate
Pacing / all atrial episodes	1560 / 4466 (34.9%)	28.0%
Pacing / AT episodes only	1212 / 2696 (41.9%)	35.5%
ATP / AT episodes only	1049 / 2720 (38.6%)	32.1%
HFB / AT episodes only	163 / 1394 (11.7%)	10.6%
HFB / AT episodes only	286 / 1570 (18.2%)	14.1%

6.4.6 Effect of atrial prevention therapies on frequency of AT/AF

Methods – A subset of 75 patients completed both a 3-month period when atrial prevention therapies (Atrial Rate Stabilization and Switchback Delay) were ON and another 3-month period when atrial prevention therapies were OFF. The order of therapies (ON/OFF or OFF/ON) was assigned at random; 38 patients (50.7%) were in the ON/OFF group and 37 patients (49.3%) were in the OFF/ON group. Frequency of atrial episodes was calculated for each period as the number of episodes in the period divided by the follow-up time in the period, normalized to 3 months. For each patient, the difference between the frequency of atrial episodes when atrial prevention therapies are OFF minus the frequency when therapies are ON was obtained. Positive differences indicated a reduction in frequency when therapies were ON.

Results – The difference in the frequency of atrial episodes when atrial prevention therapies are ON (Table 17) is not statistically significantly different from zero (Wilcoxon signed-rank test, p=0.72).

Table 17. Efficacy of Atrial Prevention Therapies, AF-Only Study

Difference, ON vs. OFF	p-value
0.0	0.72

6.4.7 Mean atrial defibrillation threshold at implant and at 3-month follow-up

Methods – Atrial DFT testing involved a two-tiered step-up protocol. Using this method, an atrial DFT (A-DFT+) was determined for 86 patients at implant and four patients at 3-month follow-up.

Results – The mean A-DFT+ at implant was 6.8 +/- 4.8 joules, and at 3 months was 2.5 +/- 1.0 joules. All four patients' A-DFT+ decreased from implant to 3-month follow-up.

Time of Assessment	# of Patients Assessed	Mean A-DFT+ (joules)
Implant	86	6.8 ± 4.8
3-month follow-up	4	2.5 ± 1.0

6.4.8 Incidence of atrial shock-induced ventricular arrhythmia

Methods – Post-atrial shock, episode records were inspected for evidence of shock-induced ventricular arrhythmia.

Results – Of the 1200 spontaneous atrial episodes treated with at least one atrial shock, no incidences of documented atrial shock induced ventricular arrhythmia occurred. The two-sided 95% confidence interval based on the exact binomial distribution for the incidence of documented atrial shock induced ventricular arrhythmia is (0%, 0.3%).

Table 18. Atrial Shock-Induced Ventricular Arrhythmias

# A-Shock-Induced VT/VF / # Atrial Episodes with Shock	Binomial Estimate	Upper Confidence Bound
0 / 1200	0.0%	0.3%

6.5 Model 9464 Patient Activator

The Model 9464 Patient Activator is a battery-powered, radio-frequency device used to self-activate atrial shock therapy in conjunction with the implanted Model 7250 device. For a patient to self-activate atrial shock therapy, the patient-activated therapy must be programmed ON in the implanted Model 7250 device. Pending patient-activated atrial shock therapy takes priority over automatic atrial fibrillation (AF) or atrial tachycardia (AT) therapies that may also be programmed ON.

Whenever a patient feels he may be in AF/AT and desires to receive therapy, he can send a request for atrial shock therapy to his implanted Model 7250 device by pressing the button on the Patient Activator. The Patient Activator is designed to provide information back to the patient after the button is pushed by way of audible tones and colored lights.

Although use of the Model 9464 Patient Activator was optional, the majority of the Model 7250 AF-Only patients opted to use it. Currently 70.8% of the AF-Only study patients have patient-activated shocks programmed ON.

Although the Model 9464 Patient Activator was used most heavily by the Model 7250 AF-Only patients, four patients from a previous Model 7250 study of patients with AF+VT/VF who suffered from symptomatic atrial arrhythmias also used the Patient Activator. Table 19 presents follow-up information for the patients from each study who ever used the Model 9464 Patient Activator through May 31, 2000. These 71 patients represent 1003 months of Model 9464 Patient Activator experience.

Table 19. Follow-up Information: Users of Model 9464 Patient Activator

	AF-only (n=67)	AF+ VT/VF (n=4)	Total (N=71)
Mean ± S.D. (months)	13.6 ± 6.4	22.3 ± 8.9	14.1
Range (months)	2.1 - 25.9	11.9 - 32.4	2.1 - 32.4

Table 20 shows the frequency of patient use of the Model 9464 Patient Activator for episodes lasting at least 30 minutes; i.e., those episodes of sufficient length to make spontaneous termination less likely. Use of the Patient Activator is divided into three-month intervals post-implant. The data indicates that patients consistently used the Patient Activator for treatment of atrial arrhythmias, with generalized estimating equations (GEE) estimates of frequency of use ranging from 40.9% to 52.1% for the 1551 episodes considered. The 459 episodes for which the Patient Activator was used represent 82.1% of all uses of the activator, indicating that the 30-minute cutoff is successfully capturing actual use. After three months post-implant, for the GEE model no trend in time is evident (p=0.23), indicating that patient use of the Model 9464 was consistent over time.

Table 20. Frequency of Use of Model 9464 Patient Activator In Episodes > 30 Minutes

Months post-implant	Episodes lasting >30 minutes		Uses of Patient Activator in episodes lasting >30 minutes			GEE estimate of frequency of use
	# of episodes	# of patients	# of episodes	# of patients	% of patients	
0 - 3	685	57	176	46	80.7 %	52.1 %
3 - 6	192	39	57	25	64.1 %	42.3 %
6 - 9	203	34	76	23	67.6 %	40.9 %
9 - 12	188	23	64	12	52.2 %	41.9 %
12 - 15	176	25	65	10	40.0 %	42.1 %
15 - 18	107	14	21	8	57.1 %	42.5 %

A summary of adverse events is shown in Table 21. There were 14 occasions in 11 patients when there was a failure to cardiovert or defibrillate an episode of AT/AF following the successful delivery of a patient activated shock. There were 13 adverse events related to the operation of the Model 9464 Patient Activator that occurred in 12 patients. Ten events were due to a patient's inability to activate a shock due to either too high of a ventricular rate, suspension of therapies, or the absence of an atrial arrhythmia (this last cause was categorized as a non-system/procedure related adverse event and occurred one time in one patient). The remaining three events were due to the Patient Activator reportedly not sounding warning tones prior to the shock, most likely because the activator was moved out of range of the device before receiving confirmation of therapy delivery.

Table 21. Summary of Model 9464 Patient Activator Adverse Events

Adverse Event	Number of events	Number of patients (%)	Percent of patients (%)
Failure to Cardiovert/Defibrillate	14	11	7.6 %
Patient Activator - Inability to Activate Shock	10	9	6.2 %
Patient Activator - Shocks Without Prior Warning Tones	3	3	0.7 %
Total	**27**	**23**	**14.5 %**

6.6 Model 6937A CS/SVC Lead

Patients in both the AF-Only study and a previous Model 7250 study of patients with AF+VT/VF were implanted with the Model 6937A coronary sinus lead. In the AF+VT/VF study, 35/530 patients (7%) were implanted with 36 Model 6937A leads at 10 investigative centers. In the AF-Only study, 79/146 patients (54%) were implanted with 79 Model 6937A leads at 17 investigative centers.

The Model 6937A follow-up experience by study appears in Table 22.

Table 22. Follow-up Information: Model 6937A CS/SVC Lead

	AF-only (n=79)	AF+ VT/VF (n=35)	Total (N=114)
Mean ± S.D. (months)	12.8 ± 6.0	12.8 ± 6.5	12.8 ± 6.2
Range (months)	0.1 - 24.4	0.8 - 24.7	0.1 - 24.7

A-DFT+ testing was completed in 63 Model 6937A patients at implant. The mean A-DFT+ for all Model 6937A patients was 6.2 ± 4.6 joules, and 6.6 ± 4.8 joules for patients enrolled in the AF-Only study in particular.

Table 23 details adverse events (complications and observations) related to the Model 6937A in both the AF-Only and AF+VT/VF studies.

Table 23. Model 6937A Lead-Related Adverse Events

Patient ID	Days post-Implant	Description and outcome
AF-Only Study		
022-313200-008	1	Lead dislodgment. Abnormal chest x-ray revealed CS lead was dislodged into the pulmonary artery, confirmed by angiogram two days later. 6937A lead was successfully repositioned into CS.

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Table 23. Model 6937A Lead-Related Adverse Events

Patient ID	Days post-implant	Description and outcome
022-410980-003	7	Subclavian vein thrombosis. The patient experienced swelling in his left arm. The patient's dose of Coumadin was increased.
AF+VT/VF Study		
010-109620-007	1	Lead dislodgement. Abnormal chest x-ray revealed CS lead was dislodged. The lead was successfully repositioned into the CS.
010-119510-003	4	Lead dislodgment. Inappropriate VF therapy due to noise/ oversensing on ventricular channel associated with 6937A lead being dislodged into the outflow tract and interacting with the RV distal coil of 6945 lead. 6937A lead was explanted after failed attempts to reposition it.

6.7 Gender Bias Analysis (AF-Only Study)

Differences between males and females with respect to the primary clinical objectives of complication-free survival and effectiveness in terminating atrial arrhythmias were inspected. Based on univariate analyses, there were no statistically significant associations between gender and either of the primary outcomes. With respect to the primary objective associated with the safety of the Model 7250 Jewel® AF, a Cox proportional hazards regression model of the time to the first system/procedure related complication was used. The coefficient in the model representing differences between genders was not significant (p=0.74). A generalized estimating equations (GEE) model was used to examine the difference in the effectiveness of atrial shock therapy between males and females. The results show no statistically significant difference between genders (p=0.65).

7 PATIENT SELECTION AND TREATMENT

7.1 Individualization of Treatment

Pectoral or abdominal implant site – Evaluate the prospective patient's size and activity level to determine whether a pectoral or abdominal implant is suitable.

Exercise stress testing – If the patient's condition permits, use exercise stress testing to:

- Determine the maximum rate of the patient's normal rhythm
- Identify any supraventricular tachyarrhythmias
- Identify exercise induced tachyarrhythmias.

The maximum exercise rate or the presence of supraventricular tachyarrhythmias may influence selection of programmable parameters. Holter monitoring or other extended ECG monitoring also may be helpful.

Electrophysiologic (EP) testing – It is strongly recommended that candidates for ICD therapy have a complete cardiac evaluation including EP testing. EP testing should identify the classifications and rates of all the ventricular and atrial arrhythmias, whether spontaneous or induced during EP testing.

Drug resistant supraventricular tachyarrhythmias (SVTs) may initiate frequent unwanted device therapy. A careful choice of programming options is necessary for such patients.

Antiarrhythmic drug therapy – If the patient is being treated with antiarrhythmic or cardiac drugs, the patient should be on a maintenance drug dose rather than a loading dose at the time of ICD implantation. If changes to drug therapy are made, repeated arrhythmia inductions are recommended to verify ICD detection and conversion. The ICD also may need to be reprogrammed.

Changes in a patient's antiarrhythmic drug or any other medication that affects the patient's normal cardiac rate or conduction can affect the rate of tachyarrhythmias and/or effectiveness of therapy.

Selection of atrial tachyarrhythmia therapies – The therapy sequence for treatment of AF/AT was not controlled in the study of the ICD. The relative effectiveness of various AF/AT therapy programming sequences cannot be determined from the study data.

Direct any questions regarding the individualization of patient therapy to Medtronic's representative at 1-800-PCD-INFO (1-800-723-4636).

7.2 Specific Patient Populations

Pregnancy – If there is a need to image the ICD, care should be taken to minimize radiation exposure to the fetus and the mother.

Nursing Mothers – Although appropriate biocompatibility testing has been conducted for this implant device, there has been no quantitative assessment of the presence of leachables in breast milk.

Pediatric Patients – This ICD has not been studied in patients younger than 13 years of age.

Geriatric Patients – Most (67%) of the patients receiving this ICD in clinical studies were over the age of 60 years – see "CLINICAL STUDIES (AF-Only Patients)").

Handicapped and Disabled Patients – Special care is needed in using this ICD for patients using electrical wheelchairs or other electrical (external or implanted) devices.

8 PATIENT COUNSELING INFORMATION

Physicians should consider the following points in counseling the patient about this ICD:

- Persons administering CPR may experience the presence of voltage on the patient's body surface (tingling) when the patient's ICD system delivers a shock.
- Encourage patients to use identification cards (issued by Medtronic) and/or identification bracelets documenting their ICD system.

Discuss information in the Patient Manual (*Restoring the Rhythms of Life*) with patients before and after ICD implantation so they are fully familiar with operation of the ICD. Advise patients how to obtain additional copies of the patient manuals.

9 CONFORMANCE TO STANDARDS

This ICD was developed in conformance with all or parts of the following standards:

- ISO 5841-3:1992(E), IS-1 IPG Connector Standard.
- ISO 11318:1993(E), DF-1 Defibrillator Connector Standard.

This information should not be used as a basis of comparisons among devices since different parts of the standards mentioned may have been used.

10 HOW SUPPLIED

The Model 7250 Jewel® AF is packaged one per package in a sterile package.

11 CLINICIAN USE INFORMATION

11.1 Physician Training

Physicians should be familiar with sterile ICD implant procedure and familiar with follow-up evaluation and management of patients with a defibrillator (or referral to such a physician).

11.2 Directions for Use

ICD operating characteristics should be verified at the time of implantation and recorded in the patient file. Complete the Device Registration Form and return it to Medtronic as it provides necessary information for warranty purposes and patient tracking.

The Model 7250 Product Information Manual (PIM) is a separate document supplied with each ICD. This manual includes product specifications, operating characteristics, and implant and follow-up recommendations. The Jewel® AF System Reference Guide (SRG), supplied with the 9961E software, provides complete programming instructions and recommendations. Copies can be obtained by contacting the Medtronic representative, or by calling 1-800-PCD-INFO (1-800-723-4636). The PIM and SRG were last updated in April 2001.

This Prescriber's Package Insert was last updated April 2001.

11.3 Maintaining Device Effectiveness

11.3.1 ICD Storage

FOR SINGLE USE ONLY. Do not resterilize and reimplant an explanted ICD. Medtronic has sterilized the ICD with ethylene oxide prior to shipment. Resterilizing the ICD is necessary if the seal on the sterile package is broken. Resterilization does not affect the "Use Before" date because this date is based on battery life and sterility.

Do not implant the ICD when:

- It has been dropped on a hard surface from a height of 45 cm (18 inches) or more because this could have damaged pulse generator components;
- Its storage package has been pierced or altered, because this could have rendered it non-sterile;
- It has been stored or transported outside the environmental temperature limits of -18 to 55 °C (0 to 131 °F), as the ICD circuitry may have been damaged; or
- Its "Use Before" date has expired, because this can adversely affect ICD longevity or sterility.

11.3.2 Sterilization Instructions

Do not resterilize the ICD or the torque wrench using an autoclave, gamma radiation, organic cleaning agents (e.g., alcohol, acetone, etc.), or ultrasonic cleaners.

Should sterilization be required:

- Repackage all items in a gas permeable container;
- Use a validated ethylene oxide gas process;
- Follow the manufacturer's operation instructions so long as the maximum temperature does not exceed 55 °C (131 °F);
- Store the resterilized components for an appropriate period to permit aeration of ethylene oxide gas.

12 PATIENT INFORMATION

Information for the patient is available in a separate booklet, *Restoring the Rhythms of Life*, from Medtronic. To obtain a copy, contact the Medtronic representative or call 1-800-PCD-INFO (1-800-723-4636). This information should be given to each patient with their ICD, and offered to the patient on each return visit or as deemed appropriate.

Restoring the Rhythms of Life was developed using patient and clinician input to ensure that it is understandable. *Restoring the Rhythms of Life* was last updated November 1999.

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When Life Depends on Medical Technology

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