Temporal Decline in Defibrillation Thresholds With an Active Pectoral Lead System

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OBJECTIVES
The objective of this study was to characterize temporal changes in defibrillation thresholds (DFTs) after implantation with an active pectoral, dual-coil transvenous lead system.

BACKGROUND
Ventricular DFTs rise over time when monophasic waveforms are used with non-thoracotomy lead systems. This effect is attenuated when biphasic waveforms are used with transvenous lead systems; however, significant increases in DFT still occur in a minority of patients. The long-term stability of DFTs with contemporary active pectoral lead systems is unknown.

METHODS
This study was a prospective assessment of temporal changes in DFT using a uniform testing algorithm, shock polarity and dual-coil active pectoral lead system. Thresholds were measured at implantation, before discharge and at long-term follow-up (70 ± 40 weeks) in 50 patients.

RESULTS
The DFTs were 9.2 ± 5.4 J at implantation, 8.3 ± 5.8 J before discharge and 6.9 ± 3.6 J at long-term follow-up (p < 0.01 by analysis of variance; p < 0.05 for long-term follow-up vs. implantation or before discharge). The effect was most marked in a prespecified subgroup with high implant DFTs (≥15 J). No patient developed an inadequate safety margin (<9 J) during follow-up.

CONCLUSIONS
The DFTs declined significantly after implantation with an active pectoral, dual-coil transvenous lead system, and no clinically significant increases in DFT were observed. Therefore, routine defibrillation testing may not be required during the first two years after implantation with this lead system, in the absence of a change in the cardiac substrate or treatment with antiarrhythmic drugs. (J Am Coll Cardiol 2001;38:1150–5) © 2001 by the American College of Cardiology

Implantable cardioverter-defibrillators (ICDs) decrease mortality among patients who present with sustained ventricular arrhythmias (1) and those with ischemic cardiomyopathy who have inducible, sustained ventricular arrhythmias during electrophysiologic studies (2,3). It is likely that the expected survival of patients with an ICD will continue to improve as effective new treatments for congestive heart failure are incorporated into clinical practice (4,5). The improved survival of patients with an ICD and the expanding indications for ICD placement have contributed to a dramatic increase in the number of patients who require longitudinal follow-up for their devices. Although the efficacy of the ICD for terminating ventricular arrhythmias is well established, it is contingent on the presence of an adequate safety margin for defibrillation and the integrity of the pulse generator and lead system. Certain malfunctions, such as lead dislodgment, fracture, insulation defects or random failure of pulse generator components can be discovered during routine ICD interrogation, including measurement of lead impedance and pacing and sensing thresholds (6,7). However, some patients may develop an inadequate safety margin for defibrillation over time, which would not be recognized without defibrillation testing. Such late increases in defibrillation thresholds (DFTs) have been reported with several transvenous and hybrid lead systems (8–15). Although many different lead systems were previously used for ventricular defibrillation, the most common configuration now consists of an active pectoral can with a transvenous lead, because of the simplicity of the implantation procedure and enhanced treatment efficacy (16–18). In the present study, we report the first long-term follow-up of temporal changes in DFT with a dual-coil, active pectoral lead system.

METHODS

Patient group. The inclusion criterion for this prospective study was initial pectoral ICD placement for standard clinical indications. The indications for ICD placement were sustained monomorphic ventricular tachycardia or ventricular fibrillation arrest (48%), syncope with inducible, sustained ventricular tachycardia at electrophysiologic testing (30%) and ischemic cardiomyopathy with asymptomatic, nonsustained ventricular tachycardia and inducible, sustained ventricular tachycardia at electrophysiologic testing (22%). Exclusion criteria were a medical condition that precluded ICD testing, inability to return for follow-up testing, implantation of a subcutaneous array or patch, unwillingness or inability to give informed consent or participation in another research protocol.

The null hypothesis was that long-term DFTs would be unchanged, compared with DFTs at implantation. The sample size of 50 patients was chosen to provide >90% power to detect a 25% change in DFT, which would be
the right ventricle and a proximal platinum coil (660 mm²) vein. This is a tripolar lead consisting of a distal electrode (Endotak DSP, models 0125 and 0145, Guidant Corp.) was placed under fluoroscopic guidance at the right atrium–superior vena cava junction. The distance from the lead tip to the proximal coil is 18 cm. The active can was either a defibrillator emulator (model 6967) or a pulse generator, which was placed subcutaneously in the left (n = 45) or right (n = 5) prepectoral space. The pulse generators used in the study included the Mini (models 1640, 1742 and 1743, Guidant Corp.) in 9 patients, Mini II (models 1762 and 1763, Guidant Corp.) in 31 patients, Mini III or IV (models 1782 and 1790, Guidant Corp.) in 6 patients and AV or AVII (models 1810 and 1821, Guidant Corp.) in 4 patients.

Defibrillator implantation. A uniform lead system and biphasic waveform were used in this study to eliminate any confounding influence of these factors on the results. All defibrillator components used in this study were manufactured by Cardiac Pacemakers Inc. (Guidant Corp., St. Paul, Minnesota). The transvenous passive-fixation defibrillation lead (Endotak DSP, models 0125 and 0145, Guidant Corp.) was placed under fluoroscopic guidance at the right ventricular apex through a subclavian, cephalic or axillary vein. This is a tripolar lead consisting of a distal electrode for sensing and pacing, a distal platinum coil (450 mm²) in the right ventricle and a proximal platinum coil (660 mm²) at the right atrium–superior vena cava junction. The distance from the lead tip to the proximal coil is 18 cm. The active can was either a defibrillator emulator (model 6967) or a pulse generator, which was placed subcutaneously in the left (n = 45) or right (n = 5) prepectoral space. The pulse generators used in the study included the Mini (models 1640, 1742 and 1743, Guidant Corp.) in 9 patients, Mini II (models 1762 and 1763, Guidant Corp.) in 31 patients, Mini III or IV (models 1782 and 1790, Guidant Corp.) in 6 patients and AV or AVII (models 1810 and 1821, Guidant Corp.) in 4 patients.

Defibrillation threshold testing. According to the study protocol, in each patient, DFTs were measured at implantation, before discharge (1 to 3 days after implantation) and at least six months after implantation. Although the minimal required length of follow-up was six months, long-term DFT testing was performed at later intervals whenever possible. Long-term DFT testing was done electively on an outpatient basis in the majority of patients (80%); the remaining patients (20%) underwent long-term DFT testing before initiation of antiarrhythmic drugs, when they presented with frequent ICD discharges due to atrial or ventricular arrhythmias. All testing was performed using conscious sedation with midazolam and fentanyl.

Ventricular fibrillation was induced with T-wave shocks or high-output ramp pacing through the defibrillation lead. The distal coil was the cathode, and the proximal coil and active can were connected electrically as the anode (i.e., normal polarity) for the first phase of the biphasic shock in all patients (19). At implantation, an emulator was used as the active pectoral electrode, and testing was performed with an external defibrillator (ECD, model 2815, Guidant Corp.), whereas at follow-up evaluations, device-based testing was performed with the pulse generator shell as the active pectoral electrode. Impedance measurements were made from pulse generator discharges of comparable energies at implantation and follow-up (20). The ECD, Mini and AV pulse generators have a capacitance of 140 μF, whereas the Mini II and AVII pulse generators have a capacitance of 125 μF. Mini III and IV have a capacitance of 105 μF. The biphasic waveform tilt is the same for all of these devices (60% first-phase tilt, 50% second-phase tilt).

A standard step-down DFT testing protocol was employed. The initial delivered shock energy for testing was 15 J. If successful, the energy was decreased to 10, 8, 5, 3 and 1 J on successive trials until defibrillation failed. If the initial 15-J shock failed, the energy was increased in 5-J steps on subsequent trials until defibrillation was successful. The DFT was defined as the lowest initial shock energy that successfully terminated ventricular fibrillation. The same protocol was used at follow-up, regardless of preceding measurements of DFT.

An adequate safety margin was defined as two or more consecutive successful shocks with delivered energies at least 9 J below the maximal output of the pulse generator. The maximal delivered outputs of the pulse generators employed in this study were 29 J (models 1640, 1742, 1743 and 1810; n = 11) and 27 J (models 1762, 1763, 1782, 1790 and 1821; n = 39). The first six available delivered shock energy settings for these devices are 29, 27, 25, 20, 18 and 15 J. The 9-J safety margin was chosen as the closest approximation of the arbitrary clinical standard of ≥10 J (20 J for 29-J devices, 18 J for 27-J devices), which has been associated with a very low incidence of sudden death (21). To ensure an adequate safety margin, a confirmatory defibrillation trial was performed in those patients with high DFTs (≥15 J). The results of the confirmatory trial were not used for statistical analysis.

Data analysis. Group changes in DFTs were analyzed for the entire cohort, as well as for a prospectively defined subgroup of patients with high thresholds (≥15 J) at implantation. This subgroup was chosen because a rise in thresholds in these patients is most likely to result in an inadequate safety margin. Analysis was also performed on subjects who demonstrated any increase in DFT (≥1 J) at follow-up. Standard clinical variables of age, gender, ejection fraction, etiology of heart disease and clinical congestive heart failure, as well as the measured variables of DFT and shock impedance, were compared between patients with and those without a temporal rise in DFT. One-way repeated measures analysis of variance (ANOVA) was used to assess temporal changes in DFT and shock impedance. Comparisons at different evaluation times were performed with paired t tests. To examine the hypothesis that the

<table>
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<th>Abbreviations and Acronyms</th>
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<td>ANOVA = analysis of variance</td>
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<td>DFT = defibrillation threshold</td>
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<td>ICD = implantable cardioverter-defibrillator</td>
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duration of follow-up affects temporal changes in DFT, least-squares linear regression analysis was performed using time as the dependent variable. All results are expressed as the mean value ± SD, and p ≤ 0.05 was considered significant.

RESULTS

Patient group. The mean age of this cohort of 50 patients was 62 ± 11 years. Women constituted 22% of the group. Significant coronary artery disease was present in 70% of the subjects, and 66% had a history of symptomatic congestive heart failure (New York Heart Association functional class II or III). Their mean ejection fraction was 34 ± 12%. Seven patients were treated with amiodarone at the time of ICD placement. In four patients, amiodarone was discontinued at the time of ICD placement and at long-term follow-up. Importantly, the clinical characteristics of the 50 study patients were not significantly different from those of the other 181 patients who underwent initial pectoral ICD placement with an active pectoral, dual-coil transvenous lead system at our institution during this interval (Table 1). All of the patients completed the study, and there were no deaths or other complications related to the DFT testing protocol.

Defibrillation threshold testing. The long-term DFT was assessed at 70 ± 40 weeks after ICD placement. No occult malfunctions of the shocking lead were discovered during the long-term DFT evaluation. The results of DFT testing are shown in Table 2 and Figure 1. The mean DFT was 9.2 ± 5.4 J at implantation, 8.3 ± 5.8 J at hospital discharge and 6.9 ± 3.6 J at long-term follow-up (p < 0.01 by ANOVA). The long-term DFT was significantly lower than that at implantation and before discharge (p < 0.01 for long-term follow-up vs. at implantation; p = 0.04 for long-term follow-up vs. before discharge). There were no significant differences between the implantation and pre-discharge DFTs in the entire study group or in any of the prespecified subgroups. The capacitance of the ICD did not influence temporal changes in DFT. Compared with the DFT at implantation, the long-term DFT was unchanged in 20 patients (40%), decreased in 25 patients (50%) and increased in only 5 patients (10%). The average safety margin at implantation was 18.2 ± 5.3 J, and no patient developed an inadequate safety margin (<9 J) during follow-up. One patient had a DFT at implantation of 25 J in normal polarity; however, this value was acceptable in reverse polarity (15 J). This patient had a long-term follow-up DFT of 15 J in normal polarity.

Only one of the five patients who had an increase in the long-term DFT was treated with amiodarone. In the subgroup that had an increase in the long-term DFT, the mean long-term DFT was 7.8 J and the highest long-term DFT was 10 J. All five of these patients had low DFTs (<15 J) at implantation. The largest observed increase in DFT was 5 J (n = 1). The five patients who had an increase in the long-term DFT did not differ from the rest of the group with respect to age, gender, ejection fraction, DFT at implantation or shock impedance.

Because withdrawal of amiodarone and treatment with sotalol would both be expected to contribute to a temporal decline in DFT (22), separate analyses were conducted after excluding all patients who were treated with antiarrhythmic drugs at the time of ICD placement. In this subgroup of 42 patients, the mean DFT was 9.0 ± 5.2 J at implantation, 7.9 ± 4.8 J before discharge and 6.8 ± 3.2 J at long-term follow-up (p < 0.05 by ANOVA; p < 0.01 for long-term

Table 1. Clinical Characteristics of the Study Group

<table>
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<th>Study Patients (n = 50)</th>
<th>Other Patients With an ICD (n = 181)</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>62 ± 11</td>
<td>63 ± 12</td>
</tr>
<tr>
<td>Female</td>
<td>11 (22%)</td>
<td>32 (18%)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>35 (70%)</td>
<td>127 (70%)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>33 (66%)</td>
<td>118 (65%)</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>34 ± 12</td>
<td>31 ± 14</td>
</tr>
<tr>
<td>Antiarrhythmic drugs*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amiodarone</td>
<td>7</td>
<td>28</td>
</tr>
<tr>
<td>Sotalol</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>8 (16%)</td>
<td>35 (19%)</td>
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*Treatment at time of implantable cardioverter-defibrillator (ICD) placement. Data are presented as the mean value ± SD number (% of patients).

Table 2. Temporal Changes in the DFT

<table>
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<tr>
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<th>At Implantation</th>
<th>Before Discharge</th>
<th>Long-Term Follow-Up</th>
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<tbody>
<tr>
<td>Total study group</td>
<td>50</td>
<td>9.2 ± 5.4</td>
<td>8.3 ± 5.8</td>
<td>6.9 ± 3.6*†</td>
</tr>
<tr>
<td>DFT &lt;15 J</td>
<td>39</td>
<td>6.7 ± 2.1</td>
<td>6.6 ± 3.7</td>
<td>5.8 ± 2.2‡</td>
</tr>
<tr>
<td>DFT ≥15 J</td>
<td>11</td>
<td>18.2 ± 3.4</td>
<td>15.2 ± 7.2</td>
<td>11.6 ± 4.7*</td>
</tr>
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*p < 0.01 vs. at implantation; †p = 0.04 vs. before discharge; ‡p = 0.02 vs. at implantation. Data are presented as the mean value ± SD.

DFT = defibrillation threshold.
follow-up vs. at implantation; \( p = 0.05 \) for long-term follow-up vs. before discharge). The patients who were treated with antiarrhythmic drugs at implantation were also examined separately \((n = 8)\). The mean DFT in this subgroup was \(10.3 \pm 6.4 \text{ J} \) at implantation, \(10.6 \pm 9.1 \text{ J} \) before discharge and \(7.4 \pm 5.4 \text{ J} \) at long-term follow-up \(( p = 0.34)\).

There were small but significant changes in shock impedance over time \(( p < 0.05 \) by ANOVA). The shock impedance was similar at implantation and at long-term follow-up \((42.2 \pm 6.2 \text{ and } 42.4 \pm 4.8 \text{ ohms, respectively, } p = \text{NS})\). The shock impedance before discharge was significantly lower than that at implantation and long-term follow-up \((39.6 \pm 5.4 \text{ ohms, } p < 0.01 \text{ for both comparisons})\). Because shock impedance is measured differently by the external defibrillator and the pulse generator, the most relevant comparison is between the long-term and pre-discharge impedances, which are both measured with the pulse generator in a closed pocket. The increase in long-term shock impedance \((\text{compared with that before discharge})\) is consistent with our previous observations with this lead \((23)\).

**Patients with high DFTs \((\geq 15 \text{ J})\) at implantation.** Eleven patients with high DFTs at implantation were identified \((22\% \text{ of the study group})\). There were no distinguishing clinical characteristics of this subgroup. The DFTs in this cohort were \(18.2 \pm 3.4 \text{ J} \) at implantation and \(11.6 \pm 4.7 \text{ J} \) at long-term follow-up \((38\% \text{ decrease, } p < 0.001)\). The average decline in DFT was significantly greater among patients with high DFTs at implantation \((6.5 \pm 4.5 \text{ J})\), as compared with that in the rest of the study group \((0.9 \pm 2.4 \text{ J}, p = 0.002)\). Two patients in the high DFT subgroup had no change in the long-term DFT; the other nine patients had a decrease in the long-term DFT, compared with that at implantation. In addition, no patient had an inadequate safety margin \(< 9 \text{ J} \text{ at the long-term evaluation. Only one patient in the high DFT subgroup was treated with antiarrhythmic drugs (amiodarone) at the time of implantation; the drug was discontinued when the DFT at implantation was 20 J. This patient did not have any change in DFT at long-term follow-up.\)

**Effect of duration of follow-up on temporal changes in DFT.** Although long-term DFT testing was performed at least six months after ICD placement in all patients, there was significant variability in the duration of follow-up. Importantly, there was no correlation between the duration of follow-up and temporal changes in DFT \((R^2 = 0.001, p = 0.79)\) (Fig. 2). Although the average length of follow-up was 70 weeks, the long-term DFT remained stable up to two to three years after implantation.

**DISCUSSION**

The major findings of this study are that DFTs decrease significantly over time with a dual-coil, active pectoral lead system. The temporal decline in DFT was most marked among patients with high DFTs \((\geq 15 \text{ J}) \text{ at implantation, which is the subgroup in which the long-term stability of defibrillation efficacy is most important. Patients with low DFTs \(< 15 \text{ J} \text{ at implantation also exhibited a significant, albeit smaller, decline in DFT at long-term follow-up. Although a small proportion of the patients in this study had an increase in DFT at long-term follow-up, these minor fluctuations were within the range expected with repeated step-down DFT testing in individual patients} (24).**

**Previous studies.** Long-term changes in DFTs are influenced by several factors, such as the lead system that is employed and the defibrillation waveform. Long-term DFTs are stable with epicardial lead systems, except when patients are treated with amiodarone \((25,26)\). In contrast, when monophasic waveforms are used with non-thoracotomy lead systems, a consistent long-term increase in DFT is observed \((8–12)\). We previously demonstrated that biphasic waveforms prevent the long-term rise in DFT seen with a dual-coil transvenous lead system \((23)\); however, other investigators have reported that up to 15\% of patients may develop a long-term rise in DFT that is large enough to mandate device reprogramming or system revision \((13)\). Long-term rises in DFT are also observed when biphasic waveforms are used with hybrid lead systems that incorporate transvenous and subcutaneous elements \((14,15)\). The present study is the first prospective evaluation of the long-term stability of DFTs with an active pectoral, dual-coil lead system. Active pectoral lead systems are currently the most commonly used configuration because of the simplicity of the implantation procedure and because DFTs at implantation are lower when an active pectoral can is used \((16–18)\). Our findings were recently corroborated by preliminary data from the larger multicenter Low Energy Safety Study \((LESS) (27)\). When routine ICD testing was performed at one year after implantation in this study, 99.6\% of induced ventricular fibrillation episodes were
successfully converted with programmed shock energies that were 6 to 12 J greater than the DFT at implantation.

Mechanisms of action. The mechanisms responsible for temporal changes in DFT remain poorly understood. We previously demonstrated that when monophasic waveforms are used with a transvenous lead system, a rise in shock impedance is sufficient to account for the increase in defibrillation energy at the threshold (8), assuming that current is the major determinant of defibrillation (28,29). However, when temporal changes in DFT with monophasic and biphasic waveforms were compared in a single patient cohort, biphasic DFT's were unchanged, despite a significant increase in shock impedance (23). This suggests that shock impedance is an important determinant of threshold energy for monophasic, but not biphasic, waveforms. In the present study, the long-term biphasic DFT declined significantly with an active can, dual-coil transvenous lead system. This decrease cannot be attributed to the waveform or changes associated with maturation of the transvenous lead, because long-term DFTs are unchanged when this waveform and lead are used without an active pectoral pulse generator (23). The stress of surgery is also unlikely to account for the higher DFT at implantation, because there was no significant difference between the DFT values at implantation and before discharge. However, because the pulse generator shell is a component of the defibrillation system, the temporal decline in DFT may be related to maturation of the pocket. With the dual-coil, active can configuration, there are two pathways for current flow: from the distal right ventricular coil to either the proximal coil or the pectoral pulse generator. It is possible that maturation of the pulse generator pocket results in a favorable change in the distribution of current between these two pathways, thereby improving defibrillation efficacy.

Clinical implications. Our findings indicate that routine DFT testing may not be necessary for at least the first two years after implantation with an active pectoral, dual-coil lead system if an adequate safety margin for defibrillation is present at the time of implantation. Relatively few patients in this study were treated with amiodarone, which can increase the DFT (30). This was because most of the patients who required concomitant treatment with amiodarone underwent long-term DFT testing before initiation of the drug. Accordingly, we would still recommend serial evaluation of the DFT among patients treated with antiarrhythmic drugs or in the case of a changing cardiac substrate (e.g., worsening congestive heart failure, severe left ventricular dysfunction, new myocardial infarction) (31).

Study limitations. A uniform lead system and defibrillation waveform were employed in this study to avoid any confounding influence of these factors on the results. Consequently, our findings may not be applicable to other defibrillation systems that employ different waveforms and leads. Although the pectoral electrode was an emulator at implantation and the pulse generator shell at subsequent evaluations, a decline in DFT was also observed when the long-term follow-up and predischarge measurements were compared. The defibrillation step-down protocol that we used has some limitations. The relationship between defibrillation success and energy is best described as a dose-response curve (32). The use of a step-down protocol to first failure to determine DFT's has provided a reasonable estimate of the 70% defibrillation success energy (33), and it has been shown to be reproducible (34). It is highly unlikely that our results are attributable to spontaneous variability with repeated measurements of the step-down DFT. With successive DFT determinations, one would expect equal proportions of patients to exhibit an increase or decrease in DFT (24). In contrast, we observed that DFT at long-term follow-up decreased in 50% of patients and increased in only 10% of patients. The fact that DFT's measured at implantation and before discharge did not differ significantly also suggests that the step-down DFT method was reproducible in this patient group. This study did not consist of a consecutive series of patients; however, our results are unlikely to be attributable to patient selection, because the clinical characteristics of the study patients were comparable to those of other patients who underwent initial pectoral ICD placement with an active pectoral, dual-coil transvenous lead system at our institution during this interval. Although some of our patients underwent long-term ICD testing as late as three to four years after ICD placement, the majority of the long-term ICD tests were performed within the first two years. Therefore, it is presently unclear whether DFT testing should be performed at later intervals (i.e., between two years after implantation and pulse generator replacement). Our results should not be extrapolated to patients who do not have an acceptable safety margin for defibrillation at implantation, because these patients were excluded from our study. Finally, treatment with antiarrhythmic drugs can have important effects on temporal changes in DFT (22); however, our results were unchanged when these patients were excluded from the analysis.

Conclusions. Our results demonstrate that DFT's decline significantly after implantation with an active pectoral, dual-coil lead system. The magnitude of the decline was most marked among patients with high DFT at implantation, who would have been considered to be at greatest risk for the development of an inadequate safety margin for defibrillation. These results indicate that routine DFT testing may not be required during the first two years after implantation with this lead system, in the absence of a change in the cardiac substrate or treatment with antiarrhythmic drugs.

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REFERENCES


