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1. Introduction

The implantable cardioverter defibrillator (ICD) is currently considered the first therapy option to protect patients from life-threatening ventricular arrhythmias. Several randomized studies demonstrated a reduction in total mortality of up to 55% and a reduction in arrhythmogenic mortality of up to 76% in ICD recipients.[1-7] Within a time frame of about 20 years, indications for ICD have evolved from a restricted “last resort therapy” to a secondary and primary preventive therapy. According to HRS/EHRA Expert Consensus on the Monitoring of Cardiovascular Implantable Electronic Devices [8], incidence of ICD implantation in the US and Europe in 2007 was 235,000 and 88,000, respectively, with a upward trend.

Moreover, prevention of sudden cardiac death (SCD) through the ICD is generally considered to represent a therapy, which will be needed for the rest of the patient’s life. However, regarding ICD cost-effectiveness as well as the potential risks of ICD therapy and subsequent generator changes the question rises if patients without any adequate ICD intervention during the lifespan of their index ICD really need further ICD protection. Therefore, the question whether or not to replace an ICD generator at the time of battery depletion is of great importance not only for the affected patients but also for their physicians and cost carriers.

This chapter is aimed to give an overview about the currently published data on long-term benefit of ICD therapy based on the incidence of adequate ICD therapy and in the ratio of potentially serious complications.
2. Long-term benefit of ICD therapy

2.1. Secondary prevention trials

Already in 1991, Tchou et al.[9] reported in a single center cohort of 184 patients who received an ICD between 1982 and 1989 (84% with ventricular fibrillation (VF) or sustained ventricular tachycardia (VT), 9% with non-sustained VT (NSVT) and 6% with pre-/syncope) that the actual risk of receiving an adequate shock by the fifth year after implantation was 69%, with an observed bimodal distribution: high within first year, and rise after four years. Occurrence of adequate ICD shock was defined as electrocardiographic documentation (ECG) of sustained VT at the time of shock or if it was preceded by sudden onset of severe presyncopal symptoms or syncope.

Grimm et al.[10] investigated ICD therapy episodes which occurred for the first time in patients who did not require such therapy prior to generator change. This was a prospective single center study enrolling 26 secondary prevention patients (77% with cardiac arrest and 23 with sustained VT) who received their second ICD device 30±9 months after initial ICD implantation. Notably, at that time patients had epicardial electrodes, and only a single patient had an ICD generator with the option to memorize endocardialelectrograms. Adequate shocks were defined as spontaneous ICD discharges preceded by severe symptoms like presyncope or syncope or documentation of VT/VF by Holter or telemetry monitoring or stored ECG by ICD. During a mean follow-up period of 21±9 months after ICD generator replacement, ICD therapy was reported in 13 of 26 patients (50%), classified as adequate in 9 patients (35%).

Dürsch et al.[11] aimed to evaluate retrospectively the necessity of the replacement of ICD generators in patients without any adequate, spontaneous ventricular arrhythmia episode during the life-time of the first implanted device. This study, reported in 1998, compared 62 secondary prevention patients (mean follow-up 51 ± 14 months) with an elective generator replacement due to battery depletion with 151 ICD patients without replacement (follow-up 16.5 ± 11 months). There was a preponderance of male patients (>80%) with a mean left ventricular ejection fraction (LVEF) of 31% in both groups. In contrast to the study of Grimm et al. 86% of patients had transvenousendocardial ICD electrodes and 95% of devices (following generator exchange) had the option to memorize endocardialelectrograms. At that time most of the ICD systems had the capability of antitachycardiac pacing (ATP) prior to ICD shock delivery. For the total patient group there was a 5 year event-free probability of 23%, and no differences were found between the two groups. Subanalysis of the replacement group patients revealed no difference in the probability of adequate ICD therapy occurrence prior to or after the replacement of the pulse generator. Notably, in 6 of the 62 (10%) patients, the first adequate ICD therapy was documented after generator replacement.

Tandri et al.[12] reported in 2006 a single center ICD registry of 1382 patients, who received their first ICD between 1980 and 2003 (76% men, LVEF 33 ± 11%) with mainly secondary prevention indication (77%). In 787 (57%) of these patients ICD therapy informations were available. Adequate ICD therapy was determined based either on the ICD memory or for ICDs without ECG storage capability on the symptoms that preceded
the shock. During a mean follow-up of 70 ± 51 months 53% of the patients received adequate ICD therapy, two thirds of them within the first year of implantation. Out of 127 patients (16%) without adequate ICD therapy within 5 years following the index generator implantation, 8%, 20% and 24% of patients experienced adequate ICD therapy after 6, 10 and 15 years of follow-up, respectively.

Data from another single center ICD registry were reported by Koller et al. in 2008.[13] This registry comprised data of 442 patients with predominantly secondary prevention (59%) with ischemic (76%) or dilated cardiomyopathy (24%) with a median follow-up of 3.6 years (max 12.7 years). Adequate ICD therapy of ventricular arrhythmias stored by intracardiac-electrograms had to be confirmed by an experienced electrophysiologist. The cumulative incidence of any adequate ICD therapy was 52% during a 7-year observation period with a two-fold higher risk for patients with secondary prevention compared to primary prevention. Patients without former adequate ICD therapy within 6 years after the first ICD implantation had an observed risk of only 6% for adequate ICD intervention in the following 2 years. Notably, only 35 patients (8%) had follow-up longer than 6 year.

The long-term follow-up of the Leiden Out-of-Hospital Cardiac Arrest Trial (LOHCAT)[14] was the first prospective single center observational study to assess the rate of mortality and risk of adequate ICD therapy in patients with secondary prevention. A total of 456 patients (86% males, mean LVEF 35±14%) with ischemic heart disease and secondary prevention indication were followed for 54±35 months after ICD implantation. Adequate ICD therapy was checked by printouts of the ICD memory. During follow-up 22% of the patients died. The cumulative incidence of adequate ICD therapy at 1, 5, and 8 years was 24, 52 and 61%, respectively. Independent factors for higher risk of adequate ICD intervention were previous VT, history of AF, wide QRS and poor LVEF. No predictive factors for the absence of ventricular arrhythmia could be identified. Of the 456 patients, 167 (37%) outlived the life-span of their index ICD and got generator replacement. No data were reported concerning how many of these patients had no former adequate ICD therapy and/or received the first adequate ICD Therapy after generator replacement.

The INcidence free SUrvival after ICD Replacement (INSURE)[15] trial was the first prospective multicenter observational study to evaluate the risk of adequate ATP and/or ICD shock delivery after elective ICD replacement. A total of 510 unselected ICD-patients with (48%) and without (52%) former adequate ICD therapy were enrolled in 29 germancenters from 2002 until 2007 after an average life-span of their first ICD generator of 62±18 months. After device replacement patients were followed every 3 to 6 months (mean follow-up 22±16 months) until occurrence of an adequate ICD therapy (stored by intracardiac-electrograms and confirmed by an adjudication committee consisting of three experienced electrophysiologists), death, second generator replacement or until common study termination endpoint. The vast majority (86%) of patients had initially been implanted for secondary prevention of SCD. The cumulative rates of adequate ICD interventions after one, two and three years following generator replacement were 32.4%, 41.3% and 48.1% in patients with former adequate ICD therapy and 10.6%, 17.6% and 21.4% in patients without former adequate ICD therapy, respectively (HR 3.08, CI: 2.15-4.39, p < 0.001) (Figure 2). In patients
without former adequate ICD interventions, only advanced NYHA stages were associated with higher risk of adequate ICD interventions. However, no predictive factors for lower probability of ICD therapy could be identified in this group.

**Table 1.** Baseline characteristics of patients in secondary prevention trials with long-term follow-up

<table>
<thead>
<tr>
<th>Author / Study</th>
<th>Year</th>
<th>N</th>
<th>Age (mean y)</th>
<th>Male (%)</th>
<th>LVEF (mean%)</th>
<th>ICM (%)</th>
<th>NICM (%)</th>
<th>CAD (%)</th>
<th>no HD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tchou et al. 1991</td>
<td>184</td>
<td>61±11</td>
<td>81</td>
<td>37±14</td>
<td>n.r.</td>
<td>17</td>
<td>81</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Grimm et al. 1993</td>
<td>26</td>
<td>56±15</td>
<td>73</td>
<td>38±15</td>
<td>n.r.</td>
<td>20</td>
<td>65</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Dürsch et al. 1998</td>
<td>62</td>
<td>58±11</td>
<td>89</td>
<td>31±9</td>
<td>34</td>
<td></td>
<td>66</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Tandri et al. 2006</td>
<td>1382</td>
<td>62±11</td>
<td>76</td>
<td>33±11</td>
<td>72</td>
<td>28</td>
<td>70</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Koller et al. 2008</td>
<td>442</td>
<td>63</td>
<td>89</td>
<td>30</td>
<td>76</td>
<td>24</td>
<td>76</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Borleffs et al. 2008</td>
<td>456</td>
<td>65</td>
<td>86</td>
<td>35±14</td>
<td>100</td>
<td>-</td>
<td>100</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Van Welsenes et al. 2011</td>
<td>832</td>
<td>63±13</td>
<td>82</td>
<td>37±15</td>
<td>73</td>
<td>n.r.</td>
<td>n.r.</td>
<td>73</td>
<td></td>
</tr>
<tr>
<td>Erkapic et al. 2012</td>
<td>510</td>
<td>65±10</td>
<td>83</td>
<td>39±16</td>
<td>37</td>
<td>25</td>
<td>71</td>
<td>38</td>
<td></td>
</tr>
</tbody>
</table>

LVEF: left ventricular ejection fraction; ICM: ischemic cardiomyopathy; NICM: non-ischemic cardiomyopathy; CAD: coronary artery disease; no HD: no heart disease. n.r.: not reported

**Table 2.** Incidence of adequate ICD therapy according to follow-up time in secondary prevention trials

<table>
<thead>
<tr>
<th>Author / Study</th>
<th>Kind of study</th>
<th>FU prior 1. ICD replacement (mean months)</th>
<th>FU after 1. ICD replacement (mean months)</th>
<th>Overall FU (mean months)</th>
<th>First adequate ICD therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tchou et al.</td>
<td>retro. s.c.</td>
<td>24±19</td>
<td>-</td>
<td>-</td>
<td>69% within 5y</td>
</tr>
<tr>
<td>Grimm et al.</td>
<td>pros. s.c.</td>
<td>30±9</td>
<td>21±19</td>
<td>-</td>
<td>35% within 6y</td>
</tr>
<tr>
<td>Dürsch et al.</td>
<td>retro. s.c.</td>
<td>-</td>
<td>-</td>
<td>50±14</td>
<td>77% within 5 y (thereof 10% after ICD replacement)</td>
</tr>
<tr>
<td>Tandri et al.</td>
<td>retro. s.c.</td>
<td>70±51</td>
<td>46±34</td>
<td>-</td>
<td>53% within 5 y (additional 24% after ICD replacement)</td>
</tr>
<tr>
<td>Koller et al.</td>
<td>retro. s.c.</td>
<td>-</td>
<td>-</td>
<td>43</td>
<td>52% within 7 y</td>
</tr>
<tr>
<td>Borleffs et al.</td>
<td>pros. s.c.</td>
<td>-</td>
<td>-</td>
<td>54±35</td>
<td>61% within 8 y</td>
</tr>
<tr>
<td>Van Welsenes et al.</td>
<td>retro. s.c.</td>
<td>41±34</td>
<td>-</td>
<td>-</td>
<td>51% within 5 y</td>
</tr>
<tr>
<td>Erkapic et al.</td>
<td>pros. m.c.</td>
<td>62±18</td>
<td>22±16</td>
<td>-</td>
<td>21% within 3 y after ICD replacement</td>
</tr>
</tbody>
</table>

Retro s.c.: retrospective single center-study; pros. s.c.: prospective single center-study; pros. m.c.: prospective multi-center study; FU: follow-up; y: years.
2.2. Primary prevention trials

The first trial which tried to provide data on the long-term benefit of ICD therapy in primary prevention patients was published in 2008 by Alsheikh-Ali.[16] Patients with prior myocardial infarction and LVEF ≤35% who received ICD for primary prevention between 1995 and 2005 formed the basis of this retrospective single center analysis. Of 525 predominantly male patients, 115 (22%) received adequate ICD therapy during a mean follow-up of 24 months. Patients who survived more than 5 years after ICD implantation without adequate therapy, the incidence of adequate ICD intervention was 6% after 7 years of follow-up. These observations were in accordance to the data of Koller et al. who reported the same incidence for patients with secondary prevention 7 years after ICD implantation. However, in both studies only 6-8% of patients had follow-up longer than 6 years after first ICD implantation. No predictive factors for a lower probability of ICD therapy could be identified in both studies.

The extended 8-year follow-up study of the Multicenter Automatic Defibrillator Implantation (MADIT) II trial was published in 2010.[17] Post-trial mortality data for all study participants were obtained from the enrolling centers through hospital records and death registries from 2001 until 2009. One-thousand-twenty study patients who survived to trial closure of MADIT II formed the basis of this study. The primary endpoint was the occurrence of all-cause mortality during a median follow-up of 7.6 years. Patients who were treated with an ICD showed a significant lower risk of death (34%) compared with non-ICD patients. The evident benefit of ICD therapy continued even in the long-term follow-up of up to 8 years, but only for patients with single chamber ICD. Patients with a dual chamber ICD (programmed to active DDDR-pacing regardless of conduction abnormalities) and more advanced NYHA class (≥ II) at enrolment, experienced a late increase in mortality due to unnecessary right ventricular pacing leading to progressive heart failure. This observation underlines previous reported data.[18] Regarding the long-term benefit due to adequate ICD therapy in the extended MADIT II trial, the cumulative probability of adequate ICD intervention during 8 years of follow-up was 68%. However, complete information of ICD interrogation during long term follow-up was only available in 109 patients (10.7%) during the post-trial period.

<table>
<thead>
<tr>
<th>Author / Study</th>
<th>Year</th>
<th>N</th>
<th>Age (mean y)</th>
<th>Male (%)</th>
<th>LVEF (mean%)</th>
<th>ICM (%)</th>
<th>NICM (%)</th>
<th>CAD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alsheikh-Ali et al.</td>
<td>2008</td>
<td>525</td>
<td>67±11</td>
<td>81</td>
<td>23±7</td>
<td>100</td>
<td>-</td>
<td>100</td>
</tr>
<tr>
<td>Goldenberg et al.</td>
<td>2010</td>
<td>630</td>
<td>64±11</td>
<td>85</td>
<td>≤35</td>
<td>100</td>
<td>-</td>
<td>100</td>
</tr>
<tr>
<td>Van Welsenes et al.</td>
<td>2011</td>
<td>1302</td>
<td>63±11</td>
<td>80</td>
<td>29±12</td>
<td>68</td>
<td>32</td>
<td>68</td>
</tr>
<tr>
<td>Van Welsenes et al.</td>
<td>2011</td>
<td>114</td>
<td>61±11</td>
<td>80</td>
<td>26±9</td>
<td>59</td>
<td>41</td>
<td>59</td>
</tr>
</tbody>
</table>

LVEF: left ventricular ejection fraction; ICM: ischemic cardiomyopathy; NICM: non-ischemic cardiomyopathy; CAD: coronary artery disease.

Table 3. Baseline characteristics of patients in primary prevention trials with long-term follow-up
Van Welsenes et al. published two reports in 2011 on long-term follow-up data of a single center registry of patients with primary and secondary prevention. In the first publication[19] they reported all-cause mortality and incidence of adequate ICD therapies in patients with primary (61%) and secondary (39%) prevention during the lifetime of the first implanted ICD. The mean follow-up was 3.4±2.8 years. The cumulative 5-year incidence of mortality was 25% for primary and 23% for secondary prevention, without reaching statistical significance between the two groups. The cumulative 5-year incidence of adequate ICD therapy (each episode had to be confirmed by a trained electrophysiologist by regard- ing the ICD memory/printouts) was 37% for primary and 51% for secondary prevention patients (Figure 1).

The second publication[20] comprised data of 114 patients with exclusively primary prevention who did not receive adequate therapy during the lifetime of their first ICD generator. The data were released from the same single center registry and were the first on the topic: “long-term benefit of ICD-therapy after elective device replacement in primary prevention patients”. The single center cohort consisted of mainly ischemic heart disease patients (80% male, mean age 61±11 years) with a mean LVEF of 26%. After an average life-span of their first ICD generator of 71±24 months the patients were followed after elective device replacement for 25±21 months. The cumulative event rate for adequate ICD intervention after replacement increased continuously from 7% after one, 9% after two, to 14% after 3 years (Figure 3).

Table 4. Incidence of adequate ICD therapy according to follow-up time in primary prevention trials

<table>
<thead>
<tr>
<th>Author / Study</th>
<th>Kind of study</th>
<th>FU prior 1. ICD replacement (mean months)</th>
<th>FU after 1. ICD replacement (mean months)</th>
<th>Overall FU (mean months)</th>
<th>First adequate ICD therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alsheikh-Ali et al.</td>
<td>retro. s.c.</td>
<td>24±0.4</td>
<td>-</td>
<td>-</td>
<td>22% within 7 y</td>
</tr>
<tr>
<td>Goldenberg et al.</td>
<td>retro. m.c.</td>
<td>18 (10-30)</td>
<td>n.r</td>
<td>91 (42-108)</td>
<td>68% within 8 y</td>
</tr>
<tr>
<td>Van Welsenes et al.</td>
<td>retro. s.c.</td>
<td>41±34</td>
<td>-</td>
<td>-</td>
<td>37% within 5 y</td>
</tr>
<tr>
<td>Van Welsenes et al.</td>
<td>retro. s.c.</td>
<td>71±24</td>
<td>25±21</td>
<td>-</td>
<td>14% within 3 y after ICD replacement</td>
</tr>
</tbody>
</table>

retro. s.c.: retrospective single center-study; retro. m.c.: retrospective multi-center study; FU: follow-up; y: years.
Figure 1. Cumulative incidence of adequate ICD therapies prior elective generator replacement in patients with primary and secondary prevention

Figure 2. Cumulative incidence of first adequate ICD therapies (with confidence intervals) after elective device replacement in patients with secondary prevention
3. Challenges of long term ICD therapy

The long-term benefit of ICD therapy has to be evaluated compared to the ratio of potentially serious complications.

A number of important medical and technological advances in ICD therapies have been made in the last years which helped to reduce the interventional stress for patients and to improve their daily safety[14-19]: the introduction of transvenous endocardial leads, subpectoral or subfascial implantation of smaller and more powerful ICD devices, introduction of diagnostic tools as e.g. monitoring of intrathoracic fluid status, ST segment changes as well as the introduction of remote home monitoring systems. However, ICD therapy is still associated with significant morbidity and some mortality, especially in long-term follow up.

3.1. Lead failure

One of the major risks of long-term ICD therapy is lead failure, mostly presented as lead fracture or insulation defect. The annual lead failure rate increases with time and reaches 20% in 10-year old leads.[20] Mechanical stress on leads is the most frequent cause for lead failure and can be reduced by avoiding the medial subclavian puncture during ICD implantation (preferred approach is through the cephalic vein or lateral subclavian puncture) and by avoiding subpectoral device implantation (preferred subfascial pocket, if possible). However, careful evaluation required, for the latter may result in pocket complications necessitating revision operations.
With the introduction of leads with multilumen design in 1997, lead survival curves initially improved but were still limited due to missing long-lasting insulation material. Silicon which is most often used for lead insulation has a good biocompatibility and flexibility, has a high friction resistance but prone to abrasion of lead insulation material. Even today in a certain type of ICD lead (RIATA®, SJM, Sylmar, CA) with silicon insulation (removed 2010 from distribution), time-dependent incidence of lead failure of 8-33% were reported.[21-24] The same lead model with a silicone-polyurethane copolymer (Optim™, SJM, Sylmar, CA) showed no increased incidence of lead failure, suggesting a better abrasion resistance.[22,25]

Apart from lead insulation material, very small diameter of the ICD lead seemed to be a further risk factor of lead failure.[26] The 6.6 Sprint fidelis® lead (Medtronic, Inc., Minneapolis, MN) is prone to increased chance of lead fracture due to most likely less stress resistance. In 2008 this high-voltage ICD-lead was removed from the market. Actually, incidence of lead failure of 17% at 5 years of follow-up is reported for this lead.[27] Therefore, implanted Sprint fidelis and several Riata lead models should be carefully examined at the time of generator replacement.

3.2. Inadequate ICD therapy

Inadequate ICD therapy is a significant clinical issue. In literature it’s reported that 12-30% of ICD patients receive inadequate ICD therapies, mainly caused by supraventricular tachycardias, T-wave oversensing and lead failure.[28-30] Such unnecessary ICD therapies are associated with increase of posttraumatic disorders as depression and anxiety.[31] It is still a matter of debate, if aside of morbidity, inadequate ICD shocks also have worse impact on the outcome of ICD patients.[30,32] However, it is our firm conviction, that the number of unnecessary ICD therapies triggered by SVTs can be considerably reduced by adequate ICD programming by an experienced physician. Furthermore, newer ICD algorithms reduced inadequate ICD therapy triggered by T-wave oversensing by 97% while maintaining 100% sensitivity for detection of true ventricular arrhythmia.[33] The safety, efficacy and performance of further new ICD discrimination algorithms is actually evaluated in a prospective multi-center trial.[34]

Since the introduction of the Lead Integrity Alert™ (LIA) by Medtronic in 2008, inadequate ICD therapies decreased by up to 50% in patients with fractured Sprint fidelis leads.[35,36] Moreover, it has been reported that this algorithm has the potential to early detect lead failure of the affected Riata family®.[37]

3.3. Risk of ICD generator replacement

Device replacement is associated with significant morbidity and some mortality. Data from a multicenter prospective registry of 1081 ICD patients who underwent device replacement (79% males, mean age 64±13 years) showed a complication rate of 4.3%. Major complications were observed in 2.6%, mostly infections or lead revisions. On multivariate analysis the presence of advanced Canadian Cardiovascular Society angina class (CCS ≥2), advanced NYHA stages (≥III), complex device systems (especially cardiac resynchronization systems),
any previous surgery, and low operator procedure volume were predictive factors for over-all complication after ICD replacement. Any complication was associated with an increased risk of mortality at 45, 90, and 180 days after device replacement with a HR of 8.58, 9.91 and 4.06, respectively (p=0.005 to 0.069).

It is strongly recommended that risks for complications after ICD replacement should not be underestimated. Even if generator replacement is technically less challenging than a new device implantation, it should be preferably performed by experienced operators.

4. Summary/Conclusion

The currently available literature reveals that patients with adequate ICD therapy prior elective ICD replacement have approximately 3-fold higher risk to receive adequate ICD intervention thereafter compared to patients without prior adequate ICD therapy. However, a significant number of patients without adequate ICD therapy prior elective device replacement will receive adequate ICD therapy within 3 years following elective device replacement. Patients who present at poor clinical status with more advanced stages of heart failure, especially with advanced NYHA classes (≥2), as well as patients with secondary prevention indication are at higher risk for adequate ICD therapy in long-term follow-up. No predictive factors for lower probability of ICD therapy could be identified for patients without adequate ICD therapy prior device replacement. Hence, ICD replacement appears still necessary in these patients. Risks of ICD therapy should not be underestimated but the weight of evidence for long-term benefit based on the incidence of ventricular arrhythmias with subsequent adequate ICD therapy supports the continuing use of ICD therapy for patients with adequate ICD indication. Nevertheless, through an intensive training of physicians in ICD-implantation, device replacement, programming, and aftercare of ICD patients, as well as the use of newer SVT discrimination and lead monitoring algorithms the rate of potential risks can be reduced substantially.

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[1] Wilkoff BL, Auricchio A, Brugada J, Cowie M, Ellebogen KA, Gillis AM, Hayes dL, Howlett JG, Kautzner J, Love CJ, Morgan JM, Priori SG, Reynolds DW, Schoenfeld MH, Vardas PE. HRS/EHRA Expert Consensus on the Monitoring of Cardiovascular Implantable Electronic Devices (CIEDs): description of techniques, indications, personnel, frequency and ethical considerations: developed in partnership with the Heart Rhythm Society (HRS) and the European Heart Rhythm Association (EHRA); and in collaboration with the American College of Cardiology (ACC), the American Heart Association (AHA), the European Society of Cardiology (ESC), the Heart Failure Association of ESC (HFA), and the Heart Failure Society of America (HFSA). Endorsed by the Heart Rhythm Society, the European Heart Rhythm Association (a registered branch of the ESC), the American College of Cardiology, the American Heart Association. Europace 2008;10:707-725.


