Programmed Shock Energy and Safety Margin - A Contradiction in Prophylactic Systems?

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Summary

Despite broadened implantable cardioverter-defibrillator (ICD) indications and rising numbers of ICD implantations worldwide, the high incidence of sudden cardiac death remains one of the great challenges in the field of cardiology. Resulting from the recently extended indications, the trend moves increasingly towards implantable prophylactic systems. Improvements in ICD technology have led to a reduced volume as well as a prolonged service lifetime of the implants. In parallel to these developments, the implantation procedure is being simplified and optimized. In today's clinical routine, the determination of the "true" defibrillation threshold (DFT) is more and more replaced by a simple "ICD function test" during the implantation. In recent years, the result has been that, for safety reasons, the energy programmed for the first shock is usually set higher than absolutely necessary. Requirements on prophylactic systems are for small and light-weight implants that do not limit the patients' quality of life. They should make it possible to survive a first ventricular fibrillation (VF) episode if the situation arises, then indicating the need for a standard ICD system. In this context, the question about the maximum shock energy of an implantable prophylactic system arises. To study this question, data from clinical implantation statistics and clinical studies were used.

Key Words

Defibrillation threshold (DFT), safety margin, prophylactic indicator

Introduction

Sudden cardiac death is still an unsolved problem in the field of cardiology. According to studies by Gillum et al., the incidence of out-of-hospital sudden cardiac death is 1.91 cases per 1000 people among males of an age between 35 and 74 years, and 0.75 or 0.9 cases per 1,000 people, among females [1]. In the United States, the cumulative incidence of sudden cardiac death is stated to be approximately 450,000 per year; the probability of survival is about 20 % for sudden death [2]. Among the electrotherapeutic interventions, the implantable cardioverter-defibrillator occupies an outstanding place in the therapy of ventricular tachyarrhythmias. In comparative studies, such as MADIT and AVID, the effectiveness and clinical safety of the ICD therapy to prevent sudden cardiac death was impressively shown during the last few years [3-13]. Worldwide, more than 250,000 ICD systems have been implanted to date, about 60,000 of them alone in the past year. Nevertheless, there is still a considerable discrepancy between the number of ICD implantations per year and the number of people dying of sudden cardiac death. In Germany, about 90,000 people die each year from sudden cardiac death. This number is contrasted by about 3,500 first implantations of ICDs in the past year.

In 1991, the guidelines for the indications were still formulated very strictly in the literature, however, they had already been revised in 1994, and were broadened again in 1998 [14-16]. The extensions for the possible indications indicate a trend that could point towards prophylactic indications in the future.

Recent years were marked by great efforts to identify patients at risk for sudden cardiac death, to improve the diagnostics, and to optimize the antiarrhythmic

Number of implantations	3702		
Gender	82 % males / 18 % females		
Age	8 - 92	years	
Mean age	60.7 + 12.7 years		
CAD		70.1 %	
NYHA I	534	24.0 %	
II	1214	54.5 %	
III	448	20.1 %	
IV	30	1.4 %	
Indications	1801	VT	
	796	VF	
	423	VT+VF	

Table 1. Preoperative patient data.

therapy. There were successes in narrowing in on the group of high-risk patients even more, especially by combining different diagnostic methods. However, the predictability still leaves much to be desired [17,18]. The association of sudden cardiac death with well-known cardiovascular risk factors and previous clinical manifestations of coronary heart disease has been proven [19-22].

Prophylactic Indicator System

Patients in the state following a myocardial infarction (MI), in particular, have a high risk potential for tachycardic rhythm disturbances and sudden cardiac death. The risk increases if the left-ventricular function is additionally severely limited. The incidence of tachycardic episodes is highest during the first year after the acute event. Patients who do not meet the accepted indications for a standard ICD post MI, because no ventricular fibrillation (VF) episodes have so far been documented, should undergo a suitable risk stratification. Implantable prophylactic indicator systems could lower the initial risk of sudden cardiac death and indicate the necessity of a permanent therapy with a standard ICD. A prophylactic indicator system has the task of reacting adequately to at least one first spontaneous VF episode with up to 5 shocks. The signals before and during the episode are documented in the device memory. Prophylactic indicator systems should be small, comfortable, and easy to program. This implies fixed, non-programmable shock energies.

In this context, the currently existing implantation data and published study results will be analyzed, in order to estimate the necessary maximum shock energy for a prophylactic indicator system.

Implantation Statistics

The implantation data of more than 3,700 ICD patients, who had been provided with BIOTRONIK ICDs, were studied (Table 1). The primary basic disease was coronary heart disease in 70.1 % of the patients, and cardiomyopathy, in 25.4 %.

The defibrillation or conversion capability was determined according to three currently used methods. Measuring the defibrillation threshold (DFT) in its conventional sense requires step-down testing of the shock energy until defibrillation is no longer successful. The "true" DFT requires a high number of fibrillation inductions under intubation anesthesia. Therefore, it is performed with less and less frequency. The prematurely interrupted step-down test is only carried out to the point at which an acceptable energy value is found that allows a sufficient safety margin for the first programmed shock energy of the ICD. It never reaches a sub-threshold value and, thus, never tests for the true DFT. In recent years, the device-based function test has increasingly gained importance. With this method, VF is usually induced once or twice, and the convertibility is tested directly through the implant with 15 J (sometimes also with 20 J). Local anesthesia and short-term sedation during the shock delivery are sufficient and enable implantation times comparable to those of pacemaker implantations.

Of the three methods, only the true DFT corresponds to the definition of a DFT. The interrupted step-down test, as well as the device-based function test, do not provide threshold values; at best they can be regarded as conversion tests.

The test results are summarized in Figure 1. True DFTs had a share of 29 %, interrupted step-down tests, of 23 %, and device-based tests, of 48 %. The lowest test values were measured with the interrupted step-down test. One can assume that a much lower DFT value should result from a complete test procedure. Here, 10.7 J are considered as the upper limit for the worst case. It must be discussed why the true DFT had worse results. In most cases, a conversion test is started with a test energy of 15 J. Originally, there might not be any intention to perform a complete step-down test. By chance, however, the first test might not be successful, thus necessitating further tests with higher energies

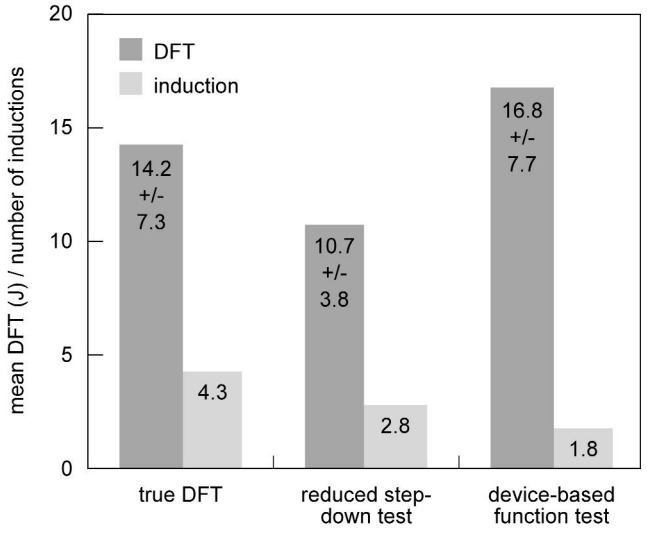


Figure 1. Results of the conversion tests.

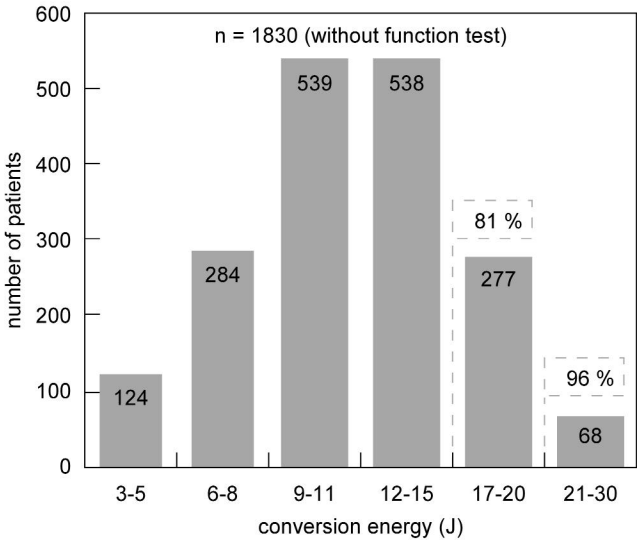


Figure 2. Distribution of conversion energies.

(step-up). Because this means that the test protocol contained at least one sub-threshold energy, the protocol now corresponds to the definition of a true DFT. As a result, a selection of patients with extremely bad DFTs is concentrated in the column for the true DFT.

To determine the true DFT, an average of 4.3 inductions of VF was necessary. Accordingly less inductions were performed for the interrupted step-down test (2.8), and for the device-based test (1.8).

If the device-based test is excluded, the test results of 1,830 patients have the distribution shown in Figure 2.

The ICD field at Biotronik has gained clinical experiences since 1994. Analyzing the implantation statistics for this time shows characteristic trends. The share of device-based function tests has increased steadily (Figure 3).

In a parallel development, there is a trend of terminating the interrupted step-down test at an ever earlier point. As a consequence, a trend to increasingly higher DFTs results (Figure 4a), caused not by the patient population, but clearly by the simplified test procedure. As a consequence, the implantation time could be significantly reduced from an average of two hours to one hour (Figure 4b). An opposite trend of the DFT development could be expected if the changes in the indicated patient population had not been superimposed by the procedure-caused falsifications. Extensions to the ICD indications that have been made since 1994 had the result that patients with a more favorable prognosis and fitness (Figure 4d), as well as better contractility reserves (Figure 4c) have been provided with an ICD.

Author		Mean DFT	Outlier
Boriani et. al.,	1998	7,7 +/- 4,4 J	23 % of values > 10 J
Munsif et. al.,	1997	9,2 +/- 5,1 J	28 % of values > 10 J
Horton et. al.,	1997	11 +/- 5 J	range 1 - 25 J
Neuzner et. al.,	1995	11,1 +/- 3,4 J	
Olsovsky et. al.,	1998	9,9 +/- 5,5 J	

Table 2. Mean DFTs of comparable implantation statistics.

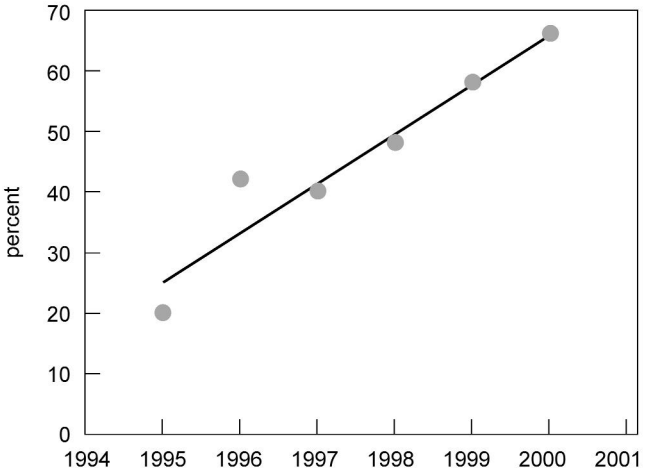


Figure 3. Percentage and trend of the device-based function test.

Author		Intraoperative DFT	Chronic DFT	Follow-up	Difference
Jung et al.,	1995	14.3 +/- 2.8 J	17.9 +/- 5.3 J	24 +/- 6 months	3.6 J
Neuzner et al.,	1998	11.1 +/- 3.4 J	11.5 +/- 2.9 J	13 months	0.4 J
Olsovsky et al.,	1998	9.9 +/- 5.5 J	7.6 +/- 5.5 J	2 months	- 2.3 J
Tummala et al.,	1996	11.7 +/- 3.0 J	15.8 +/- 10.0 J		4.1 J
Martin et al.,	1995	9.8 +/- 1.0 J	12.4 +/- 1.5 J	6 months	2.6 J

Table 3. Comparison of intraoperative and chronic DFTs.

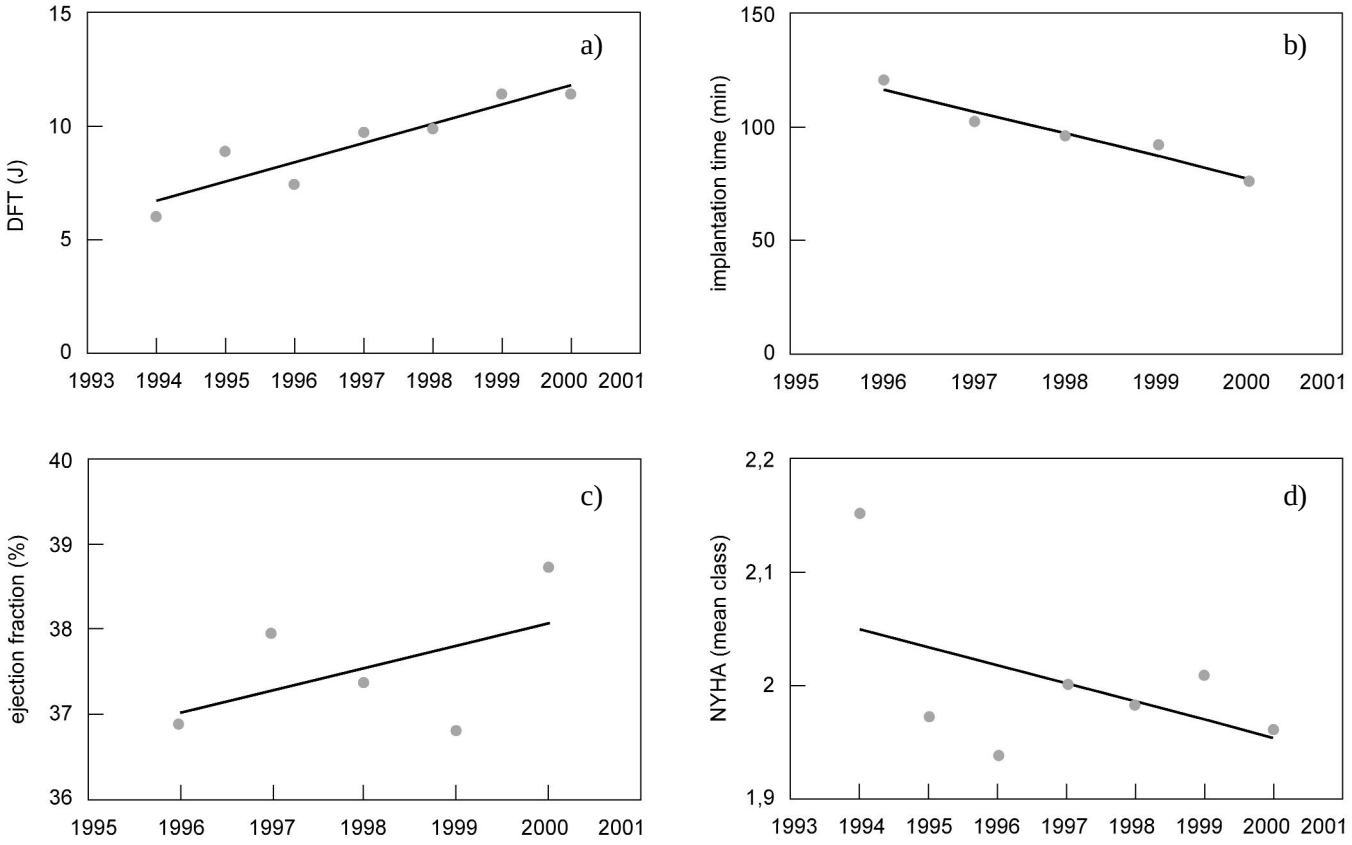
When evaluating the results reported so far, and shown in Figure 2, in regard to a prophylactic indicator device with a reduced output energy of, e.g., 20 J, 96 % of the patients could be converted without taking into account the need to program a safety margin. For a maximum energy of 15 J, the percentage already decreases to 81 %. Of course, a more reliable evaluation of the energy necessary when considering the need to program a safety margin requires study results attained under defined conditions, which necessarily include a complete DFT test (true DFT).

Evaluation of Published Studies

Defibrillation thresholds known from previously published studies (Table 2) are comparable to our results in regard to their mean values and standard deviations.

Stability of Intraoperatively Determined Defibrillation Thresholds

The evaluation of and information about the long-term stability of intraoperatively measured DFTs differ.



Figures 4. Trends of the DFT (a), the implantation time (b), the ejection fraction (c), and the NYHA classification (d).

LEET Study
In the usual clinical practice, the safety margin of the shock energy to be programmed (first shock) is calculated by doubling the DFT or adding 10 J to the DFT. The LEET study (low energy Endotak trial) was decisive in regard to the necessary safety margins. Neuzner et al. determined a mean DFT of 10.4 +/- 4.2 J in 162 patients [30]. 29 % of the determined DFT values were higher than 10 J. The safety margin for the first shock was programmed with two times the DFT value. The efficacy of the first shock was studied and found to be 84.4 %.

MINT Study
The currently still ongoing MINT study (minimum energy output trial) examines the efficacy of the first shock without consideration of a safety margin. To this end, the DFT is determined by a complete step-down test, and the same determined energy value is programmed as first shock. Studying spontaneous VF episodes, it is determined how often the programmed DFT value can terminate successfully, without having to deliver a second high-energy shock of 30 J. Patient safety is assured by a shock-success memory that immediately applies the second, high-energy shock in future VF episodes if the first shock has failed once. Thus, the low-energy first shock is skipped. The results of the MINT study will allow statements about the intra-individual stability of the DFT and the efficacy of the first shocks if low energies are used.
Study results can be expected within the year 2000.

Conclusion

Averaged DFTs ranging around 10 J result from the mentioned studies. Since the standard deviations of the DFTs are very high, there is a percentage of 25 % to 30 % of the examined patients who have a DFTs higher than 10 J.
For a prophylactic indicator system with a maximum energy of 20 J, a higher shock efficacy might possibly be expected than previously published for patients with stricter ICD indications. In view of the fact that there are currently no experiences regarding the DFTs for the target group of patients who would be considered suited for a prophylactic indicator system, an according study is desirable. Such a study should clarify whether the hypothesis of a lower DFT in patients who have not previously presented with VF episodes is correct.
It must be possible to compensate for influences on the DFT and its long-term stability (e.g., the degree and progression of the basic cardiac disease or drug therapy) by a sufficient safety margin. Guidelines can be taken from the MINT study.
A final statement about the efficacy of reduced output energies for a prophylactically treated patient group is currently not possible with sufficiently clinical reliability.

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