# Improved defibrillation efficacy with an ascending ramp waveform in humans

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**OBJECTIVES** The purpose of this study was to compare an ascending ramp waveform (RAMP) with a standard, clinically available biphasic truncated exponential waveform (BTE) for defibrillation in humans.

**BACKGROUND** In animal studies, RAMP had a lower defibrillation threshold (DFT) than BTE.

**METHODS** We studied 63 patients at implantable cardioverter-defibrillator placement using a dual-coil lead and left pectoral active can. The subjects were divided into two groups, one with a 12-ms ascending first phase and one with a 7-ms ascending first phase. Phase 2 of RAMP for both groups was a truncated exponential decay with 65% tilt and reversed polarity. The BTE had a 50% tilt in each phase. DFT and upper limit of vulnerability (ULV) were measured for both waveforms using a binary search protocol.

**RESULTS** The patient population was 77% male, with a mean age of 63 $\pm$ 10 years and ejection fraction of 33 $\pm$ 13%. Delivered energy at DFT was lower with the 7-ms RAMP vs BTE (5.4 $\pm$ 2.6 J vs 6.5 $\pm$ 3.4 J; $P < .01$) but unchanged with the 12-ms RAMP (7.4 $\pm$ 4.5 J vs 7.1 $\pm$ 4.9 J). Maximal voltage at DFT was significantly lower with either RAMP compared to BTE ($P < .01$). There was a strong correlation between ULV and DFT for both RAMP and BTE ($P < .01$).

**CONCLUSIONS** The 7-ms ascending ramp waveform significantly reduced delivered energy (18%) and voltage (24%) at DFT, whereas the 12-ms RAMP reduced only DFT voltage. This is the first report of a waveform that is superior to a BTE for defibrillation in humans. ULV correlates with DFT for RAMP, supporting the use of ULV testing for implantation of devices.

**KEYWORDS** Arrhythmia; Defibrillation; Electrophysiology; Tachyarrhythmias; Implantable defibrillators; Ventricular tachycardia

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Implantable cardioverter-defibrillators (ICDs) are commonly used to prevent sudden cardiac death. With the development of biphasic defibrillation waveforms and transvenous lead systems, the energy required for defibrillation was greatly reduced, allowing for prepectoral implantation.[1–4] Advances in capacitor and battery technology have allowed for greater reduction of pulse generator size, improving the safety and comfort of implantation. However, further advances in battery or capacitor technology likely will not yield significant decreases in ICD generator size without a decrease in the energy required for defibrillation.

All current ICDs use a truncated, biphasic exponential decaying waveform (BTE) to defibrillate. Mathematical models of defibrillation predict that defibrillation efficacy can be improved with an ascending ramp waveform (see Appendix).[5–7] Reports of animal studies indicate that ascending ramp waveforms are more effective than truncated exponential waveforms.[8,9] Advances in power electronics have made ramp waveforms feasible in an implantable defibrillator. We conducted a prospective, randomized study

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to compare the efficacy of two ascending ramp waveforms with a standard truncated biphasic waveform for ventricular defibrillation in humans.

## Methods

The study population consisted of 63 patients undergoing ICD placement for standard clinical indications. Informed consent was obtained from all patients. The study was approved by the Institutional Review Board of each institution.

Defibrillation testing was performed with the patients in the fasting or postabsorptive state under conscious sedation with fentanyl and midazolam, or propofol. During testing, 12-lead surface ECGs and simultaneous intracardiac electrograms were monitored continuously. Defibrillation thresholds (DFTs) and upper limit of vulnerability (ULV) were determined using an external waveform generator (model 2960 research defibrillator, Medtronic, Inc., Minneapolis, MN, USA), which can generate an arbitrary waveform irrespective of load resistance. The impedance of the system was measured in all patients by the delivery of a truncated exponential, monophasic 200-V synchronized shock prior to testing. All patients received a dual-coil lead (models 6944 or 6947, Medtronic, Inc.). An active can emulator was placed in the prepectoral pocket for testing. The proximal coil and active can were connected as the cathode. The distal right ventricular coil was the anode for each trial. Ventricular fibrillation (VF) was defined as a chaotic rhythm on the surface ECG leads with irregular intracardiac electrograms at a mean cycle length less than 200 ms. VF was induced using T-wave shocks during determination of the ULV (described later).

In all patients, DFT and ULV were determined using both an ascending ramp (RAMP) and standard BTE waveforms. The order of testing was randomized. The BTE had a 50%/50% tilt and a preset time constant to simulate delivery from a 125-$\mu$F capacitor (Figure1). Patients were divided into two groups. In group 1, patients were tested with a waveform that had a 12-ms ascending ramp, followed by a 1-ms exponential decay before a reverse polarity exponential decay phase of 2.5-ms duration (RAMP-12; Figure 1). This waveform was selected based on design and theoretical grounds. After analysis of the results from group 1, the waveform was modified by shortening the ascending ramp to 7-ms duration, followed by a 0.5-ms decay, increasing the leading-edge voltage of the second phase. A new cohort of patients (group 2) then was tested (RAMP-7; Figure 1). Both DFT and ULV were determined using a four-step binary search algorithm with a starting energy of 9 J. Energy for subsequent trials was increased or decreased, depending on the success of the initial shock (Figure 2). ULV was determined by a modification of the methods previously described.[10] The peak of the T wave was determined from the latest peaking, monophasic T wave that had opposite polarity to the QRS complex during ventricular pacing at a cycle length of 500 ms. The first T-wave shock was delivered after eight ventricular paced beats (500-ms interval) to coincide with the peak of this T wave. If VF was not induced, subsequent shocks were delivered 20 ms before the peak and 20 and 40 ms after the peak. If any of the four shocks induced VF, the strength of the next shock was increased. If none of the four shocks induced VF, shock strength was decreased. An interval of at least 3 minutes was required between each VF induction to allow for complete hemodynamic recovery. For each trial, delivered energy, peak voltage, peak current, and resistance were determined. DFT and ULV were determined by averaging the maximum unsuccessful and minimum successful shock strength for either defibrillation (to determine DFT) or for VF induction (to determine ULV). For ULV, "successful" was defined as failure to induce VF by any of the four shocks; "unsuccessful" was defined as induction of VF by any shock. Following completion of the experimental testing, the active can emulator was removed, and implantation of the defibrillator was completed.

Data are presented as mean $\pm$ SD. Comparisons are made using the Student's t-test for paired data. $P < .05$ was considered significant. Pearson correlation was used to assess the relationship between ULV and DFT.

## Results

The study population was typical of patients who receive ICDs (Table 1). The cohort was 77% male (mean age 63 $\pm$ 12 years). Mean left ventricular ejection fraction was 33 $\pm$ 13%. Forty-five patients (71%) had coronary artery disease, 13 (23%) had dilated cardiomyopathies, 1 (2%) had sarcoidosis, and 4 (6%) had other conditions. The indications for ICD placement were sudden cardiac death in 11 patients (17%), sustained or symptomatic ventricular tachycardia (VT) in 23 (37%), nonsustained VT with a low ejection fraction and inducible VT in 7 (11%), syncope with inducible arrhythmias in 13 (21%), low ejection fraction (<30%) and an ischemic cardiomyopathy in 8 (13%), and sarcoidosis in 1 (2%). Eight patients were taking antiarrhythmic drugs at the time of testing (seven amiodarone and one sotalol). The patients in each group were comparable except that group 2 had a higher percentage of patients who were implanted using MADIT-2 criteria (ischemic cardiomyopathy and low ejection fraction) as a result of release of these data between the two phases of this study. All patients completed the testing protocol without adverse consequences.

The results of the testing are given in Table 2. For group 1, the peak voltage at DFT was decreased with RAMP-12 compared to BTE ($P < .001$). However, the delivered energy at DFT was unchanged with RAMP compared with BTE. The results for individual patients with respect to delivered energy at DFT and DFT voltage are shown in