Effect of Biphasic Shock Duration on Defibrillation Threshold With Different Electrode Configurations and Phase 2 Capacitances
Prediction by Upper-Limit-of-Vulnerability Determination

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Background—The defibrillation threshold (DFT) may be affected by biphasic shock duration (BSD), electrode configuration, and capacitance. The upper limit of vulnerability (ULV) may be used to estimate the DFT. For different lead configurations and phase 2 capacitances, we investigated in 18 pigs whether the use of ULV may predict waveforms with lowest DFT.

Methods and Results—DFT and ULV were determined by up-down protocols for 10 BSDs. ULVs were measured by T-wave scanning during ventricular pacing (cycle length 500 ms). In protocol 1 (n=6), a pectoral “active can” was combined with an electrode in the superior vena cava as common cathode and a right ventricle electrode as anode (AC+SVC). In protocol 2 and protocol 3 (n=6 each), only the “active can” was used as proximal electrode (AC). Capacitance was 150 μF during both phases in protocol 1 and protocol 3 but 150 μF (phase 1) and 300 μF (phase 2) in protocol 2. ULV and DFT demonstrated a linear correlation in each protocol (r=0.78 to 0.84). Lowest DFTs were found at 10 ms for AC+SVC and at 14 ms for AC (P<0.001). At optimal BSDs, voltage DFTs did not differ significantly between AC (527±57 V) and AC+SVC (520±70 V). Switching capacitors for phase 2 in a way that reduced leading-edge voltage by 50% while doubling capacity did not change BSD for optimal voltage DFT but increased minimum DFT from 527±57 V to 653±133 V (P=0.04).

Conclusions—The BSD with lowest DFT is shorter for AC+SVC than for AC. There is no significant difference in voltage DFT between both at optimal BSD. A lower phase 2 capacitance reduces DFTs irrespective of BSD. Because strength-duration curves for DFT and ULV correlate for different BSDs, lead systems, and phase 2 capacitances, ULV determination may allow the prediction of waveforms with lowest DFT. (Circulation. 1999;99:1516-1522.)

Key Words: defibrillation ■ fibrillation ■ waves

Phase duration of biphasic defibrillation shocks has an important impact on defibrillation energy requirements in modern implantable cardioverter-defibrillators (ICDs). Depending on factors such as applied capacitance and electrode impedance, the optimal total shock duration (TSD) may vary from patient to patient. Testing of the defibrillation threshold (DFT) of different TSDs in individual patients would require the induction of multiple episodes of ventricular fibrillation (VF), which may lead to intolerable hemodynamic impairment. Determination of the upper limit of vulnerability (ULV) in patients may require the induction of only 1 or 2 VF episodes. Human and animal studies with either fixed-duration or fixed-tilt waveforms have demonstrated that the DFT can be estimated by determination of the ULV. Factors that influence the DFT such as electrode configuration or antiarrhythmic agents have been found to affect the ULV similarly. The first aim of this study was to assess the effect of TSD on the DFT for different defibrillation electrode configurations and phase 2 capacitances. The second objective was to investigate whether an effect of these variables on the DFT can be predicted by ULV determination.

Methods

Animal Preparation

All investigations were undertaken with permission of the competent authorities (Regierungspräsident Köln, June 1997). In 18 pigs (70±6.4 kg) anesthesia was induced with azaperone (2 mg/kg intramuscularly), atropine (0.14 mg/kg intramuscularly), and after 20 minutes with ketamine (20 mg/kg intramuscularly). The pigs were
ventilated with N\textsubscript{2}O/O\textsubscript{2} (ratio 3:1, Servo respirator, Siemens Corp). Sodium pentobarbital (1 to 2 mg/kg) was repeatedly infused to maintain a constant depth of anesthesia. Blood pressure was monitored through a carotid arterial line. Central venous and arterial blood samples were taken every 30 minutes for analysis of electrolytes and blood gases. Abnormal values were corrected as needed. Pulmonary capillary wedge pressure was monitored with a Swan-Ganz-catheter.

A defibrillation electrode (Ventritex-SF-01, Ventritex Corp) was introduced into the right ventricular apex (RVA) through the left external jugular vein. This electrode carries 2 coils, 1 positioned in the RVA and 1 in the superior vena cava (SVC). An ICD shell (Ventritex-Contour, Ventritex Corp) as second defibrillating electrode (“active can”) was placed in the pocket of the left pectoral muscle.

Electrode Configuration and Capacitors

Protocol 1

In 6 pigs, a 3-electrode system was applied. The RVA coil served as anode during phase 1 of the biphasic shock and the SVC coil together with the ICD shell as cathode (AC+SVC). Shocks were delivered by a 150-\mu F capacitor (two 300-\mu F capacitances connected in series; Ventritex-HVS-02, Ventritex Corp) during both shock phases (phase separation, 200 \mu s). Phase 2 leading-edge voltage equaled phase 1 trailing-edge voltage.

Protocol 2

In 6 pigs, shocks were delivered between the RVA electrode and the pectoral ICD shell (AC). The RVA electrode was anode during phase 1. Shocks were delivered by a 150-\mu F capacitor during phase 1 (two 300-\mu F capacitances connected in series) and a single 300-\mu F capacitor during phase 2 (phase separation, 200 \mu s; Ventritex-HVS-02). Leading-edge voltage of phase 2 was half the trailing-edge voltage of phase 1.

Protocol 3

In 6 pigs, shocks were delivered between the RVA electrode and the pectoral ICD shell (AC) as in protocol 2, whereas the waveform was identical to protocol 1.

Waveform Durations

DFTs and ULVs were determined for 10 TSDs (2, 4, 6, 8, 10, 12, 14, 16, 18, and 20 ms), with a relation of phase 1 to phase 2 duration of 50\%:50\%. The order of testing of the different TSDs was randomized within each animal. Peak voltage and current during phase 1 were recorded by a digital oscilloscope. Pathway impedance was determined by dividing peak voltage by peak current. The voltage decrease during phase 1 (phase 1 tilt) was calculated according to the formula phase 1 tilt=$\frac{1-V_{2}}{V_{1}}\times 100$ (\%), where $V_{2}$=phase 1 leading-edge voltage and $V_{1}$=phase 1 trailing-edge voltage. The phase 1 trailing-edge voltage was estimated by use of the formula $V_{t}=V_{1}\times e^{\frac{-R}{C}}$, where $V_{1}$=capacitor voltage as a function of time $t$; $V_{t}$=initial capacitor voltage, at $t=0$; $R$=impedance; and $C$=capacitance.

ULV Measurement

ULV determinations were performed during rapid pacing through the tip and ring of the RVA electrode. A train of 8 stimuli (cycle length 500 ms) was delivered at twice the diastolic pacing threshold. Six surface ECG limb leads were recorded at a paper speed of 100 mm/s (Mingograph, Siemens Corp) to select the lead with the latest peaking monophasic T-wave during pacing. The time from stimulus to the peak of this T-wave was measured and averaged during 3 consecutive beats. Throughout the whole study, new measurements of the stimulus to T-wave interval were taken every 5 VF episodes or before ULV determination for a new TSD started. ULV testing started with a shock strength of 710 V delivered to the peak of the T-wave of the 8th paced ventricular beat. A step-up–step-down protocol with a step-up size of 40 V, a step-down size of 80 V, and final steps of 20 V was used. The lowest voltage that did not induce VF was defined as the ULV. After ULV determination for the peak of the T-wave, the same protocol was started for shocks delivered at peak $-20$ ms, peak $-40$ ms, and peak $+20$ ms. Thus 4 ULVs were determined for each TSD in each animal. The highest of the 4 ULVs was defined as ULV\textsubscript{can} for each shock duration and pig. One minute elapsed between shocks that did not induce VF and subsequent shocks.

DFT Measurement

The DFTs were determined during VF episodes induced while testing the ULV for the same TSD. DFT testing started with a shock strength of 710 V by using the same step-up–step-down protocol as for the ULV determination. Defibrillating shocks were delivered 10 seconds after the onset of VF. In case of failure, an internal 990-V shock was applied. After each VF episode, a next shock was not delivered within 3 minutes and before blood pressure and heart rate had returned to normal. In addition, the DFT was determined for shocks with a TSD of 10 ms at the beginning of the experiment and hourly thereafter. If the DFT voltage differed by $>40$ V for this control waveform, the pig was excluded from analysis.

Statistical Analysis

Data are expressed as mean$\pm$1 SD. Repeated-measures ANOVA was used to compare peak voltage and current at the DFT or ULV\textsubscript{can} among the 10 waveforms in each protocol. For comparison of DFTs/ULV\textsubscript{can} between protocols, a 2-tailed unpaired Student’s t test was used. Individual DFT and ULV\textsubscript{can} values of all animals and TSDs in each protocol were pooled for calculation of linear regression. In each protocol, the DFT/ULV\textsubscript{can} values for each TSD were compared with the use of a paired t test. Differences in impedances between protocols were assessed by 2-tailed unpaired Student’s t tests. The percentages of coupling intervals relative to the peak of the T-wave that identified the ULV\textsubscript{can} were compared by use of a \chi\textsuperscript{2} test. ULV values for different coupling intervals were compared with the use of a paired t test. Probability values $\leq0.05$ were considered statistically significant.

Results

No animal had to be excluded from analysis because of an unstable DFT. In each animal, an average of 54$\pm$17 shocks was delivered for DFT determinations and 202$\pm$86 shocks for ULV measurements. DFT and ULV\textsubscript{can} values for the 3 protocols are summarized in the Table.

Protocol 1

The shock strength-duration curve for the DFT demonstrated a single minimum of peak voltage at a TSD of 10 ms (phase 1 tilt, 66\%; $P<0.001$, Figure 1). The same applied for the DFT in terms of peak current (Table). Similarly, the strength-duration curve for the ULV\textsubscript{can} showed a nadir at a TSD of 10 ms (phase 1 tilt, 64\%; $P<0.001$, Figure 1). At each TSD, the ULV\textsubscript{can} was lower than the DFT ($P<0.05$ except for a TSD of 4 ms, $P=NS$). A linear correlation existed between ULV and DFT, with $r=0.78$ (Figure 4A). The impedance did not differ significantly between DFT shocks (31$\pm$3 $\Omega$) and ULV\textsubscript{can} shocks (30$\pm$2 $\Omega$).

Protocol 2

The lowest voltage DFT was observed at a TSD of 14 ms (phase 1 tilt, 75\%; $P<0.001$, Figure 2). Likewise, the lowest ULV\textsubscript{can} was found at a TSD of 14 ms (phase 1 tilt, 70\%; $P<0.001$, Figure 2). Basically the same results were observed for the DFT and ULV\textsubscript{can} in terms of peak current (Table). At each TSD, the ULV\textsubscript{can} was lower than the DFT ($P<0.05$ except for a TSD of 6 and 20 ms, $P=NS$). There was a linear correlation between ULV and DFT, with $r=0.84$ (Figure 4B).
The defibrillation impedance was 37±8 Ω compared with 38±7 Ω for ULV shocks (P=NS). Both impedances were higher compared with AC+SVC during protocol 1 (each P<0.001).

Protocol 3

The lowest voltage DFTs and ULV\textsubscript{scan} were present at a TSD of 14 ms (P<0.001, Figure 3). The corresponding phase 1 tilts were 71% for DFT shocks and 69% for ULV shocks. The
DFT and ULV scan values in terms of peak current were also lowest at 14 ms. At each TSD, the ULV scan was consistently lower than the DFT ($P < 0.05$ except for a TSD of 4 ms, $P = \text{NS}$). The linear regression line is shown in Figure 4C ($r = 0.8$). The impedance for DFT shocks was $36 \pm 5 \Omega$ compared with $38 \pm 7 \Omega$ during ULV scan determination ($P = \text{NS}$).

**Comparison Between Waveforms of Protocol 2 and Protocol 3**

The only difference between protocol 2 and protocol 3 was the use of a 300-$\mu$F capacitor during phase 2 of the biphasic pulse in protocol 2, resulting in reducing the leading-edge voltage of phase 2 to half the value used in the other protocols as a result of the technical method used (removing one of the two 300-$\mu$F capacitors switched in series to obtain 150 $\mu$F for phase 1). The optimal TSD was equal for both waveforms (14 ms). However, the voltage DFT was significantly lower for the 14-ms waveform in protocol 3 ($527 \pm 57 \text{ V}$) compared with the 14-ms waveform in protocol 2 ($653 \pm 133 \text{ V}$, $P = 0.04$). The same holds true for the peak current at the DFT (protocol 3, $14 \pm 2 \text{ A}$ vs protocol 2, $18 \pm 5 \text{ A}$; $P = 0.05$). These results would have been predicted by the ULV scan: Both voltage ULV scan were lowest at a TSD of 14 ms. At this TSD, protocol 3 rendered a significantly lower ULV scan ($403 \pm 75 \text{ V}$) than protocol 2 ($553 \pm 124 \text{ V}$, $P = 0.02$). Similar results were observed for the ULV scan in terms of peak current (protocol 3 at TSD of 14 ms, $11 \pm 2 \text{ A}$ vs protocol 2 at TSD of 14 ms, $15 \pm 5 \text{ A}$; $P = 0.04$). A significant difference between both protocols was not found for the defibrillation impedance or for the impedance of ULV shocks.

**Comparison Between Electrode Configurations of Protocol 1 and Protocol 3**

The difference between protocol 1 and protocol 3 was the incorporation of an additional defibrillation electrode in the

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**Figure 3.** Peak voltage at DFT and ULV scan during protocol 3. An "active can" system without vena cava superior electrode was applied. The active can was the cathode and the right ventricular electrode was the anode during phase 1. Capacitance was 150 $\mu$F during both phases. Waveform duration significantly affected DFT and ULV scan ($P < 0.001$, ANOVA).

**Figure 4.** A through C, Pearson correlation coefficients ($r$) and lines of regression for DFT and ULV scan values of all waveforms and animals tested in protocol 1 (A, $n = 60$), protocol 2 (B, $n = 60$), and protocol 3 (C, $n = 60$). Some data points overlap.
Influence of Waveform on ULV-DFT Relation

Figure 5. Superimposition of DFT curves (peak voltage) of protocol 1 and protocol 3. DFT was lowest at 10 ms in protocol 1 (active can plus vena cava electrode) but at 14 ms in protocol 3 (active can without vena cava electrode). There was no significant DFT difference between both at optimized duration. Comparison of both configurations at the same shock duration revealed a trend toward lower DFTs during protocol 1 for durations ≤10 ms (P=NS). By contrast, except for 20 ms, DFTs for durations ≥12 ms were higher during protocol 1 than during protocol 2. This reached significance at duration of 14 ms. *P=0.05, +P=0.12.

SVC connected as common cathode with the pectoral ICD shell in protocol 1 (AC+SVC). This resulted in a significantly lower mean impedance for both DFT and ULVscan for AC+SVC compared with the AC system in protocol 3 (P<0.001). Moreover, the TSD with lowest DFT was shorter for AC+SVC (10 ms) than for AC (14 ms). There was an insignificant trend toward lower DFTs for AC+SVC as opposed to AC for TSDs, being ≤10 ms (Figure 5). By contrast, except for a TSD of 20 ms, the DFTs for TSDs ≥12 ms were higher for AC+SVC compared with AC. This reached statistical significance at a TSD of 14 ms (P=0.05). Comparing both electrode configurations each at the optimal TSD with the lowest DFT, no significant difference was present between both (AC+SVC, 10 ms: 520±70 V vs AC, 14 ms: 527±57 V, P=NS). Of interest, because of a lower impedance of the AC+SVC configuration, peak current for AC+SVC at 10 ms (18±2 A) was significantly higher than for AC at 14 ms (14±2 A, P=0.02). The results of ULVscan determination paralleled those of the DFT measurements: Whereas the lowest ULVscan was observed for a TSD of 10 ms during protocol 1 (433±53 V), the ULVscan was minimal for a TSD of 14 ms during protocol 3 (403±75 V). Similar to the DFT measurements, differences of peak voltage at the ULVscan between AC and AC+SVC at optimal TSD were not significant. Also, peak current at the ULVscan was significantly higher for AC+SVC at 10 ms (15±2 A) than for AC at 14 ms (11±2 A, P=0.002).

Coupling Intervals at the ULVscan
The mean stimulus to T-wave interval was 382±23 ms. Shocks delivered to the peak of the T-wave were more likely to identify the ULVscan than were shocks of other coupling intervals (peak of T-wave: 48% vs peak−20 ms: 29%, peak+20 ms: 30% or peak−40 ms: 3%, P<0.001 each, n=180). In those instances in which a coupling interval of peak−40 ms identified the ULVscan, the ULVs at peak−40 ms were higher (594±138 V) than at a coupling interval of peak−20 ms (546±114 V, P=NS). When a coupling interval of peak+20 ms identified the ULVscan, the ULV at peak+20 ms (577±159 V) was significantly higher than the ULVs at the peak of the T-wave (490±137 V, P<0.001).

Discussion
Electric shocks delivered to the heart during the vulnerable period of the cardiac cycle have been shown to induce VF.13 If a critical shock strength (ULV) is exceeded, these shocks no longer induce VF.14 Linear correlation between ULV and DFT has been demonstrated in several human and animal studies.7–12 All these studies compared the DFT and ULV for a single shock duration or phase 1 tilt. Yet, the optimal shock duration or phase 1 tilt with the lowest DFT may vary considerably, depending on electrode impedance or capacitance size.2,5,15 The present study underscores the value of using ULV to predict the optimal TSD for internal defibrillation. A similar correlation between ULV and DFT over different shock durations has recently been reported for monophasic shocks and biphasic shocks of varying phase 2 duration.16 Despite differences in ULV determination protocols and lead systems, both studies demonstrate that factors that change the DFT change the ULV in parallel. If these findings translate to humans, prediction of the waveforms, capacitances, and electrode configurations with the lowest DFT may be possible without the need for repeated induction of VF with the use of the ULV concept.

The DFT data of the present study may be important with respect to some recent studies on different pectoral lead systems in patients. Whereas one study17 did not find a significant DFT difference between AC and AC+SVC (60% phase 1 tilt, both), another study18 reported a decrease of the DFT for the AC+SVC system as compared with the AC system (65% phase 1 tilt, both). It is important to note that the pathway impedance was significantly lower for AC+SVC than for AC in both clinical studies17,18 and our animal study. In fact, theoretical concepts suggest that with decreasing capacitance and impedance, the shock duration with the lowest DFT decreases.15,19 As predicted, the TSD with minimal DFT voltage in our study was shorter for the lower impedance AC+SVC system (10 ms) than for the higher impedance AC configuration (14 ms). The respective phase 1 tilt was slightly higher for AC (71%) compared with AC+SVC (66%). The latter would not have been expected from a theoretical standpoint, which predicts that the phase 1 tilt with the lowest DFT increases with decreasing impedance and capacitance.15 Notably, for time constants T (T=impedance×capacitance) between 2 and 12 ms, changes of the optimal phase 1 tilt were suggested to be less pronounced than changes of phase 1 duration.15 The phase 1 tilt in the current study was calculated by using the impedance measured at the leading edge of phase 1. This is only an estimate of the real phase 1 tilt as it would have been obtained by measuring phase 1 leading and trailing-edge voltage. In
fact, the impedance has been reported to change during phase 1 of biphasic shocks. Therefore, one could imagine that the tilts calculated in the present study may not have exactly reflected the real voltage drop during phase 1. This may partly explain why the tilts found in the present study differed from the tilts that would have been predicted on the basis of mathematical models. The results of the present study indicate that the comparison of lead systems with different impedances by using the same phase 1 tilt or shock duration may in fact misestimate the DFT difference. As such, the use of the same phase 1 tilt within each study but different phase 1 tilts between the studies may have contributed to the diverging results in recent studies that investigated the DFTs for an AC+SVC system as compared with an AC system.

Another intention of our study was to compare the DFT and the ULV for different capacitances during phase 2 of the biphasic shocks. Changing phase 2 capacitance from 90 to 22.5 μF (phase 1, 90 μF) has previously been shown to decrease the DFT in patients. However, besides different phase 2 capacitances and phase 2 leading-edge voltages, differences in phase 1 duration might have contributed to the lower DFT for the 22.5-μF second-phase waveform. The present study showed that the TSD and phase 1 duration with the lowest DFT was equal for waveforms with different phase 2 capacitances. At optimal shock duration, the DFT for the 150-μF second phase was significantly lower than for the 300-μF second phase. It is important to note that besides differences of phase 2 capacitances there also was a difference of phase 2 leading-edge voltage for the 2 waveforms. This renders it difficult to explain by which mechanism the waveform used in protocol 3 decreased the DFT compared with protocol 2. A model developed by Kroll proposed that phase 2 unloads the residual charge that is left on the cardiac cell membrane after delivery of the first phase (“charge-burping” hypothesis). This residual charge is thought to cause postshock arrhythmias, thus diminishing defibrillation success. For a fixed pulse duration, the charge delivered by a capacitor equals $C \times V_o \times \left[1 - e^{-t/R_3 C}\right]$ ($C =$ capacitance; $V_o =$ initial capacitor voltage, at $t=0$; $t =$ pulse duration; $R_3 =$ impedance). Comparing protocol 2 and protocol 3, the product $C \times V_o$ remains constant (halving C, doubling $V_o$). Thus for an equal pulse duration and a similar impedance, a lower C value means more charge delivered. Conceptually, this could mean that protocol 2, with the higher C, provides less effective “charge-burping,” causing higher DFTs. However, we did not specifically test this hypothesis, which remains to be checked in the Kroll model in a quantitative way and then verified in experiments that vary capacity and leading-edge voltage for phase 2 independently.

Limitations
In our study, the ULV$_{\text{scan}}$ was significantly lower than the DFT. In dogs, it was demonstrated that with rapid ventricular pacing the ULV approximately equaled the DFT, whereas it was lower than the DFT when the pacing cycle length was increased. Therefore, the choice of a faster pacing rate in our study might have resulted in a ULV$_{\text{scan}}$ level closer to the DFT level. In addition, only limited T-wave scanning was performed in our study, which may have caused an underestimation of the ULV$_{\text{scan}}$. Additional T-wave shocks delivered at peak +40 ms or peak −50 ms might have resulted in higher ULV$_{\text{scan}}$ values.

To determine most accurately the DFT and ULV strength-duration relation, we used a step-up–step-down protocol with final steps of 20 V. This required a maximum of 3 VF inductions to determine the ULV for a single time point of the T-wave. Recent clinical studies reported that other ULV protocols need only 1 or 2 VF inductions for ULV determination. Moreover, during clinical ULV testing, larger voltage steps will require fewer VF inductions, thus providing higher safety during ULV and DFT testing. This may, however, worsen the correlation between the ULV and DFT.

In this animal model, the interval from the pacing stimulus to the peak of the latest peaking monophasic T-wave was $382 \pm 23$ ms and therefore longer than reported in a clinical study ($358 \pm 56$ ms) with the same pacing rate. However, all patients in that study had organic heart disease, which may have accounted for this difference. The lack of organic heart disease also may have affected the level of the ULV$_{\text{scan}}$ and the correlation between ULV$_{\text{scan}}$ and DFT in the present study.

No pig had to be excluded from analysis because of unstable DFT for the control waveform. Therefore, the number of previous shocks did not affect subsequent DFT results for this control waveform. Because we did not repeatedly determine the ULV for a control waveform throughout the experiment, we do not know whether the same might have applied for the ULV results.

Conclusions
The TSD for lowest DFT is $\approx 40\%$ longer for AC (36 Ω) than for AC+SVC (31 Ω). The respective tilts are more similar for these 2 configurations: 71% for AC and 66% for AC+SVC. At optimal TSD, the DFT did not differ significantly between both lead systems.

Application of a 150-μF capacitor during both phases of the biphasic shocks led to a significant DFT reduction compared with shocks with a 150-μF first phase and a 300-μF second phase. The latter waveform is currently applied in some clinical devices. A lower phase 2 capacitance did not affect the TSD with the lowest DFT.

The DFT results would have been predicted by ULV$_{\text{scan}}$ determinations because strength-duration curves for DFT and ULV$_{\text{scan}}$ correlated for different electrode configurations and phase 2 capacitances. If results in patients are shown to be similar to our results in pigs, ULV determination may allow comparison of different electrode systems and capacitances, each at optimal TSD without the need for extensive DFT testing.

References


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Circulation. 1999;99:1516-1522
doi: 10.1161/01.CIR.99.11.1516

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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