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Feasibility of Atrial Fibrillation Detection and Use of a Preceding Synchronization Interval as a Criterion for Shock Delivery in Humans With Atrial Fibrillation

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Objectives. **This study assessed the feasibility of detecting atrial fibrillation (AF) and delivery of appropriately timed R wave shocks using an implantable atrial defibrillator.**

Background. **For atrial defibrillation therapy to be feasible in an implantable form, AF must be detected in a specific fashion, and the risk of ventricular proarrhythmia should be minimized.**

Methods. **Eleven patients with AF underwent testing with an implantable atrial defibrillator (METRIX 3000 Automatic Atrial Defibrillator, InControl, Inc.). Wideband electrograms (EGMs) were recorded from the right ventricular (RV) bipolar catheter and from the multipolar catheters located in the right atrium (RA) and coronary sinus (CS). Atrial fibrillation detection was performed using two serial algorithms—quiet interval analysis and baseline crossing analysis—that detect atrial activity on the RA–CS channel. Ventricular sensing using a minimal preceding synchronization interval of 500 ms as a criterion for synchronous shock delivery was performed from filtered RV and RV–CS EGMs.**

Results. **The AF detection algorithms were applied to 53 AF data segments and 18 normal sinus rhythm data segments. Atrial fibrillation was detected appropriately in 49 instances, and the specificity for detecting AF and normal sinus rhythm was 100%. Synchronization criterion efficacy was assessed by delivering shock markers and shocks. Of the 2,025 R waves processed, 557 (27.5%) were marked as suitable for shock delivery. In addition, 69 therapeutic and 11 test shocks were delivered during AF. All shock markers and shocks were delivered synchronously with the R wave, and the synchronization criterion was never violated.**

Conclusions. **Atrial fibrillation can be detected in a specific fashion using the RA–CS lead configuration and serial detection algorithms for atrial sensing. The delivery of properly timed shocks is feasible and should minimize the risk of ventricular proarrhythmia.**

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Low energy transvenous defibrillation has been used successfully to convert atrial fibrillation (AF) to normal sinus rhythm (1–10). However, previous studies (11–13) have documented that shocks delivered during some portion of the T wave can consistently cause ventricular fibrillation. The delivery of synchronized shocks after a short preceding ventricular cycle length has also been shown (14) to cause ventricular fibrillation. The dispersion of ventricular refractoriness has been associated with ventricular vulnerability to reentry (15). It has been shown (16–20) that abrupt changes in stimulation sequences can induce ventricular arrhythmias in humans and in animal models. A reliable AF detection algorithm and delivery of synchronized shock after a minimal preceding ventricular cycle length should thus minimize the risk of ventricular proarrhythmia. Because the lead configuration in the right atrium (RA) and coronary sinus (CS) forms the best atrial defibrillation vector (7–10), to avoid the complexity of using multiple transvenous leads, this RA–CS lead configuration could also be used for atrial sensing.

However, the feasibility of detecting AF in an appropriate fashion and using a minimal preceding ventricular cycle lengths as a synchronization criterion for shock delivery during AF has not been studied before in humans. The present study evaluated the performance of an AF detection method and synchronization criterion for shock delivery by means of an automatic implantable atrial defibrillator in patients with a history of AF.

Methods

Patients. The study group included 11 patients with AF (3 men, 8 women; mean [±SD] age 51 ± 9 years, range 32 to 63). Ten patients had a history of paroxysmal AF that ranged in duration from 18 months to 20 years. The remaining patient had chronic AF lasting >3 months in duration. Atrial fibrillation–defibrillation testing was performed after all antiarrhythmic

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Abbreviations and Acronyms

AF = atrial fibrillation
AV = atrioventricular
CS = coronary sinus
EGM = electrogram
RA = right atrial, right atrium
RV = right ventricle, right ventricular

medications had been discontinued for at least 5 half-lives in nine patients. Of the remaining two patients, one had discontinued amiodarone 3 weeks before testing because of side effects. The remaining patient with AF was taking sotalol (160 mg twice daily) at the time of testing. The protocol was approved by the institutional review board, and all patients gave written informed consent.

Transvenous lead system. Two temporary multipolar transvenous catheters (InControl model 7903) were introduced percutaneously through the right internal jugular and right femoral veins and positioned into the CS and the RA. Each of these catheters incorporates 11 platinum electrodes (interelectrode spacing of 2 mm) of which the tip and the fourth ring electrode can be used for pacing and sensing and the remaining nine electrodes, with a surface area of 2.31 cm^2, for defibrillation. These nine defibrillation electrodes also form the vectors used for detecting intracardiac electrical activity. A third 6F standard quadripolar electrode (Bard) was also introduced percutaneously through the femoral vein and positioned in the right ventricular (RV) apex. However, only the distal two electrodes were used for the RV bipolar configuration. Figure 1 depicts the location of different catheters and the vectors used for AF detection, synchronization and shock delivery.

Atrial defibrillator. The METRIX atrial defibrillator was not implanted in any of the patients but was inserted into a device fixture that connected the transvenous catheters to the device. The METRIX defibrillator weighs 79 g and has a displacement volume of 53 cm^3. The device can monitor intracardiac atrial and ventricular electrical activity for the presence of AF and, after a synchronization process, deliver R wave synchronous 3/3-ms biphasic shocks using an 80-μF capacitor. The therapy options are programmable up to four levels, and the voltage ranges from 30 to 300 V. The device is also capable of providing full-time ventricular asynchronous, or VVI, pacing. The METRIX defibrillator can also be used to induce AF by using R wave synchronous shocks and can store intracardiac electrograms (EGMs) for up to 2 min from the most recent six AF episodes.

Atrial fibrillation detection algorithms. The EGM data over 8 s are analyzed using two sensing channels; that is, one from the vectors formed by the RV bipolar configuration and the second from multipolar catheters located in the RA and CS. The filtered RV (22 to 45 Hz) and RA–CS (10 to 45 Hz) channels are downsampled by a factor of 4 to 250 Hz. For R wave sensing, the RV channel gain was automatically adjusted so that the fixed detection threshold was 25% of the average peak amplitude of the largest four peaks in the segment processed. For atrial sensing on RA–CS, a detection window of 300 ms was used after the detected R waves were blanked out to avoid ventricular contamination. The gain was automatically adjusted so that the detection threshold was 33% of the average peaks in the data segment. The EGM data were then

Figure 1. Schema of vectors used for sensing and shock delivery. Catheter locations in the RA, CS and RV and the different vectors used for monitoring cardiac electrical activity and delivering defibrillation pulses are shown in the three panels. During AF detection (**left panel**), an 8-s EGM data segment is collected utilizing two sensing channels, one from the vector formed by the RV bipolar catheter (RV vector) and the second from the vector formed by the multipolar RA–CS catheters (RA–CS vector). On successful qualification of data, RA–CS EGMs are analyzed for detection of AF. Synchronization (**middle panel**) utilizes sensing channels from the vectors formed by the RV bipolar catheter (RV vector) and from the tip electrode of the RV catheter and the multipolar CS catheter (RV–CS vector). Atrial defibrillation pulses (**right panel**) after synchronization are delivered over the RA–CS electrodes.

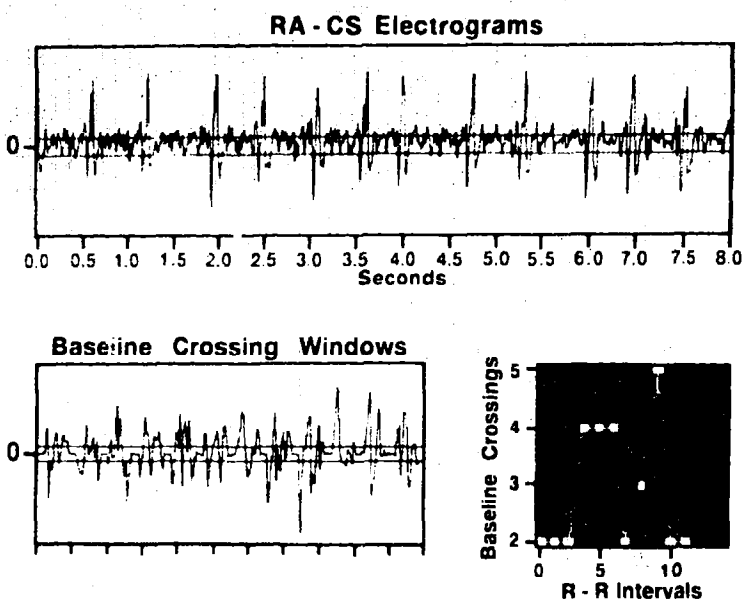


Figure 2. Baseline crossing analysis for AF detection. The **top panel** shows an 8-s EGM segment from a vector formed by multipolar catheters located in the RA and CS used for baseline crossing analysis. The **lines** above and below 0 in the **top** and **bottom left panels** represent the positive and negative sensitivity thresholds for baseline crossings. A 200-ms detection window separated by the **short 0 line segment,** as shown in the **bottom left panel,** was programmed beginning 80 ms after each R wave except the last. The baseline crossing count is the average number of baseline crossings per R wave. To be counted, the crossing has to occur over both positive and negative sensitivity thresholds. The **right bottom panel** shows the computer generation of baseline crossings in each window. The total baseline crossings over 11 RR intervals analyzed was 32. The average baseline crossing count of 2.9 was thus well above the programmed value of 2.0 in this patient, and AF was detected appropriately.

processed by the detection algorithms; namely, quiet interval analysis and baseline crossing analysis.

Quiet interval analysis. The quiet interval analysis algorithm is used to discriminate between a sinus and a nonsinus rhythm in the 8-s EGM segment. The *quiet interval* is defined as an interval greater than the preselected interval during which no sensed events occur on the RA–CS channel and is programmable from 130 to 220 ms. The percent quiet time is calculated by dividing the total time by 8 s and multiplying by 100%. The percent quiet time is programmable from 10% to 30% in increments of 5%. If the percent quiet time is equal to or rises above the programmed value, the cardiac rhythm is diagnosed as normal sinus rhythm. If the percent quiet time falls below the programmed value, the rhythm is determined to be nonsinus, and the baseline crossing algorithm is invoked to detect AF.

Baseline crossing analysis. The baseline crossing analysis is a configuration analysis method that examines the average number of baseline crossings on the ST-T region. Using an RA–CS EGM, a detection window is set beginning 80 ms after the R wave and ending 200 ms later, except in the last R wave. The device then analyzes the filtered RA–CS EGM data to count the number of times the signal crosses both the negative and positive baseline crossing thresholds within each detection window. The baseline crossing count is the average number of baseline crossings per R wave. It is programmable from 1.6 to 3.0 in increments of 0.1. If the average baseline crossing count in the 8-s window exceeds the programmed count, the cardiac rhythm is defined as AF (Fig. 2).

Synchronization. The RV and RV–CS channels are used for synchronization process (Fig. 1). The minimal synchronization interval can be programmed from 500 to 800 ms. Because each R wave is sensed at a slightly different time on the RV and the RV–CS channels, a *minimal synchronization interval* is therefore defined as the interval between the later of the two S wave components of a QRS complex sensed on the two channels and the earlier of the two Q wave components of the next QRS complex sensed on the two channels (the SQ interval). A qualifying synchronization interval for shock delivery must be greater than the programmed minimal interval, and, if <800 ms long, the qualifying SQ interval must be no more than 140 ms shorter than the preceding QQ interval on the RV channel. No study patients had left bundle branch block, which, as a result of the involvement of two different channels, could potentially affect the synchronization process.

Programming and testing protocol. Testing was performed under light anesthesia using intravenous propofol. Quiet interval was programmed at 170 ms, and the percent quiet time was programmed at 25%. The baseline crossing count was programmed at 2.0. The synchronization (SQ) interval was programmed at 500 ms. Initial attempts were made to induce AF by delivering R wave synchronous shocks at 30 V. If unsuccessful, burst pacing was performed from the first and fourth electrodes of the RA catheter using a Bloom stimulator. Once AF was sustained for at least 60 s, several 8-s AF and normal sinus rhythm data segments were initially processed by the detection algorithms. To assess synchronization, the METRIX defibrillator was initially programmed to deliver shock markers once the synchronization criterion had been fulfilled. Subsequently, after assessing the integrity of the lead system by delivering a 20-V test shock, the synchronization process was evaluated during therapeutic shock delivery. The device was programmed to deliver the first shock at 180 V. Additional shocks were delivered at 40-V increments or decrements, depending on the initial success. The atrial defibrillation threshold was defined as the lowest amount of energy that

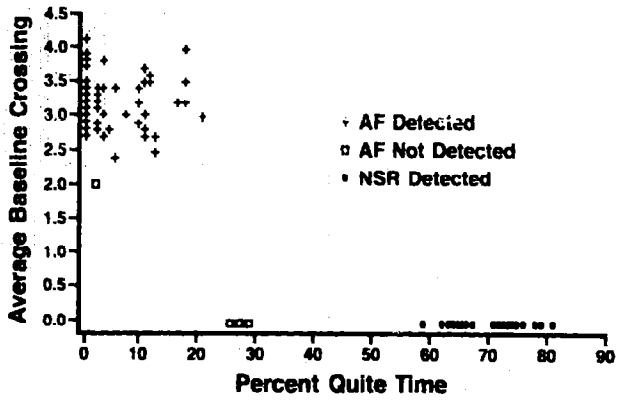


Figure 3. Scattergram of percent quiet time during sinus rhythm and AF and average baseline crossing count during AF. Eighteen normal sinus rhythm (NSR) and 53 AF EGM segments were processed by these algorithms. During quiet interval analysis, the cardiac rhythm equal to or above the programmed value of 25% was classified as normal sinus rhythm and that below the programmed value of 25% was classified as nonsinus rhythm (AF), at which time the baseline crossing algorithm was invoked. Baseline crossing analysis detected AF from the EGM segment determined to be nonsinus rhythm by quiet interval analysis when the average baseline crossing count was >2.0. Using these criteria, the NSR and AF detection specificity of quiet interval analysis was 100%, and the AF detection specificity of baseline crossing analysis was 100%. During three episodes of AF, the percent quiet time ranged from 27% to 29%, and the baseline crossing algorithm was not invoked. During one episode of AF, the baseline crossing count was 2.0, and AF was not detected.

successfully defibrillated AF on two successive attempts. However, no systematic attempts were made to evaluate different lead locations to achieve the lowest defibrillation energy. All patients were followed up in the clinic 1 week after discharge from the hospital.

Results

Atrial fibrillation could be reproducibly induced and sustained in all patients for repeated testing. Forty-five low energy shocks were delivered during sinus rhythm in an attempt to induce AF in 10 patients. However, only four episodes of sustained AF were induced in two patients. Burst pacing was thus required to induce AF in the majority of instances. Therapeutic shocks were delivered during all 69 AF–defibrillation sequences tested in the 11 patients. In addition, 11 test shocks were also delivered during AF. No complications were encountered in any patient. No ventricular proarrhythmia occurred during the delivery of shocks.

Performance of AF detection algorithms. Eighteen 8-s EGM data segments during normal sinus rhythm and fifty-three 8-s EGM segments during sustained episodes of AF in the 11 patients were processed by the detection algorithms. The scatter diagram of percent quiet time during normal sinus rhythm and AF, and the average baseline crossing count during AF, are depicted in Figure 3. The percent quiet time was 70 ± 6.4% (mean ± SD, range 59% to 81%) during normal sinus rhythm and 5.9% ± 7.4% (range 0% to 29%) during AF. Using a percent quiet time <25% as a criterion for classifying the cardiac rhythm as AF, the specificity of quiet interval analysis in detecting AF was 100%. Similarly, when a percent quiet time ≥25% was used to classify normal sinus rhythm, the specificity of quiet interval analysis for detecting sinus rhythm was 100%. However, during three AF episodes in three patients, the percent quiet time ranged from 27% to 29%, respectively. The AF was thus categorized as a normal sinus rhythm, and the baseline crossing algorithm was not invoked.

The average baseline crossing count analyzed during AF detection was 3 ± 0.8 (range 2.0 to 4.1). When a baseline crossing count >2.0 was used as a criterion for detecting AF, the AF detection specificity of baseline crossing analysis was 100%. During one episode of AF in one patient, however, the baseline crossing count was 2.0, and AF was not detected. The analysis of ECMs showed that this patient had converted to an organized atrial rhythm at the time the AF detection algorithm had been invoked. During the subsequent two episodes of AF, the average baseline crossing count was 3.3 and 3.5, respectively, and AF was detected appropriately both times.

Efficacy of synchronization criterion and shock delivery. During AF, 104 EGM segments for delivery of shock markers, 11 test shocks and 69 therapeutic shocks were analyzed. The 104 EGM data segments analyzed for delivery of shock markers contained 2,025 R waves, of which 557 (27.5%) were marked as suitable for shock delivery. In the remaining 1,468 instances, the synchronization criterion was not met. All shock markers delivered were synchronized to the R wave. All patients had intervals that met the synchronization criterion. R wave synchronous shocks (Fig. 4) during 11 test shocks and 69 sequences of AF–defibrillation tested were delivered appropriately in all instances.

Depicted in Figure 5 is the plot showing the relation between the synchronization (SQ) interval preceding the delivery of shock markers and shocks during AF and the QQ intervals preceding the SQ intervals. The minimal preceding synchronization (SQ) interval of 500 ms as a criterion was met during all instances of delivery of shock markers and shocks. The mean preceding synchronization (SQ) interval was 682 ± 190 ms (range 510 to 1,360). The mean QQ interval preceding the SQ interval was 641 ± 198 ms (range 300 to 1,430). However, this interval was below the specified range of 140 ms. The synchronization criterion was not violated during any of the 637 episodes, and all shock markers and shocks were delivered in an appropriate fashion.

In one patient, sinus rhythm could not be restored despite the maximal shock strength of 300 V. In the remaining 10 patients, the leading edge voltage defibrillation threshold was 246 ± 38 V (range 180 to 300). The delivered energy threshold was 2.0 ± 0.6 J (range 1.1 to 3.1). One patient had asystole (with no sinus or ventricular escape rhythm) ranging from 4.4 to 7.2 s after the delivery of therapeutic shocks. The postshock escape interval in the remaining 10 patients ranged from 860 to 1740 ms.

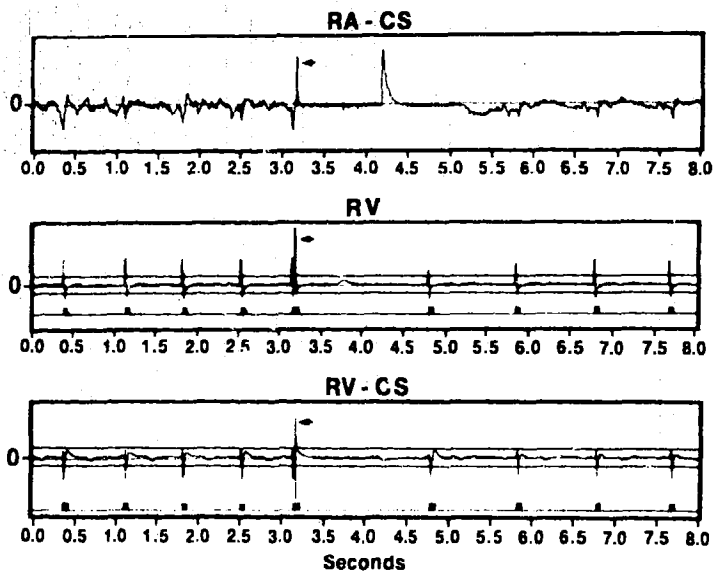


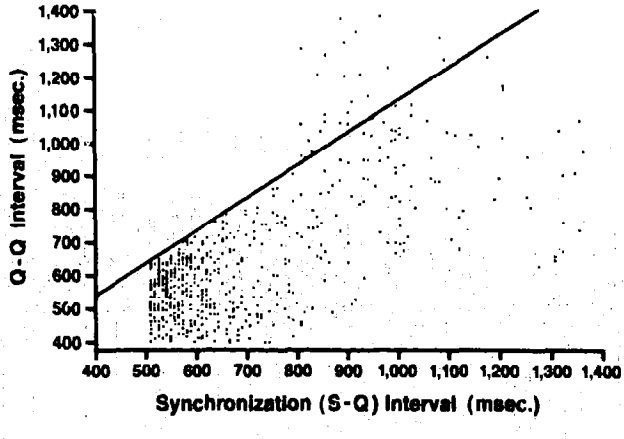
Figure 4. Synchronization and shock delivery. An 8-s EGM segment recorded from a vector formed by multipolar catheters located in the RA and CS (**top panel**), bipolar RV catheter (**middle panel**) and from a vector formed by the tip electrode of the RV and multipolar CS catheters (**bottom panel**) is shown. **Lines** above and below 0 in the **bottom two panels** represent the positive and negative sensitivity thresholds, and the **short vertical lines** represent the synchronization markers. A therapeutic R wave synchronous shock at 260 V (**arrow**) delivered over the RA–CS catheters restores normal sinus rhythm. The preceding synchronization interval before shock delivery is well above the programmed minimal value of 500 ms.

Discussion

The *principal finding* of this study was that, using vectors from the multipolar catheters located in the RA, CS and RV, AF can be detected appropriately. The two serial algorithms of quiet interval and baseline crossing analysis can discriminate AF and normal sinus rhythm with a high degree of specificity. Furthermore, the use of a minimal preceding synchronization interval as a criterion for shock delivery is feasible and should minimize the risk of inducing ventricular arrhythmias.

Atrial sensing and AF detection algorithm. Detecting AF in a specific fashion is critical for appropriate atrial defibrillation therapy. A new set of serial algorithms were tested in this study to detect AF. To obtain high specificity, it was necessary for both algorithms to analyze the cardiac rhythm. During normal sinus rhythm, the filtered RA–CS signal values are likely to lie between the detection thresholds and produce long intervals during which there are no sensed events. The quiet interval analysis should thus detect normal sinus rhythm in a specific way. Using 25% as a criterion for quiet interval analysis, initially three episodes of AF in three patients were determined to be sinus rhythm. Thus, whereas it is possible that every form of nonsinus rhythm may not be detected by quiet interval analysis, when normal sinus rhythm is detected, it is highly probable that it is genuine sinus rhythm. The quiet interval algorithm also seems to be specific for detecting a nonsinus rhythm such as AF; all episodes determined to be nonsinus rhythm by a percent quiet time <25% were genuine AF episodes, after which the baseline crossing algorithm was invoked to detect AF.

Figure 5. Plot of the relation between the synchronization (SQ) intervals preceding the delivery of shock markers and shocks and the QQ intervals preceding the SQ intervals is shown. A total of 557 shock markers, 69 therapeutic shocks and 11 test shocks were delivered during AF. In all instances the synchronization (SQ) interval was >500 ms. When the synchronization (SQ) interval was <800 ms, the preceding QQ interval was either shorter than the SQ interval or no longer than the SQ interval by the maximal specified range of 140 ms. The synchronization criterion was thus not violated in any of the instances, and all shock markers and shocks were delivered appropriately.



The baseline crossing algorithm takes into account the unique electrophysiologic properties of AF. Atrial fibrillation has been characterized as chaotic and disorganized and non-acetylcholine animal model studies (7, 21, 22) have suggested that the cycle length of AF is ~90 to 120 ms. In one study (23), where bipolar atrial EGMs were used, significant differences were found between regular rhythm and AF for atrial rate, percent of power in the 4 to 9-Hz band during spectral analysis and amplitude probability density close to the isoelectric line. The number of deflections during AF in the ST-T region is thus typically higher than in normal sinus rhythm. As shown in Figure 2, during AF, due to an increased atrial rate, the intervals between sensed events are relatively short. It is thus highly likely that despite a short detection window, enough signal activity during AF in the ST-T region would cross both the negative and positive baseline crossing thresholds to detect

AF. Combining the two algorithms in a serial fashion also provides a high degree of specificity for detecting AF.

Synchronization and risk of ventricular proarrhythmia. Although the reported overall risk of inducing ventricular arrhythmias during atrial defibrillation is low (6,24), studies have reported (2–4,25) the occurrence of ventricular fibrillation during transvenous atrial defibrillation. This factor has been the most critical issue regarding the use of atrial defibrillation therapy in an implantable form (26). The induction of ventricular arrhythmia during atrial defibrillation does not seem to be a random event and can occur as a result of different mechanisms: 1) Lack of synchronization of the defibrillation shock in relation to the intrinsic ventricular depolarization can result in a shock being delivered during the ventricular vulnerability period (e.g., during the T wave). 2) Since the ventricular vulnerable period is also affected by the preceding cycle length, ventricular fibrillation could occur even if a synchronized shock is delivered during ventricular depolarization that occurs before complete repolarization of the previous beat (14).

In the previously mentioned study of a sheep model (14), 11 episodes of ventricular fibrillation were observed during the delivery of 1,870 shocks. However, all episodes of ventricular fibrillation occurred with a preceding ventricular cycle length <300 ms. Nine of these 11 episodes were thought to be caused by shock being synchronized to ventricular depolarization that was encroaching on the terminal portion of the preceding T wave due to short preceding RR intervals. It has also been shown (27) that at long preceding cycle lengths, ventricular action potential duration approaches a maximum of 300 ms. A synchronization criterion, which, apart from delivering R wave synchronous shocks, takes into account the preceding ventricular cycle lengths, should thus minimize the risk of ventricular arrhythmia. Because patients were sedated and supine during testing, the possibility of delayed synchronization due to rapid ventricular response during a fully conscious state remains.

A recent study (28) of 40 recorded EGMs from 23 patients in AF showed that 53% of the 3,813 RR intervals were found to be >500 ms in duration. Many factors, such as impulse efficacy, different atrioventricular (AV) junction inputs, longitudinal dissociation and electrotonic modulation, can influence AV conduction during AF, and a recent study (29) also demonstrated that an inverse relation exists between the atrial and ventricular rates during AF. Furthermore, because AF is rarely an emergency, immediate conversion of AF to sinus rhythm is not an important factor. These properties should make it possible for some of the conducted RR intervals to be long enough for appropriate synchronization.

Limitations of the study. Previous studies (10) have shown that patient discomfort increases steadily with increasing shock strength. Studies have also shown (30) that the atrial defibrillation threshold can be influenced by several factors, including lead position. However, this may require testing numerous AF–defibrillation sequences in each patient. The main purpose of the present study was to assess the performance of AF detection algorithms and the feasibility of a synchronization criterion that required the induction of AF during numerous occasions and testing of several AF–defibrillation sequences. For the sake of patient comfort and safety, the testing protocol was performed under light anesthesia, and the issues of patient tolerance and defibrillation thresholds could not be addressed in a systematic fashion. Furthermore, in the clinical setting, the presence of antiarrhythmic medications, electrolyte abnormalities and myocardial ischemia could all affect AF detection, redetection and the ventricular vulnerability period. Use of temporary catheters also only provides a test of feasibility of the variables evaluated and cannot be accurately extrapolated to a clinically implanted system. Further research is needed to address these issues.

Summary and clinical implications. In this study, the feasibility of the performance of AF detection algorithms and a synchronization criterion for shock delivery was demonstrated. To avoid inappropriate shock delivery, atrial sensing needs to be performed in a specific fashion. Using a preceding synchronization interval as a criterion for shock delivery, as demonstrated in this study, is also possible and should minimize the risk of ventricular arrhythmias during atrial defibrillation. The findings of the present study thus may have implications for the feasibility of this therapy in an implantable form. Several other important issues, such as patient tolerance and achieving the lowest energy for atrial defibrillation using different lead locations; the type of patient population that may benefit from this form of therapy; long-term safety; efficacy; and cost effectiveness, will also need to be resolved. Findings of AF detection and synchronization in this feasibility study will also need to be corroborated in a large population of patients in future studies.

References

1. Jain SC, Bhatnagar VM, Azami RU, Awasthey P. Elective countershock in atrial fibrillation with an intracardiac electrode—a preliminary report. J Assoc Physicians India 1970;18:821–4.
2. Nathan AW, Bexton RS, Spurrell RA, Camm AJ. Internal transvenous low energy cardioversion for the treatment of cardiac arrhythmias. Br Heart J 1981;52:377–84.
3. Dunbar DN, Tobler HG, Fetter J, Gornick CC, Benson DW, Benditt DG. Intracavitary electrode catheter cardioversion of atrial tachyarrhythmias in the dog. J Am Coll Cardiol 1986;7:1015–27.
4. Powell AC, Garan H, McGovern BA, Fallon JT, Krishnan SC, Ruskin JN. Low energy conversion of atrial fibrillation in the sheep. J Am Coll Cardiol 1992;20:707–11.
5. Kumagai K, Yamanouchi Y, Tashiro N, Hiroki T, Arakawa K. Low energy synchronous transcatheter cardioversion of atrial flutter/fibrillation in the dog. J Am Coll Cardiol 1990;16:497–501.
6. Levy S, Lauribe P, Dolla E, et al. A randomized comparison of external and internal cardioversion of chronic atrial fibrillation. Circulation 1992;86:1415–20.
7. Cooper RAS, Alferness CA, Smith WM, Ideker RA. Internal cardioversion of atrial fibrillation in the sheep. Circulation 1993;87:1673–86.
8. Wharton JM, Johnson EE. Catheter based atrial defibrillation. PACE Pacing Clin Electrophysiol 1994;17:1058–66.
9. Alt E, Schmitt C, Ammer R, et al. Initial experience with intracardiac atrial defibrillation in patients with chronic atrial fibrillation. PACE Pacing Clin Electrophysiol 1994;17:1067–78.
10. Murgatroyd F, Slade AKB, Sopher M, Rowland E, Ward DE, Camm AJ. Efficacy and tolerability of low energy cardioversion of paroxysmal atrial fibrillation in humans. J Am Coll Cardiol 1995;25:1347–53.

11. Lown B. Electrical reversion of cardiac arrhythmias. Br Heart J 1967;26: 469–89.
12. Ferris LP, King BG, Spence PW, Williams HB. Effect of electric shock on the heart. Elect Eng NY 1936;55:498–515.
13. Wiggers CJ, Wegria R. Ventricular fibrillation due to single localized induction and condenser shocks applied during the vulnerable phase of ventricular systole. Am J Physiol 1940;128:500–5.
14. Ayers GM, Alferness CA, Ilina M, et al. Ventricular proarrhythmic effects of ventricular cycle length and shock strength in a sheep model of transvenous atrial defibrillation. Circulation 1994;89:413–22.
15. Vassalo JA, Cassidy DM, Kindwall KE, Marchlinski FE, Josephson ME. Nonuniform recovery of excitability in the left ventricle. Circulation 1988; 78:1365–72.
16. Janse MJ, van der Steen ABM, van Dam R, Durrer D. Refractory period of the dog's ventricular myocardium following sudden changes in frequency. Circ Res 1969;24:251–62.
17. Denker S, Lehmann MH, Mahmud R, Gilbert C, Akhtar M. Facilitation of macroreentry within the His-Purkinje system with abrupt changes in cycle length. Circulation 1984;69:26–32.
18. Denker S, Lehmann M, Mahmud R, Gilbert C, Akhtar M. Facilitation of ventricular tachycardia induction with abrupt changes in ventricular cycle lengths. Am J Cardiol 1984;53:508–15.
19. Gomes JA, Alexopoulos D, Winters SL, Deshmukh P, Fuster V, Suh K. The role of silent ischemia, the arrhythmic substrate and the short-long sequence in the genesis of sudden cardiac death. J Am Coll Cardiol 1989;14:1618–25.
20. El-Sherif N, Gough WB, Restivo M. Reentrant ventricular rhythms in which a short-long-short cardiac sequence facilitates the induction of reentry. Circulation 1991;83:268–78.
21. Wells JL Jr, Karp RB, Kouchoukos NT, MacLean WA, James TN, Waldo AL. Characterization of atrial fibrillation in man: studies following open heart surgery. PACE Pacing Clin Electrophysiol 1978;1:426–33.
22. Kirchhof C, Chorro F, Scheffer GJ, et al. Regional entrainment of atrial fibrillation studied by high resolution mapping in open-chest dogs. Circulation 1993;88:736–49.
23. Slocum J, Sahakian A, Swiryn S. Computer discrimination of atrial fibrillation and regular atrial rhythms form intra-atrial electrograms. PACE Pacing Clin Electrophysiol 1988;11:610–21.
24. Murgatroyd FD, Johnson EE, Cooper RA, et al. Safety of low energy transvenous atrial defibrillation—world experience [abstract]. Circulation 1994;90 Suppl I:I-14.
25. Saksena S, Krol RB, Varanasi S, Matthew P. Internal atrial defibrillation in symptomatic atrial flutter/fibrillation [abstract]. Circulation 1994;90 Suppl I:I-377.
26. Levy S, Camm J. An implantable atrial defibrillator: an impossible dream? Circulation 1993;87:1673–86.
27. Elharrar V, Surawicz B. Cycle length effects on restitution of action potential duration in dog cardiac fibers. Am J Physiol 1983;244:H782–H92.
28. Adams JM, Ayers GM, Infinger KR, Bocek JM, White HG, Alferness CA. Preceding ventricular interval: a programmed criterion for an implantable atrial defibrillator [abstract]. Am Heart J 1994;128:636.
29. Chorro FJ, Kirchhof CJ, Brugada J, Allessie JA. Ventricular response during irregular atrial pacing and atrial fibrillation. Am J Physiol 1990;259:H1015–H21.
30. Ayers GM, Ilina MI, Wagner DO, Sirokman WA, Griffin JC, Alferness CA. Right atrial electrode location for transvenous atrial defibrillation [abstract]. J Am Coll Cardiol 1994;23:125A.