Review

Transvenous Atrial Defibrillation—Techniques and Clinical Applications

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Summary: Atrial fibrillation (AF) is the most common arrhythmia requiring treatment. The most desirable therapy may be restoration and maintenance of sinus rhythm. Limitations of the current methods for cardioversion of AF have prompted the development of transvenous atrial defibrillation (TADF) as an alternative and more effective technique for converting AF. Recent advances in the technique of TADF, particularly in the design and configuration of the electrodes, and the use of an optimal biphasic shock waveform have dramatically improved the efficacy of TADF for the termination of all types of AF. The reduction in voltage and energy requirements for cardioversion by TADF may allow the procedure to be performed with little or no sedation and the risk of general anesthesia may be avoided. Both experimental and clinical studies have demonstrated the feasibility, safety, and efficacy of using TADF as a new temporary or “permanent” mode of electrical therapy for AF. It has several potential applications, from acute termination of AF in the electrophysiology laboratory and in patients who have failed to respond to external cardioversion, to its use as an implantable device for treating recurrent AF. This article reviews the current technique and clinical applications of TADF for treatment of AF.

Key words: atrial fibrillation, transvenous atrial defibrillation

Introduction

Atrial fibrillation (AF) is the most common arrhythmia encountered in clinical practice, accounting for a substantial morbidity and resource consumption.^{1–4} Restoration of normal sinus rhythm may be the preferred goal of therapy when treating patients with persistent AF, as it should eliminate symptoms, improve exercise capacity, reduce thromboembolic complications, and may potentially improve survival.^{5–7} Furthermore, recent experimental studies by Wijffels *et al.* have demonstrated that AF itself alters the electrophysiologic properties of the atrium which facilitate the initiation and maintenance of AF (AF begets AF).⁸ This process appears to be reversible and supports the notion that early cardioversion of AF episodes may ultimately prevent further arrhythmia recurrence.

However, the established methods for converting AF to sinus rhythm have shortcomings. Antiarrhythmic therapy is effective for converting AF of short duration but has limited efficacy for long-lasting AF and is associated with proarrhythmic risk.^{9–13} External cardioversion of AF using high-voltage DC shocks delivered between skin paddle electrodes was first described by Lown in 1962¹⁴ and is still the standard technique for restoring sinus rhythm. It is effective in approximately 70–95% of patients with AF (depending on patient selection) and is associated with minimal risk.^{14, 15} However, the high-energy shocks, in the range of 100 to 360 joules (J), can be detrimental to the heart^{16–18} and are painful to conscious patients. Thus, external electrical cardioversion usually requires general anesthesia. Furthermore, this method is not always successful and is not suitable for patients when AF subsequently recurs: the concept of repeated defibrillation in an outpatient setting under general anesthesia is unsatisfactory. As a result, various invasive approaches using epicardial or endocardial electrodes have been used in an attempt to increase the efficacy of cardioversion by delivering energy closer to the atrial myocardium. A technique that substantially reduces the atrial defibrillation threshold would enable cardioversion to be achieved without the need for general anesthesia and could be applied to patients in whom conventional transthoracic cardioversion has failed. Furthermore, this would open the door to the development of an implantable atrial defibrillator for patients with recurrent AF. Recent animal^{19–22} and human^{23–31} studies have demonstrated the safety

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and efficacy of low-energy transvenous atrial defibrillation (TADF). It is the purpose of this article to review the techniques and clinical applications of TADF.

Techniques of Transvenous Atrial Defibrillation

During the last two decades, many experimental and clinical studies have been performed and have refined the techniques of TADF. Early attempts at TADF using conventional intracavitary electrodes were disappointing. However, recent advances in the development of specific catheters for defibrillation and the use of different shock waveforms have prompted a reevaluation of this technique. To perform TADF safely and to reduce its energy requirement, several important technical considerations relating to the defibrillation electrodes, the pulse characteristics, and the timing of atrial shock delivery should be taken into account.

Defibrillation Electrode

Electrode configuration: The feasibility of TADF was first described by Jain *et al.* in 1970, using a single endocardial right atrial lead with an external electrode on the chest wall in animals and humans.³² In 1974, Mirowski *et al.* reported their preliminary results of TADF using an acetylcholine-induced AF model.³³ Subsequent studies by Levy *et al.*²³ and Kumagai *et al.*²⁴ have reproduced these initial results, each in 10 patients who were resistant to pharmacologic or transthoracic cardioversion. In a multicenter, randomized study, in which this technique was compared with conventional external cardioversion in 112 patients, TADF achieved a 91% success rate of restoration of sinus rhythm compared with a 67% rate using conventional external cardioversion.²⁵ Therefore, by increasing the intracardiac current density, the use of one endocardial electrode in combination with an external electrode has achieved a greater efficacy than the conventional external transthoracic technique, but high energies (200–300 J) were still required.

Subsequently, several investigators^{19, 20} undertook animal testing of TADF using endocardial electrodes confined to the right atrium. These studies demonstrated the feasibility and the greater efficacy of TADF using a bipolar right atrial configuration over conventional external cardioversion. However, early clinical studies by Hartzler and Kallock and Nathan *et al.* using this electrode configuration were less successful.^{34, 35} It is unlikely that the placement of both electrodes in the right atrium would incorporate sufficient atrial myocardium, especially the left atrium, for effective defibrillation. Cooper *et al.*²² conducted a comprehensive study to evaluate multiple waveforms and electrode/lead configurations for TADF using a pacing-induced model of AF in sheep. In this study, four right atrial electrodes (superior vena cava, right atrial appendage, mid- and low right atrium) and three left atrial positions (coronary sinus, left pulmonary artery, and a left axillary subcutaneous patch) were examined. The efficacy of TADF using electrode configurations confined to the right atrium were compared with those involving the right and left atrium. The lowest defibrillation thresholds were obtained using a right-left atrial electrode con-

figuration, with the best results from an electrode pair in the right atrium and the coronary sinus.

Following the findings of Cooper *et al.*,²² several centers have investigated the use of biatrial shocks for TADF in patients with paroxysmal and chronic AF.^{26–31} These studies have demonstrated the superior efficacy of TADF by using shock vectors to encompass both the right and left (via coronary sinus or pulmonary artery) atria. The energy requirement for TADF is in the range of 2–6 J and is only ~ 2 to 5% of the energy required for transthoracic defibrillation^{11, 14, 15} and ~ 2% of the energy requirement in those early investigations that used an intracardiac defibrillation catheter and an external patch.^{23–25} Only a few clinical studies have compared different transvenous lead configurations for TADF in human. Both the data from Desai *et al.*³⁶ and Saksena *et al.*²⁸ suggest that a right atrium to coronary sinus vector may be associated with the lowest threshold. Furthermore, patients with chronic AF are associated with a higher defibrillation threshold.^{27, 28, 31, 37}

Electrode location: In addition to the shock vector, the location of the electrodes within the right atrium and coronary sinus may also affect the efficacy of TADF. Ayers *et al.* demonstrated that the atrial defibrillation threshold may be further reduced by positioning the electrodes in various locations within the great cardiac vein³⁸ and in the right atrium.³⁹ A recent clinical study by Lok *et al.*⁴⁰ suggested that high right atrial appendage together with a distal coronary sinus electrode location is associated with a lower atrial defibrillation threshold than an anterolateral right atrial electrode. Furthermore, the location of electrodes may also affect the incidence of post-shock conduction disturbances. Cooper *et al.*²² found that sinoatrial block only occurred during shocks administered between the superior vena cava and the right atrial appendage leads, while atrioventricular block only occurred with either the low or middle right atrium to coronary sinus electrode system. It appears that electrode locations that result in high electrical potential gradients near the sinoatrial and atrioventricular node may cause postshock conduction disturbance.

Electrode length: Previous studies^{19, 22} suggested that larger surface areas of defibrillation electrodes were associated with lower defibrillation thresholds in animal models. Subsequent studies in animals⁴¹ and humans⁴² have demonstrated that a shorter electrode length (< 3 cm) increased defibrillation threshold. Theoretically, a longer electrode length with a larger surface area could lower defibrillation threshold by generating a larger and more homogeneous electrical field within the atria and reduce the shock impedance to increase the current flow. However, both animal⁴³ and human⁴⁴ studies failed to demonstrate that the use of longer electrodes (> 6 cm) in the right atrium and coronary sinus lower the defibrillation threshold. This might have occurred because the electrodes were too long and too close together, resulting in shunting of current flow away from the myocardium. Furthermore, leads with longer electrodes are more difficult to build, have a larger diameter, and are more difficult to position in optimal locations. Thus, it appears that defibrillation electrodes of about 6 cm for both right atrium and coronary sinus allow optimal TADF in humans.

Pulse Characteristics

Shock waveforms: The shock waveforms and pulse durations have significant impact on the efficacy of transvenous defibrillation in the atrium. Biphasic waveforms consisting of two phases of opposite polarity decrease the shock strength required for TADF compared with equal duration monophasic waveforms in animals²² and humans.⁴⁵⁻⁴⁸ Johnson *et al.*⁴⁵ compared a biphasic with a monophasic waveform of the same pulse duration and found that 3/3 ms biphasic waveform had a significantly lower atrial defibrillation threshold than a 6 ms monophasic waveform. A subsequent study by Cooper *et al.*⁴⁸ confirmed the superior efficacy of biphasic waveform compared with monophasic waveforms of the same total pulse duration. Furthermore, they found that for symmetrical biphasic waveforms, shorter (3 ms) and longer (12 ms) total pulse durations were associated with higher threshold voltages than were 6 ms waveforms.

Characteristics of biphasic waveforms: Although biphasic waveforms have been shown to be superior to monophasic waveforms, the characteristics of the biphasic waveforms may also affect their efficacy for TADF. Tomassoni *et al.*⁴⁹ and Sra *et al.*⁵⁰ demonstrated that the efficacy of TADF can be improved by using biphasic waveforms with 50% tilt in both phases, although the optimal biphasic waveform tilt modification in each individual patient is different. Cooper *et al.*⁴⁸ have shown that for the same total pulse duration of 10 ms, an asymmetrical biphasic waveform with the second phase shorter than the first (7.5/2.5 ms) was more efficacious than pulses that were symmetrical biphasic (5/5 ms) or asymmetrical biphasic, with the second phase longer than the first (2.5/7.5 ms). Furthermore, recent animal studies⁵¹ suggest that reducing the peak leading edge shock voltage and its rate of rise (waveform rounding) could further reduce the atrial defibrillation threshold. Although the optimal biphasic waveform for TADF is not yet known, it is clear that defibrillation efficacy may be improved by optimizing waveform characteristics.

Sequential and dual current pathways defibrillation: Animals mapping studies have demonstrated that the site of earliest atrial activation after unsuccessful TADF is dependent on the electrode location.⁵² After unsuccessful TADF, earliest atrial activations are located in areas in which the potential gradient field created by the shock is predicted to be low. Based on these findings, Cooper *et al.* examined the efficacy of TADF by using dual current defibrillation pathways with sequential shock in animals⁵³ and humans.⁵⁴ The dual electrode configurations were designed to use a second shock and current pathway that encompassed the area of the atria in which the potential gradient field was predicted to be low after a single current shock delivered from the right atrial appendage and distal coronary sinus. Both animal⁵³ and human⁵⁴ studies have demonstrated that the use of a second sequential shock delivered between the proximal coronary sinus and left subclavian vein reduces the atrial defibrillation energy requirement by >50% compared with single current pathway of right atrial appendage to distal coronary sinus. Clinical application of a dual current pathway is limited by the increased lead complexity.

Timing of Atrial Shock Delivery

Accurate timing of atrial shock delivery is critical for the safety of performing TADF. The proarrhythmic potential of an atrial shock for TADF has been well documented in animal^{19,21} and human³⁰ studies. In most instances, the ventricular proarrhythmic episodes resulted from shocks that were not synchronized with the R wave. These findings emphasize the importance of achieving reliable R-wave synchronization for shock delivery. However, optimal R-wave synchronization alone may not be sufficient to prevent the ventricular proarrhythmia. R-wave synchronized shocks can result in ventricular arrhythmias if delivered during the ventricular vulnerability period. The ventricular vulnerability period is affected by the preceding cycle length and rhythm. The proarrhythmic risk was higher with shocks delivery after a short preceding R-R interval as the second R wave may occur simultaneously with the terminal portion of the preceding T wave. Previous studies^{55,56} found that even properly R wave-synchronized shocks could induce ventricular arrhythmias when the preceding RR interval during ventricular pacing was <300 ms.

Recent studies^{57,58} showed that during atrial pacing, the conduction delay occurring in the atrioventricular node and the His-Purkinje system could prevent the terminal portion of the T wave of the preceding QRS complex from encroaching on the R wave, and that this reduced the risk of induction of ventricular arrhythmias by R wave-synchronized shocks. However, in the presence of bundle-branch block or during ventricular pacing, atrial shocks should not be synchronized to an R wave with a preceding R-R interval of <380 ms, as this protection is no longer sufficient to prevent proarrhythmia.⁵⁸ Furthermore, the occurrence of a preceding long-short cycle length sequence was also associated with a higher risk of ventricular proarrhythmia because of an increase in the dispersion of ventricular refractoriness that results from this sequence.^{54,56} Thus, delivery of an atrial shock to an R wave with a preceding long-short sequence should be avoided and this can be accomplished by preventing shock delivery when there is a large difference in the cycle length of the preceding rhythm.

Clinical Applications of Transvenous Atrial Defibrillation

Efficacy

Transvenous atrial defibrillation can be achieved with remarkably low energy using biphasic waveform shocks delivered between transvenous defibrillation catheter/electrodes positioned to provide a shock vector that encompasses both the left and right atria (Fig. 1). The efficacy of TADF using a biphasic waveform and a biatrial shock has been examined in patients with paroxysmal and persistent AF.²⁶⁻³¹ Alt *et al.*²⁶ reported their initial experience with TADF using a right atrial to pulmonary artery electrode vector in 13 patients with persistent AF; 10 patients were successfully cardioverted with a mean energy of 3.7 J. Murgatroyd *et al.*²⁷ performed TADF

FIG. 1 Twelve-lead electrocardiogram recording of a successful transvenous atrial defibrillation. After delivery of a 340 V (3.2 J) biatrial shock, atrial fibrillation is converted immediately to sinus rhythm.

by using 3/3 ms biphasic, biatrial shocks in 19 patients with short duration of AF; atrial fibrillation was spontaneous in only 4 of these patients and AF was electrically induced in the remaining 15 patients. In this study, AF was terminated in all patients by using TADF with a leading-edge voltage ranging from 140–340 V (0.7–4.4 J). By using the same technique, several investigators^{30, 31, 36} have shown a successful rate of TADF in 78–92% of patients with spontaneous AF episodes of short duration (< 7 days), with a mean leading-edge voltage ranging from 223–272 V (1.8–2.8 J). Subsequent studies by other investigators^{29–31} have demonstrated a 70–89% TADF efficacy rate using a mean leading edge voltage ranging from 297–317 V (3.3–3.7 J) in patients with long established AF. Although the reported success rate of TADF in patients with paroxysmal AF and established AF was similar, the leading edge voltage and energy requirements were significantly higher with persistent than with paroxysmal AF.^{30, 31, 37} Although there is no study directly comparing the efficacy of external cardioversion with TADF using biphasic, biatrial shock, Schmitt *et al.*⁵⁹ demonstrated that TADF was successful in up to 90% of patients who had failed external cardioversion. These results suggest that TADF is more efficacious than external cardioversion and is a feasible approach in those who have failed external cardioversion.

Safety

The major concern in applying TADF for cardioversion of AF is the potential risk of provoking life-threatening ventricular arrhythmias. Although previous studies have suggested that the right atrium to coronary sinus electrodes configuration could minimize the inclusion of ventricular myocardium within the defibrillation field,⁶⁰ ventricular fibrillation can still be induced by a very low-energy atrial defibrillation shock deliv-

ered during the ventricular vulnerable period.⁶¹ Thus, as discussed before, the timing of atrial shock delivery is critical to their safety. Previous animal studies^{55, 57, 58} have demonstrated that biatrial shocks should be safe if synchronized to the R wave, delivered after a minimum RR interval (at least 300 ms), and not preceded by a long-short sequence. During clinical application, a minimum R-R interval of 500 ms was suggested to allow a safety margin.

The data from a multicenter registry on the safety of biatrial shock have confirmed these findings.⁶² No proarrhythmias have been observed from more than 3000 biatrial, synchronized shocks delivered between the right atrium and coronary sinus. Nevertheless, unsynchronized shocks delivered between the right atrium and the coronary sinus or high-energy synchronized shocks delivered between the right atrium and the pulmonary artery have triggered ventricular proarrhythmia. A recent study⁶³ in patients with a history of ventricular tachycardia and left ventricular dysfunction has demonstrated that the risk of proarrhythmia is low from an R wave-synchronized atrial defibrillation shock delivered during narrow complex rhythm. Furthermore, the registry has shown that a higher energy (> 4 J) biatrial shock can depress the function of sinus and atrioventricular nodes, causing slowing of ventricular rate during AF and sinus pause before the resumption of sinus rhythm after successful cardioversion.⁶² Thus, backup pacing should be available during the procedure.

Tolerability

As the energies required for biatrial TADF are directly applied to the heart rather than passing through the thoracic cage, the atrial defibrillation thresholds are considerably lower than those for conventional external cardioversion. Therefore, patient tolerability and acceptance of therapy might improve

since general anesthesia is no longer needed and postconversion morbidity is reduced. Unfortunately, atrial defibrillation shocks, even at a lower energy, are far from imperceptible. Zipes *et al.* reported that in patients fitted with an implantable defibrillator for ventricular tachycardia, shocks of an intensity of <0.5 J were generally well tolerated while shocks of >0.5 J were less well tolerated.⁶⁴ In contrast, a recent study by Steinhilber *et al.*⁶⁵ demonstrated that patients perceived no difference in discomfort between shocks of 0.4 J and 2 J. Although the mechanism of shock-related discomfort remains unclear, it is probably related to a variety of factors, including the defibrillation threshold, stimulation of nerve fibers, contraction of skeletal muscle, and psychological components.⁶⁶

In clinical studies^{27, 28} where a step-up protocol with increasing defibrillation energy was used, the degree of discomfort increased steadily with the shock strength in all patients. On the other hand, there is a wide difference in the reported discomfort threshold values at which patients requested sedation before further shock delivery. These differences may be related to the number of delivered shocks and starting intensity of shocks. For example, in one study²⁷ that started TADF at 10 V, the atrial defibrillation threshold was above the tolerability threshold. In another study,²⁸ in which a clinically relevant shock intensity was used at the first shock (180 V), significantly more patients could be cardioverted without sedation (Fig. 2). It appears that the tolerability of atrial defibrillation shocks may be related more to the cumulative effect of shock delivery, that is, the total number of shocks delivered, than to the intensity of the individual shock. In fact, recent studies^{65, 67} have also demonstrated that patients perceived that the second delivered shock, independent of energy strength, was more uncomfortable than the first one. Thus, to improve patient tolerability to TADF, a starting shock level close to the defibrillation threshold to minimize the numbers of shocks delivered should be used in a shock delivery protocol.⁴⁰

Methods that can lower atrial defibrillation may have an impact on tolerability either directly or by ensuring defibrillation success with the minimum number of shocks. The use of concomitant antiarrhythmic agents such as sotalol,³⁷ different electrode locations,⁴⁰ and technological advances in defibrillation waveform^{48–54} can lower atrial defibrillation thresholds and may improve patient tolerability. As the shock-induced

discomfort is more likely related to shock voltage than energy,⁶⁶ methods that decrease peak voltage, such as the use of a larger capacitor to deliver biphasic shocks with longer pulse duration^{49, 68} and rounding of the leading and second edge of a defibrillation waveform⁵⁰ may increase the patient tolerability to TADF without impairing the efficacy. Psychological factors, such as mental preparation before the shock delivery and patient-perceived benefit from shock delivery, may also play a critical role with respect to patient tolerability. Finally, the use of rapidly absorbed and short-acting medication to relieve shock-related discomfort and anxiety prior to TADF may also increase patient acceptability of the TADF.⁶⁶

Early Reinitiation of Atrial Fibrillation after Transvenous Atrial Defibrillation

Recurrences of AF are commonly observed after successful cardioversion. Previous studies have reported that unstable sinus rhythm followed by AF recurrence occurred in 13–36% of patients shortly (within min) after successful electrical cardioversion, using either external or internal electrical cardioversion.^{69–72} These studies suggest that the occurrence of this phenomenon was not related to the previous arrhythmia duration and any of the clinical parameters (age, gender, left atrial size, left ventricular ejection fraction, defibrillation energy and voltage, and type of heart disease), was usually preceded by atrial premature beats with a short coupling interval, and occurred within the first mins after cardioversion. Recent study in patients with implantable atrial defibrillators also demonstrated that early reinitiation of AF occurred in half of them and was observed in 27% of treated AF episodes.⁷³ Therefore, suppression of early reinitiation of AF has an important implication for the use of temporary low-energy internal cardioversion and may necessitate more frequent therapy with an implantable atrial defibrillator. The mechanisms of spontaneous AF reinitiation after internal cardioversion seem to be heterogeneous and the optimal treatment remains unclear. The same studies^{69–72} have demonstrated that antiarrhythmic agents (class I or class III) may be useful in the prevention and acute suppression of spontaneous reinitiation of AF. In a subset of patients, AF may be reinitiated by atrial premature beats with a consistent coupling interval and similar P-wave morphology which suggests a focal source of AF. This type of focal AF may be amenable to radiofrequency ablation of the source of the atrial premature beats as shown in recent studies.⁷⁴ The potential role of atrial pacing in the prevention of early reinitiation of AF requires further evaluation.

Clinical Applications

Acute termination of atrial fibrillation: Temporary defibrillation catheters and an external device may be useful for acute termination AF (Fig. 3). Atrial fibrillation frequently complicates diagnostic electrophysiologic study or radiofrequency ablation procedures. Under these circumstances, cardioversion under general anesthesia or the use of antiarrhythmic agents may prolong and complicate the procedure. On the other hand, TADF can effectively terminate AF and allow

FIG. 2 Comparison of atrial defibrillation threshold (ADFT) and tolerability threshold in terms of leading edge voltage in the studies of Murgatroyd *et al.*²⁷ and Lok *et al.*²⁸ □ = ADFT, ■ = tolerability threshold.

FIG. 3 Posteroanterior (PA) fluoroscopic image of the position of defibrillation electrodes in the anterolateral right atrium (RA) and coronary sinus (CS). Two quadripolar catheters are positioned in the His position and at the right ventricular apex (RV) for recording intracardiac electrograms and for providing postshock ventricular backup pacing.

completion of the study or therapy. It may be used to treat patients with postoperative AF by using a temporary catheter. Alternatively, in those patients who underwent open heart surgery, temporary epicardial wires sutured to the pericardium may be used for postoperative pacing and atrial defibrillation.⁷⁵ Transvenous atrial defibrillation should also be considered in patients who fail external cardioversion⁵⁹ and in patients in whom general anesthesia may be hazardous, such as those with severe obstructive lung disease. However, the advantage of TADF is limited to a higher acute efficacy in terminating AF in that the probability of recurrence of AF appears to be identical whether AF is terminated using external or internal techniques.^{25, 26} Nevertheless, the use of TADF may result in an overall larger number of patients with successful cardioversion of AF and maintenance of sinus rhythm.

Implantable atrial defibrillator: The promising results achieved with TADF and the success of the implantable cardioverter defibrillator (ICD) for treatment of ventricular tachycardias and fibrillation (VT/VF) have prompted the development of an implantable atrial defibrillator. Two main concepts have been applied to the practical realization of an implantable atrial defibrillator: (1) the addition of atrial defibrillation as a feature of an ICD, that is, a dual-chamber (atrial and ventricular) defibrillator; and (2) the development of a stand-alone implantable atrial defibrillator.

Atrial fibrillation occurs frequently in patients with an ICD and is probably the most common cause of inappropriate discharges.⁷⁷ The incorporation of AF detection and defibrillation therapy as a subsidiary mode in an ICD appears to be desirable. Recent reports have shown that TADF can be ac-

complished using existing ICD electrode systems, but the required energy is of the order of 5–10 J for paroxysmal AF, and 10–20 J for chronic AF.^{28, 35, 78, 79} A dual-chamber ICD can provide backup ventricular defibrillation for VT/VF that might complicate AF therapy. However, the device is still biased toward the detection and therapy of VT/VF to prevent delay or failure to deliver appropriate therapy for VT/VF. The dual-chamber ICD may be more appropriate for use in patients with concomitant atrial and ventricular arrhythmias.

For patients without coexisting ventricular arrhythmias, a stand-alone implantable atrial defibrillator may be a feasible option.^{73, 80} The primary aims of an implantable atrial defibrillator are to relieve the patients' symptoms, improve their quality of life, and potentially alter the progressive natural history of the disease. Thus, the implantable atrial defibrillator is designed to provide a very specific and more conservative therapy to treat an often highly symptomatic, but not life-threatening arrhythmia. In comparing the implantable atrial defibrillator with the dual-chamber defibrillator, the potential advantage of a stand-alone implantable atrial defibrillator is its smaller size, lower cost, lesser complexity, and greater flexibility with regard to the use of electrode configurations. This advantage causes a decrease in device-related discomfort and an increase in patient acceptability of therapy. On the other hand, the efficacy of an implantable atrial defibrillator in accurate AF detection and R-wave synchronization for shock delivery is critically important with regard to the possible provocation of ventricular proarrhythmia by a device without backup ventricular defibrillation capability.⁸¹

Hybrid therapies: The application of TADF does not preclude the use of other modalities of treatment for AF. In fact, as AF is a heterogeneous disease, multiple complementary therapies are more likely to result in a satisfactory outcome. Concomitant use of antiarrhythmic agents may decrease the atrial defibrillation threshold³⁶ and prevent the early^{15, 69–71} or late recurrence^{9–11} of AF following cardioversion. Recent animal studies⁸² have suggested that linear radiofrequency ablation in the right atrium might reduce the incidence of AF and decrease the atrial defibrillation threshold. Another approach to facilitate TADF may be the use of rapid atrial pacing to entrain and organize AF before defibrillation. However, preliminary data have failed to demonstrate any beneficial effect of overdrive atrial pacing on atrial defibrillation threshold.⁸³ On the other hand, recent studies⁸⁴ have shown that single- or dual-site atrial pacing could prevent the recurrence of AF and may have an important application as an adjunct to the implantable atrial defibrillator for treatment of AF.

Conclusions

Recent advances in the technique of TADF, particularly in the design and configuration of the electrodes and the use of an optimal biphasic shock waveform, have dramatically improved the efficacy of TADF for the termination of all types of AF. Both experimental and clinical studies have demonstrated the superior efficacy of TADF over conventional external car-

dioversion. The reduction in voltage and energy requirements for cardioversion by TADF may allow the procedure to be performed with little or no sedation and the risk of general anesthesia may be avoided. Furthermore, TADF has proved to be safe so long as the shocks are correctly synchronized to the R wave and are delivered without a short preceding RR interval or long-short sequence. Further studies are underway to refine every aspect of the technique in order to optimize its efficacy, safety, and tolerability.

Several substantial clinical trials have indicated that TADF can be considered as a new temporary or "permanent" mode of electrical therapy for AF. It has several potential applications, from acute termination of AF in the electrophysiology laboratory and in patients who have failed to respond to external cardioversion, to its use as an implantable device for treating recurrent AF. The clinical role of the implantable atrial defibrillator for the treatment of patients with AF awaits further evaluation. The interaction of multiple hybrid therapies with TADF is likely to be a focus of intense future research.

References

- Kannel WB, Abbott RD, Savage DD, McNamara PM: Epidemiologic features of chronic atrial fibrillation: The Framingham study. *N Engl J Med* 1982;306:1018-1022
- Gajewski J, Singer RB: Mortality in an insured population with atrial fibrillation. *J Am Med Assoc* 1981;245:1540-1544
- Petersen P, Godtfredsen J: Atrial fibrillation: A review of course and prognosis. *Acta Med Scand* 1984;216:5-9
- Wolf PA, Mitchell JB, Baker CS, Kannel WB, D'Agostino RB: Impact of atrial fibrillation on mortality, stroke, and medical costs. *Arch Intern Med* 1998;158:229-234
- Grogan M, Smith HC, Gersh BJ, Wood DL: Left ventricular dysfunction due to atrial fibrillation in patients initially believed to have idiopathic dilated cardiomyopathy. *Am J Cardiol* 1992;69:1570-1573
- Petersen P, Madsen EB, Brun B, Pedersen F, Gyldensted C, Boysen G: Silent cerebral infarction in chronic atrial fibrillation. *Stroke* 1987;18:1098-1100
- Van Gelder IC, Crijns HJ, Blanksma PK, Landsman ML, Pasma JL, Van Den Berg MP, Meijler FL, Lie KI: Time course of hemodynamic changes and improvement of exercise tolerance after cardioversion in chronic atrial fibrillation unassociated with cardiac valve disease. *J Am Coll Cardiol* 1993;72:560-566
- Wijffels MC, Kirchhof CJ, Dorland R, Allesie MA: Atrial fibrillation begets atrial fibrillation: A study in awake chronically instrumented goats. *Circulation* 1995;92:1954-1968
- Zehender M, Hohnloser S, Muller B, Meinertz T, Just H: Effects of amiodarone versus quinidine and verapamil in patients with chronic atrial fibrillation: Results of a comparative study and a 2-year follow-up. *J Am Coll Cardiol* 1992;19:1054-1059
- Hohnloser SH, Van de Loo A, Baedeker F: Efficacy and proarrhythmic hazards of pharmacologic cardioversion of atrial fibrillation: Prospective comparison of sotalol versus quinidine. *J Am Coll Cardiol* 1995;26:852-858
- Tieleman RG, Gosselink AT, Crijns HJ, Van Den Berg MP, De Kam PJ, Van Gilst WH, Lie KI: Efficacy, safety, and determinants of conversion of atrial fibrillation and flutter with oral amiodarone. *Am J Cardiol* 1997;79:53-57
- Coplen SE, Antman EM, Berlin JA, Hewitt P, Chalmers TC: Efficacy and safety of quinidine therapy for maintenance of sinus rhythm after cardioversion. A meta-analysis of randomized control trial. *Circulation* 1990;82:1106-1116
- Maisel WH, Kuntz KM, Reimold SC, Lee TH, Antman EM, Friedman PL, Stevenson WG: Risk of initiating antiarrhythmic drug therapy for atrial fibrillation in patients admitted to a university hospital. *Ann Intern Med* 1997;127:281-284
- Lown B: Electrical cardioversion of cardiac arrhythmias. *Br Heart J* 1967;29:469-487
- Van Gelder IC, Crijns HJ, Van Gilst WH, Verwer R, Lie KI: Prediction of uneventful cardioversion and maintenance of sinus rhythm after direct-current electrical cardioversion of chronic atrial fibrillation and flutter. *Am J Cardiol* 1991;68:41-46
- Yabe S, Smith WM, Daubert JP, Wolf PD, Rollins DL, Ideker RE: Conduction disturbances caused by high current density electric fields. *Circ Res* 1990;66:1190-1203
- Pansegau DU, Abboud FM: Hemodynamic effects of ventricular defibrillation. *J Clin Invest* 1970;49:282-297
- Dahl CF, Ewy GA, Warner ED, Thomas ED: Myocardial necrosis from direct current countershock: Effect of paddle size and time interval between discharge. *Circulation* 1974;50:956-961
- Dunbar DN, Tobler HG, Fetter J, Gornick CC, Benson DJ, Benditt DG: Intracavity electrode catheter cardioversion of atrial tachyarrhythmias in the dog. *J Am Coll Cardiol* 1986;7:1015-1027
- Kumagai K, Yamanouchi Y, Tashiro N, Hiroki T, Arakawa K: Low energy synchronous transcatheter cardioversion of atrial flutter/fibrillation in dog. *J Am Coll Cardiol* 1990;16:497-501
- 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;20:707-711
- Cooper RAS, Alfemess CA, Smith WM, Ideker RE: Internal cardioversion of atrial fibrillation in sheep. *Circulation* 1993;87:1673-1686
- Levy S, Lacombe P, Cointe R, Bru P: High energy transcatheter cardioversion of chronic atrial fibrillation. *J Am Coll Cardiol* 1988;12:514-518
- Kumagai K, Yamanouchi Y, Hiroki T, Arakawa K: Effects of transcatheter cardioversion on chronic lone atrial fibrillation. *PACE* 1991;14:1571-1575
- Levy S, Lauribe P, Dolla E, Kou W, Kadish A, Calkins A, Paganelli F, Moyal C, Bremond M, Schork A: A randomized comparison of external and internal cardioversion of chronic atrial fibrillation. *Circulation* 1992;86:1415-1420
- Alt E, Schmitt C, Ammer R, Coenen M, Fotuhi P, Karch M, Blasini R: Initial experience with intracardiac atrial defibrillation in patients with chronic atrial fibrillation. *PACE* 1994;17:1067-1078
- Murgatroyd FD, Slade AKB, Sopher SM, Rowland E, Ward DE, Camm AJ: Efficacy and tolerability of low energy cardioversion of paroxysmal atrial fibrillation in humans. *J Am Coll Cardiol* 1995;25:1347-1353
- Saksena S, Prakash A, Mongeon L, Varanasi S, Kolettis T, Mathew P, De Groot P, Mehra R, Krol RB: Clinical efficacy and safety of atrial defibrillation using biphasic shocks and current nonthoracotomy endocardial lead configurations. *Am J Cardiol* 1995;76:913-921
- Lok NS, Lau CP, Ho DSW, Tang YW: Hemodynamic effects and clinical determinants of defibrillation threshold for low energy transvenous atrial defibrillation in patients with chronic atrial fibrillation. *PACE* 1997;20:899-908
- Levy S, Richard P, Lau CP, Lok NS, Camm AJ, Murgatroyd FD, Jordaens LJ, Kappenberger LJ, Brugada P, Ripley KL: Multicenter low energy transvenous atrial defibrillation (XAD) trial results in different subsets of atrial fibrillation. *J Am Coll Cardiol* 1997;27:750-755
- Levy S, Richard P, Gueunoun M, Yapo F, Trigano J, Mansouri C, Paganelli F: Low-energy cardioversion of spontaneous atrial fibrillation. Immediate and long term results. *Circulation* 1997;96:253-259
- 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;19:821-824

33. Mirowski M, Mower MM, Langer AA: Low energy catheter cardioversion of atrial tachyarrhythmias (abstr). *Clin Res* 1974;22:290
34. Hartzler GO, Kallock MJ: Low energy transvenous intracavitary cardioversion of tachycardias. In *Cardiac Pacing* (Eds. Steinbach K, Glogar D, Laszkovics A, Scheibelhofer W, Weber H), p. 853–858. Proceedings of the VIIth World Symposium on Cardiac Pacing. Darmstadt: Steinkopff, 1983
35. Nathan AW, Bexton RS, Spurrell RAJ, Camm AJ: Internal transvenous low energy cardioversion for the treatment of cardiac arrhythmias. *Br Heart J* 1984;52:377–384
36. Desai PK, Mongeon L, Conlon S, Casavant D, Moon R, Pacetti P, Marchese T, Haffajee C: Is energy for transvenous defibrillation with active pectoral can feasible? (abstr). *Circulation* 1994;90:I-376
37. Lau CP, Lok NS: A comparison of transvenous atrial defibrillation of acute and chronic atrial fibrillation and the effect of intravenous sotalol on human atrial defibrillation threshold. *PACE* 1997;20:1–11
38. Ayers GM, Iliina M, Wagner D, Kreyenhagen P, Bernard S, Alferness C: Cardiac vein electrode locations for transvenous atrial defibrillation (abstr). *J Am Coll Cardiol* 1993;21:306A
39. Ayers GM, Iliina M, Wagner DO, Sirokman WA, Griffin JC, Alferness CA: Right atrial electrode location for transvenous atrial defibrillation (abstr). *J Am Coll Cardiol* 1994;23:125A
40. Lok NS, Lau CP, Tse HF, Ayers GM: Clinical shock tolerability and effect of different right atrial electrode locations on efficacy of low energy human transvenous atrial defibrillation using an implantable lead system. *J Am Coll Cardiol* 1997;30:1324–1330
41. Ortiz J, Niwano S, Abe H, Gonzalez X, Ayers GM, Waldo AL: Transvenous atrial defibrillation in two canine models of atrial fibrillation (abstr). *J Am Coll Cardiol* 1994;23:125A
42. Hillsley RE, Yarger MD, Greenfield RA, Sorrentino RA, Wharton JM: Effect of catheter electrode length on internal atrial defibrillation thresholds in humans (abstr). *Circulation* 1995;92:I-473
43. Tacker WA, Schoenlein WE, Janas W, Ayers GM, Wagner DO: Catheter electrode evaluation for transvenous atrial defibrillation (abstr). *PACE* 1993;16:853
44. Timmermans C, Rodriguez LM, Ayers GM, Lambert H, Smeets J, Wellens HJ: Effect of electrode length on atrial defibrillation thresholds. *J Cardiovasc Electrophysiol* 1998;9:582–587
45. Johnson EE, Yarger MD, Wharton JM: Monophasic and biphasic waveforms for low-energy internal cardioversion of atrial fibrillation in human (abstr). *Circulation* 1993;88:I-592
46. Keane D, Sulke N, Cooke R, Jackson G, Sowton E: Endocardial cardioversion of atrial flutter and fibrillation (abstr). *PACE* 1993;16:928
47. Keane D, Boyd E, Anderson D, Robles A, Deverall P, Morris R, Jackson G, Sowton E: Comparison of biphasic versus monophasic waveforms in epicardial atrial defibrillation. *J Am Coll Cardiol* 1994;24:171–176
48. Cooper RAS, Johnson EE, Wharton JM: Internal atrial defibrillation in humans: Improved efficacy of biphasic waveforms and the importance of phase duration. *Circulation* 1997;95:1487–1496
49. Tomassoni G, Newby KH, Kearney MM, Brandon MJ, Natale A: Testing different biphasic waveforms and capacitances: Effect on atrial defibrillation threshold and pain perception. *J Am Coll Cardiol* 1996;28:695–699
50. Sra J, Bremner S, Krum D, Blanck Z, Deshpande S, Bieh M, Li H, Jazayeri MR, Akhtar M: The effect of biphasic waveforms tilt in transvenous atrial defibrillation. *PACE* 1997;20:1613–1618
51. Harbinson MT, Allen JD, Imam Z, Dempsey G, Anderson JM, Ayers GM, Adgey AA: Rounded biphasic waveform reduces energy requirements for transvenous catheter cardioversion of atrial fibrillation and flutter. *PACE* 1997;20:226–229
52. Cooper RAS, Smith WM, Ideker RE: Early activation sites after unsuccessful internal atrial defibrillation shock: The effect of electrode configuration (abstr). *PACE* 1996;19:706
53. Cooper RAS, Smith WM, Ideker RE: Internal cardioversion of atrial fibrillation: Marked reduction in defibrillation threshold with dual current pathways. *Circulation* 1997;96:2693–2700
54. Cooper RAS, Plumb VJ, Epstein AE, Kay GN, Ideker RE: Marked reduction in internal atrial defibrillation threshold with dual-current pathways and sequential shocks in human. *Circulation* 1998;97:2527–2535
55. Ayers GM, Alferness CA, Iliina MB, Wagner DO, Sirokman WA, Adams JM, Griffin JC: Ventricular proarrhythmic effects of ventricular cycle length and shock strength in a sheep model of transvenous atrial defibrillation. *Circulation* 1994;89:413–422
56. Barold HS, Wharton JM: Ventricular fibrillation resulting from synchronized internal atrial defibrillation in a patient with ventricular preexcitation. *J Cardiovasc Electrophysiol* 1997;8:436–440
57. Sokoloski MC, Ayers GM, Kumagai K, Khrestian CM, Niwano S, Waldo AL: Safety of transvenous atrial defibrillation: Studies in the canine sterile pericarditis model. *Circulation* 1997;96:1343–1350
58. Keelan ET, Krum D, Hare J, Mughal K, Li H, Akhtar M, Jazayeri MR: Safety of atrial defibrillation shocks synchronized to narrow and wide QRS complexes during atrial pacing protocols simulating atrial fibrillation in dogs. *Circulation* 1997;96:2022–2030
59. Schmitt C, Alt E, Plewan A, Ammer R, Leibig M, Karch M, Schomig A: Low energy intracardiac cardioversion after failed conventional external cardioversion of atrial fibrillation. *J Am Coll Cardiol* 1996;28:994–999
60. Min X, Mongeon L, Mehra R: Analysis of CS-RA, Can-RA, Can-RV and SVC-RV systems for atrial defibrillation by using finite element human thorax model and comparisons with the clinical studies (abstr). *PACE* 1996;19:696
61. Gray RA, Jalife J: Effects of atrial defibrillation shocks on the ventricles in isolated sheep hearts. *Circulation* 1998;97:1613–1622
62. Murgatroyd FD, Johnson EE, Cooper RA, Lau CP, Alt E, Kappenburger LJ, Smith JM, Camm AJ, Wharton JM: Safety of low energy transvenous atrial defibrillation: World experience (abstr). *Circulation* 1994;90:14
63. Simons GR, Newby KH, Kearney MM, Brandon MJ, Natale A: Safety of transvenous low energy cardioversion of atrial fibrillation in patients with history of ventricular tachycardia: Effects of rate and repolarization time on proarrhythmic risk. *PACE* 1998;21:430–437
64. Zipes DP, Jackman WM, Heger JJ, Chilson DA, Browne KF, Naccarelli GV, Rahilly GT Jr, Prystowsky EN: Clinical transvenous cardioversion of recurrent life-threatening ventricular tachyarrhythmias: Low energy synchronized cardioversion of ventricular tachycardia and termination of ventricular fibrillation in patients using a catheter electrode. *Am Heart J* 1982;103:789–794
65. Steinhilber DM, Cardinal D, Mongeon L, Mattson L, Waters M, Foley L, Corrigan S: Atrial fibrillation: Are low energy shocks acceptable to patients? (abstr). *PACE* 1996;19:625
66. Ayers GM: How can atrial defibrillation be made more tolerable? In *Nonpharmacological Management of Atrial Fibrillation* (Eds. Murgatroyd FD, Camm AJ), p. 474–487. Armonk, NY: Futura Publishing Co., 1997
67. Jung J, Heisel A, Fries R, Kollner V: Tolerability of internal low-energy shock strengths currently needed for endocardial atrial cardioversion. *Am J Cardiol* 1997;80:1489–1490
68. Ammer R, Alt E, Ayers G, Lehmann G, Schmitt C, Pasquantonio J, Putter K, Schmidt M, Schomig A: Pain threshold for low energy intracardiac cardioversion of atrial fibrillation with low or no sedation. *PACE* 1997;20:230–236
69. Bianconi L, Mennuni M, Lukic V, Castro A, Chieffi M, Santini M: Effects of oral propafenone administration before electrical cardioversion of chronic atrial fibrillation: A placebo-controlled study. *J Am Coll Cardiol* 1996;28:700–706
70. Tse HF, Lau CP, Lok NS: Early recurrence of atrial fibrillation after successful defibrillation in patients with chronic atrial fibrillation (abstr). *PACE* 1997;20:2305
71. Timmermans C, Rodriguez LM, Smeets JLRM, Wellens HJJ: Immediate reinitiation of atrial fibrillation following internal atrial defibrillation. *J Cardiovasc Electrophysiol* 1998;9:122–128

72. Sra J, Biehl M, Blanck Z, Dhala A, Jazayeri MR, Deshpande S, Akhtar M: Spontaneous reinitiation of atrial fibrillation following transvenous atrial defibrillation. *PACE* 1998;21:1105-1110
73. Wellens H, Lau CP, Lüderitz B, Akhtar M, Waldo AL, Camm AJ, Timmermans C, Tse HF, Jung W, Jordaens L, Ayers G: Atrioverter, an implantable device for the treatment of atrial fibrillation. *Circulation* 1998;98:1651-1656
74. Lau CP, Tse HF, Ayers GM: Defibrillation-guided radiofrequency ablation of atrial fibrillation secondary to an atrial focus. *J Am Coll Cardiol* 1999;33:1217-1226
75. Ortiz J, Sokoloski MC, Ayers GM, Cmolik BL, Niwano S, Geha AS, Waldo AL: Atrial defibrillation using temporary epicardial defibrillation stainless steel wire electrodes: Studies in canine sterile pericarditis model. *J Am Coll Cardiol* 1995;26:1356-1364
76. Alt E, Ammer R, Lehmann G, Ayers GM, Pasqantonio J, Schomig A: Patient characteristics and underlying heart disease as predictors of recurrent atrial fibrillation after internal and external cardioversion in patients treated with sotalol. *Am Heart J* 1997;134:419-425
77. Pinski SL, Fahy GJ: The proarrhythmic potential of implantable cardioverter-defibrillators. *Circulation* 1995;92:1651-1664
78. Chung MK, Niebauer BL, Wilkoff BL, Jaeger FJ, Kidwell GA, Morant VA, Tchou PJ: Internal cardioversion of atrial fibrillation using standard ventricular implantable cardioverter-defibrillators (abstr). *J Am Coll Cardiol* 1998;31:38A
79. Heisel A, Jung J, Fries R, Schieffer H: Influence of active pectoral can on transvenous atrial cardioversion threshold in patients with implantable cardioverter-defibrillators (abstr). *J Am Coll Cardiol* 1998;31:38A
80. Lau CP, Tse HF, Lok NS, Lee KL, Ho DS, Sopher M, Murgatroyd F, Camm AJ: Initial clinical experience with an implantable human atrial defibrillator. *PACE* 1997;20:220-225
81. Tse HF, Lau CP, Sra JS, Crijns HJ, Edvardsson N, Kacet S, Wyse DG: Atrial fibrillation detection and R-wave synchronization by Metrix implantable atrial defibrillator: Implications for long term efficacy and safety. *Circulation* 1999;99:1446-1451
82. Kalman JM, Olgin JE, Karch MR, Steiner PR, Stillson C, Chin MC, Lesh MD: Effect of right atrial linear lesions on atrial defibrillation threshold: Implications for 'hybrid therapy' (abstr). *PACE* 1996;19:625
83. Darpo B, Ayers GM, Bergfeldt L, Linde C, Johansson K, Rosenqvist M: Overdrive pacing does not lower atrial defibrillation threshold in patients with atrial fibrillation (abstr). *PACE* 1998;21:812
84. Delfaut P, Saksena S, Prakash A, Krol RB: Long term outcome of patients with drug refractory atrial flutter and fibrillation after single and dual site right atrial pacing for arrhythmia prevention. *J Am Coll Cardiol* 1998;32:1900-1908