Conclusions—With the Atrioverter, prompt and safe restoration of sinus rhythm is possible in patients with recurrent atrial fibrillation. The atrial defibrillation threshold had to be ≤240 V during preimplant testing. Atrial fibrillation detection, R-wave shock synchronization, and defibrillation threshold were tested at implantation and during follow-up. Shock termination of spontaneous episodes of atrial fibrillation was performed under physician observation. Results are given after a minimum of 3 months of follow-up. During a follow-up of 72 to 613 days (mean, 259±138 days), 96% of 227 spontaneous episodes of atrial fibrillation in 41 patients were successfully converted to sinus rhythm by the Atrioverter. In 27% of episodes, several shocks were required because of early recurrence of atrial fibrillation. Shocks did not induce ventricular arrhythmias. Most patients received antiarrhythmic medication during follow-up. In 4 patients, the Atrioverter was removed: in 1 because of infection, in 1 because of cardiac tamponade, and in 1 because of frequent episodes of atrial fibrillation requiring His bundle ablation.

Methods and Results—The study included 51 patients with recurrent atrial fibrillation who had not responded to antiarrhythmic drugs, were in New York Heart Association Heart failure class I or II, and were at low risk for ventricular arrhythmias. The atrial defibrillation threshold had to be ≤240 V during preimplant testing. Atrial fibrillation detection, R-wave shock synchronization, and defibrillation threshold were tested at implantation and during follow-up. Shock termination of spontaneous episodes of atrial fibrillation was performed under physician observation. Results are given after a minimum of 3 months of follow-up. During a follow-up of 72 to 613 days (mean, 259±138 days), 96% of 227 spontaneous episodes of atrial fibrillation in 41 patients were successfully converted to sinus rhythm by the Atrioverter. In 27% of episodes, several shocks were required because of early recurrence of atrial fibrillation. Shocks did not induce ventricular arrhythmias. Most patients received antiarrhythmic medication during follow-up. In 4 patients, the Atrioverter was removed: in 1 because of infection, in 1 because of cardiac tamponade, and in 1 because of frequent episodes of atrial fibrillation requiring His bundle ablation.

Conclusions—With the Atrioverter, prompt and safe restoration of sinus rhythm is possible in patients with recurrent atrial fibrillation. (Circulation. 1998;98:1651-1656.)

Key Words: atrial fibrillation • atrial defibrillation • atrium

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia1 with hemodynamic, thromboembolic, and health and economic consequences. Usually, restoration of sinus rhythm is attempted by pharmacological or electrical therapy.2,3 In chronic AF, therapy is directed toward maintenance of an acceptable ventricular rate and prevention of thromboembolic complications with anticoagulant therapy. When ventricular rate control cannot be obtained by medication, interruption or modification of AV conduction with or without ventricular pacing can be performed.4,5 The concept that multiple atrial reentrant wavelets are present6,7 in AF resulted in the approach to divide the atria into several segments, either surgically (the MAZE operation) or by a catheter.8,9 In most patients with AF, other cardiovascular disease is present, affecting the consequences of the arrhythmia and the selection of therapy.

In the goat model,10 persistent AF results in electrophysiological changes in the atrium that favor maintenance of fibrillation and early recurrence after successful conversion. Therefore, to shorten the episode of AF as much as possible seems important to prevent recurrence of AF after conversion to sinus rhythm. This article describes the initial results with an implantable device (the METRIX Atrioverter) that allows rapid and successful conversion of AF by low-energy intracardiac shocks. The objective of our study was to evaluate the safety and efficacy of this new therapy.

Methods

Patients

We enrolled 51 patients from 19 centers in 9 different countries in this study. They had had prior episodes of AF that had spontaneously terminated or been converted to normal sinus rhythm with intervals of recurrence of AF episodes between 1 week and 3 months. Treatment with at least 1 class I or III antiarrhythmic drug was ineffective or only partially effective, resulting in arrhythmia recurrences, or not tolerated because of side effects. Exclusion criteria are given in Table 1. The 51 patients underwent clinical evaluation, including history and physical examination, 12-lead ECG, chest
TABLE 1. Exclusion Criteria for Atrial Defibrillator Implant

<table>
<thead>
<tr>
<th>Exclusion Criteria</th>
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<tbody>
<tr>
<td>Implanted heart valve</td>
</tr>
<tr>
<td>AF of reversible cause (eg, after cardiac surgery, hyperthyroidism)</td>
</tr>
<tr>
<td>Wolff-Parkinson-White syndrome</td>
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<tr>
<td>Myocardial infarction or myocardial revascularization ≤year</td>
</tr>
<tr>
<td>Active angina or cardiac ischemia</td>
</tr>
<tr>
<td>History of left atrial thromboembolic events</td>
</tr>
<tr>
<td>Congestive heart failure</td>
</tr>
<tr>
<td>ECG documentation of sustained or nonsustained ventricular tachycardia (&gt;3 consecutive beats)</td>
</tr>
<tr>
<td>Defibrillation level &gt;240 V at inclusion testing procedure</td>
</tr>
</tbody>
</table>

radiography, echocardiography, and laboratory tests. The protocol received approval from the ethics committee or institutional review board of each participating center. Informed consent was obtained from each patient.

The Device
The InControl METRIX Atrioverter system consists of an implantable atrial defibrillator (model 3000 or 3020) connected to right atrial (perimeter right atrial model 7205) and coronary sinus (perimeter coronary sinus model 7109) defibrillation leads and a bipolar endocardial ventricular pacing lead (Figure 1), a programmer, and a defibrillation systems analyzer. The defibrillator is a battery-powered, pectorally implanted device with a displacement of 53 cm² and a weight of 79 g (model 3000) or 82 g (model 3020). With specific algorithms, the device detects AF and delivers R-wave synchronous defibrillation shocks to convert AF to sinus rhythm. It is also able to pace the ventricle after shock delivery in case of bradycardia. Shocks can be delivered at a selected voltage, with a maximal intensity of 300 V. The model 3000 defibrillator has an 80-μF capacitor and can deliver a maximal shock of 3 J with a biphasic waveform of 3 ms/3 ms. The model 3020 defibrillator has a 160-μF capacitor with a maximal shock of 6 J with a biphasic waveform of 6 ms/6 ms. The device stores the intracardiac electrograms from the last 6 successfully terminated episodes of AF. Real-time telemetry of 3 simultaneous intracardiac electrograms can be obtained via the programmer. The device can be programmed in an automatic mode with automatic, periodic activation of the detection algorithm and shock delivery after a preset delay from onset of AF, or it can be used in a patient- or physician-activated mode in which the detection algorithm and shock therapy are initiated by placing a magnet over the Atrioverter. During this study, the device was programmed in the monitor mode, and shock therapy was delivered in hospital by a physician.

Study Protocol
Preimplant, Implant, and Postimplant Procedures
During the patient inclusion testing procedure, either temporary catheters or permanent leads were placed in the coronary sinus, right atrium, and right ventricle. Patients were sedated according to the normal clinical practice of each institution. Right ventricular pacing and sensing thresholds were obtained. All leads were connected to the defibrillation systems analyzer or model 3020 device fixture. Atrial signals were examined by performing the AF detection algorithm. After AF detection testing, the synchronization algorithm was tested. Synchronization markers were examined during sinus rhythm to ensure that the device was synchronizing properly with the ventricular depolarization. When proper synchronization was confirmed, the device was programmed to deliver shocks synchronized to the R wave during sinus rhythm to induce AF. If the device did not induce AF, rapid atrial pacing was used as an alternative induction method. The AF detection and synchronization tests were also performed during AF. To be eligible for implantation, 2 successes at 240 V had to be obtained during testing. This was later revised to allow 1 success out of 3 attempts at 260 V for model 3000 and 240 V for model 3020.

At implantation, permanent leads were placed in the coronary sinus, right atrium, and right ventricle. Right ventricular pacing and sensing thresholds were obtained. AF detection and R-wave synchronization were again assessed. Two of 4 successes at 240 V had to be attained at the final lead location. Atrial defibrillation threshold (ADFT) was estimated as follows. Starting with a 180-V shock, the shock intensity was increased in 20-V steps until successful defibrillation was achieved. After this initial success, AF was induced, and a shock 20 V less than the previously successful shock was given. Thereafter, the shock intensity was decreased in 20-V steps until a shock intensity was delivered that failed to convert the AF despite the delivery of 2 shocks at this intensity. Shocks were then delivered at 20-V steps of increasing intensity until AF was successfully converted with the delivery of 2 shocks at this intensity.

To implant the device, ADFT had to be ≤240 V. Automatic mode operation, which consisted of AF detection, capacitor charge, AF redetection, synchronization, shock delivery, postshock pacing (if needed), and AF detection, was also tested during the implant procedure.

Postimplant evaluation was performed at predischarge; at 1, 3, and 6 months; and at 6-month intervals thereafter until the completion of the study. AF detection and R-wave synchronization tests were performed at predischarge and at 1- and 3-month follow-ups. The defibrillation level was tested during the predischarge and at 1-month follow-up. Long-term ADFT testing was repeated at the 3-month follow-up. Follow-up with device interrogation was performed at 6 months and every 6 months thereafter. At those times, AF was induced during sinus rhythm by low-intensity shocks or by rapid atrial pacing by use of a separate catheter. AF was permitted to last for ≥5 minutes before test shocks were given.

During preimplant, implant, and postimplant shock delivery, cardiac rhythm was continuously recorded to document the possible induction of ventricular arrhythmias. The decision to use anticoagulant therapy in the preimplant, implant, and postimplant periods was left to the investigator, with protocol suggesting the use of anticoagulant therapy if the patient did not have the device.
Treatment for Spontaneous Episodes

When the patient sought treatment of a spontaneous episode, data pertaining to shock effectiveness were recorded. Clinical factors, such as antiarrhythmic medications and changes in system performance in case of lead position changes, were also recorded.

Results

After the first implant on October 31, 1995, 51 patients received the Atrioverter, and all patients had ≥3 months of postimplant follow-up as of July 4, 1997. These 51 patients were selected from 119 patients undergoing a screening testing procedure. Of 50 patients screened, 17 received the model 3000, and 34 of 69 screened patients received the model 3020. Of the failed screenings, 43 were due to high ADFT. The remaining patients did not proceed to implant because of either physician/patient decision or exclusions for enrollment. Patient demographics are given in Table 2. Two patients had a history of PTCA, and 2 patients had had CABG. All patients had been treated with ≥1 class I or III antiarrhythmic drug (average, 3.9 drugs) that had been discontinued, was not tolerated, or was only partially effective. The average duration of follow-up was 259 ± 138 days (≈8.6 months), with a median of 232 days (≈7.7 months).

Safety

A total of 3719 shocks were delivered: 3049 during testing and 670 for spontaneous episodes of AF. All shocks for spontaneous episodes were given during physician observation. There were no reported cases of induction of ventricular arrhythmias or inaccurately synchronized shocks during the study. Analysis of the AF detection algorithm performance during observed operations revealed a 100% specificity for the recognition of sinus rhythm (as opposed to AF) and 92.3% sensitivity for the detection of AF (as opposed to sinus rhythm). A total of 1062 tests of the detection algorithm were performed in sinus rhythm and 1178 in AF.

Efficacy

Treatment of Spontaneous Episodes

Forty-one patients had 231 episodes of AF for which they sought therapy (average, 5.6 episodes per patient; range, 1 to 26 episodes). Four episodes of AF occurred immediately before the time of threshold testing, and these episodes were used for clinical testing of the device. Because these episodes were not treated as spontaneous episodes but rather were used for this testing, they are excluded from further analysis and

![Image](https://example.com/image.png)

**Figure 2.** Example of early recurrence of AF after successful shock-induced conversion to sinus rhythm.

| TABLE 2. Profile of 51 Patients Studied |
|---|---|
| Sex | 40 men, 11 women |
| Age, y | 31–77 |
| Mean | 58 |
| Average number of AADs | 3.9 |
| LVEF,* % | 38–87 |
| Mean | 58±11 |
| LA size, cm | 3.3–6.6 |
| Mean | 4.4±0.8 |
| NYHA class, no. of patients | I 36, II 15 |

*AAD indicates antiarrhythmic drug; LVEF, left ventricular ejection fraction; and LA, left atrium.

*Measured during sinus rhythm.
ADFTs were measured at implantation and at the 3-month follow-up were in sinus rhythm at that time. Given. All 47 patients having their devices at the end of hospital, no Atrioverter treatment of these episodes was allowed to convert spontaneously at a later time. For 22 episodes in which stable sinus rhythm was eventually observed, 19 were chemically converted before additional shock delivery, and 1 was converted with external cardioversion after antiarrhythmic drug pretreatment.

Early recurrence of AF (ERAF) (Figure 2) was present during the treatment of 62 episodes (27% of all episodes) and seen in 21 of 41 patients (51%). ERAF was defined as the resumption of AF within 1 minute after a shock that resulted in sinus rhythm for ≥ 1 beat. This prevented restoration of persistent sinus rhythm for 26 of the episodes. Six episodes were chemically converted before additional shock delivery, 1 was converted with external defibrillation, and 19 were allowed to convert spontaneously at a later time. For 22 episodes in which stable sinus rhythm was eventually obtained, antiarrhythmic drugs were injected intravenously followed by repeated cardioversion. With ERAF taken into account, the overall clinical efficacy of the device was 86.3%.

One patient with frequent episodes (1 to 2 per week) and a drug-resistant rapid ventricular rate underwent His bundle ablation and permanent ventricular pacing. One patient had a failed conversion attempt before the 1-month follow-up and underwent successful lead repositioning with the next spontaneous episode and subsequent spontaneous episodes were successfully terminated with the device. Three patients had successful conversions early but experienced late failure. In 1 of these patients, spontaneous episodes were successfully converted after repositioning of the right atrial electrode. One patient had a high implant threshold, and 50% of the episodes could be converted after implantation.

Ten patients did not receive Atrioverter treatment for spontaneous episodes of AF. As shown by examination of the episodes log, 5 patients had no episodes of AF (follow-up duration, 58 to 354 days; mean, 164 ± 112 days). Five patients did have episodes of AF (1 patient had 1 episode, 1 had 2, 1 had 5, 1 had 6, and 1 had 15) during a follow-up of 52 to 382 days (mean, 177 ± 124 days). Because they did not go to a hospital, no Atrioverter treatment of these episodes was given. All 47 patients having their devices at the end of follow-up were in sinus rhythm at that time.

**AF Thresholds**
ADFTs were measured at implantation and at the 3-month follow-up. The data collected were the shock voltage and energy of 2 consecutive successes and 2 consecutive failures; the average of these 2 values was defined as the ADFT. As shown in Figure 3, ADFTs were slightly higher at 3 months for the 3000 model and slightly lower in the 3020 model, without reaching statistical significance.

**Antiarrhythmic Medication After Implantation**
All but 3 the patients who entered the study were on antiarrhythmic medication at the time of trial closure. At implantation, 27 patients were on D-L sotalol (18 patients) or amiodarone (9 patients). These numbers were 18 and 15 patients, respectively, at the end of the study.

**Shock Tolerability**
Use of sedation preceding shock delivery was left to the treating physician in conference with the patient. Marked variability in shock tolerance between patients was reported by the investigators. The interinstitutional variability in the level of sedation used made it impossible to address the shock tolerance issue in detail.

**Complications**
Two patients with the device implanted had subclavian venous thrombosis. One was treated successfully with urokinase. In the other patient, it was considered to be a chronic problem, and no intervention was performed. In 1 patient, a pericardial effusion developed a few hours after testing during the 1-month follow-up study. During the testing session, 19 shocks were delivered, 17 at low voltage for induction of AF and 2 for defibrillation. When the patient returned to hospital because of chest pain, shortness of breath, and hypotension, the echocardiogram revealed cardiac tamponade. At operation, perforation of the atrial wall by the right atrial electrode was found. The right atrial and right ventricular leads were extracted, and the right atrial perforation site was repaired. The coronary sinus lead and the Atrioverter were removed a few days later. The patient made an uneventful recovery. Post hoc review of the serial chest x-rays from the 4-day postimplant period revealed that the lead was floating in the atrium on postimplant day 1. The unstable position of the right atrial lead probably resulted in atrial perforation during repeated shock applications 1 month after implantation. Two patients developed infection, requiring explantation of the device and leads.

Four patients required repositioning of the right atrial lead: 1 patient because of lead dislocation and 3 because of an acute increase in the ADFT. One patient had dislodgement of the right ventricular lead that resulted in a change in signal quality, inhibiting appropriate shock delivery. The lead was successfully repositioned.

**Discussion**
Thirty-six years ago, Lown et al showed that AF could be converted to sinus rhythm by a transthoracic high-energy shock. In 1970, Jain et al demonstrated that AF could be treated successfully by giving shocks with 1 electrode in the right atrium and the other over the chest wall. In 1992, Levy et al reported that a high-energy shock given within the atrium had a higher immediate success rate than transthoracic defibrillation. More recently, it was shown that the energy
required to defibrillate could be markedly reduced by the use of large-surface right atrial and coronary sinus electrodes and biphasic shock waveforms.\textsuperscript{13–23} The present study was designed to determine the safety, efficacy, and complications of an implanted device able to recognize AF and to treat the arrhythmia by delivery of an appropriately timed defibrillation voltage. To prevent a possible long period of ventricular electrical standstill after successful defibrillation, the device was equipped with an on-demand ventricular pace function. A large number of defibrillation shocks were given, both during the testing phase (3049 shocks) and during attempts (670 shocks) to convert spontaneous episodes of AF during a follow-up period of 72 to 613 days (mean, 259±138 days). In all patients, the shocks were given under the observation of a physician. No ventricular arrhythmias were induced in any patient, indicating that the device was safe in the patient population studied. This safety record, ie, the absence of inadvertent precipitation of a ventricular tachyarrhythmia, reflects the application of the lessons learned from prior testing in animal models\textsuperscript{13–18} and in patients.\textsuperscript{18–21} This resulted in programming the atrial shock synchronized to a QRS complex, which occurs ≥500 milliseconds after the preceding QRS complex, to avoid the T wave of the preceding beat. Such an approach is possible because conversion of AF is not an emergency.

Efficacy of the device was evaluated by determining its ability to recognize AF, to reject sinus rhythm, and to convert AF to sinus rhythm by a low-energy shock. Arrhythmia recognition occurred with high specificity. In contrast to the ventricular defibrillator in which the life-threatening character of the arrhythmia requires a short time from onset to therapy and therefore a high sensitivity, the atrial defibrillator, which is treating a non–life-threatening arrhythmia, should be able to recognize AF with a very high degree of specificity. The device was effective in terminating AF, restoring 74% of episodes to sinus rhythm without further intervention. With drug intervention for ERAF or failed conversion, the overall efficacy of the device was 86%. As discussed elsewhere,\textsuperscript{22} ERAF within minutes after a successful cardioversion is an important problem. They were observed in our patients in 27% of episodes and occurred at least once in approximately half the patients. About half the time, it could be controlled by the intravenous administration of antiarrhythmic drugs, followed by repeated cardioversion. This might present a problem when the device is used outside the hospital. Not only control of ERAF but also the tolerance of the defibrillator shock are important aspects of a long-term success of the implantable Atrioverter. As shown by Ammer et al,\textsuperscript{25} whereas shock energy determines the success of a shock, shock voltage determines the pain perceived by the patient. By using waveforms that deliver greater energy at lower peak voltages, internal cardioversion of AF can be performed with less sedation and greater patient tolerance. The discomfort from intracardiac low-energy shocks is still poorly understood. Most investigators\textsuperscript{18–25} found marked individual variations in shock tolerability. The number of shocks is important, with discomfort growing as the number of shocks increases. This suggests that the first shock should be well above the ADFT to make the shock successful. Lok et al\textsuperscript{20} showed that most patients can tolerate a shock level of 260 V without sedation.

It is well known that longer-lasting AF is more difficult to convert to sinus rhythm and has a higher incidence of recurrences.\textsuperscript{23,28,29} It has been shown in the animal model that electrophysiological remodeling of the atria leads to marked shortening of the atrial refractory period and a loss of the normal relation between heart rate and the duration of the atrial refractory period favoring ERAF.\textsuperscript{11}

If this electrophysiological remodeling of the atria can be prevented by defibrillation as early as possible, it is likely that recurrences of AF will decrease and the number of necessary shocks will diminish over time. Careful follow-up of the number of episodes of AF after implantation of the Atrioverter should answer that question.

The complications observed were mostly related to the use of intracardiac catheters and the implantation of a device, such as the necessity to reposition the catheter (6 patients) and infection (2 patients). In 1 patient, His bundle ablation and pacemaker implantation were performed because of very frequent episodes of AF with a high ventricular rate. A serious complication, atrial perforation with cardiac tamponade, occurred in 1 patient. In retrospect, inappropriate fixation of the atrial lead seems to be the explanation of this complication. The relatively high complication rate is probably related to the learning curve of using the device but may also be caused by its use in 19 centers with differences in techniques, management, and experiences. This resembles the early implantable ventricular defibrillator experience.\textsuperscript{30}

Conclusions

The implantable Atrioverter recognizes AF with high specificity, and in the patients studied, low-energy defibrillation shocks can be given safely and effectively, resulting in prompt restoration of sinus rhythm. Early recurrences of AF after a successful shock occurred at least once in 21 of the 41 patients and usually required the additional administration of antiarrhythmic drug therapy. Shock tolerance varied markedly between patients. Lowering of the ADFT by changing catheter characteristics and shock waveform and the availability of a short-acting, nonaddictive analgetic/anxiolytic drug should facilitate the acceptance of this device. The patients studied fulfilled strict selection criteria, and the performance of the device was observed in hospital. Several pharmacological and nonpharmacological treatment options are currently available to patients with AF. The proper place of the implantable Atrioverter in the treatment of atrial fibrillation requires further investigation.

Appendix

List of Participating Centers and Investigators

Academic Hospital Gent, Gent, Belgium (L. Jordaeus, R. Tavernier, F. Provenier); Hôpital Nord Marseille, Marseille, France (S. Levy, V. Taramasco, E. Dolla); Hôpital Cardiologique, Lille, France (S. Kacet, D. Lacroix, P. le Franc, D. Klug, C. Kouakam); Hôpital “Hôtel Dieu,” Rennes, France (C. Daubert, D. Gras, P. Mabo, D. Pavin); University of Bonn, Bonn, Germany (B. Lüderitz, W. Jung); Klinikum der Stadt Ludwigshafen, Ludwigshafen, Germany (K. Seidl); Academic Hospital Maastricht, Maastricht, Netherland (H. Wellens, C. Timmermans, L.M. Rodriguez); Academic Hospital
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Atrioverter: An Implantable Device for the Treatment of Atrial Fibrillation
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Circulation. 1998;98:1651-1656
doi: 10.1161/01.CIR.98.16.1651

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1998 American Heart Association, Inc. All rights reserved.
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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