Multichamber Pacing in Patients with an Implantable Cardioverter Defibrillator

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Summary

Multichamber pacing may become useful in a number of conditions to achieve either hemodynamic or antiarrhythmic results. Biatrial pacing has been demonstrated to increase arrhythmia-free intervals in patients with frequent drug refractory paroxysmal atrial fibrillation. However, the antiarrhythmic mechanism is not well understood. Therefore, controlled randomized trials will be needed to better identify responsive patients. A dual-chamber implantable cardioverter defibrillator combined with biatrial pacing and a coronary sinus shock coil may be useful in patients with paroxysmal atrial fibrillation and ventricular tachyarrhythmias. The most important feature of this device is its capacity for both synchronous dual chamber and biatrial pacing as well as dual chamber tachyarrhythmia detection and therapy. Biventricular pacing has recently been proposed for treating patients with drug refractory heart failure associated with severe left ventricular systolic dysfunction and intraventricular conduction delay. It is increasingly likely that heart failure patients with poor functional status and a high risk for sudden death will be considered for both an implantable cardioverter defibrillator and a biventricular pacemaker.

Key Words

Implantable cardioverter defibrillator (ICD), biventricular pacing, biatrial pacing

Introduction

A number of new and innovative multichamber pacing modalities have recently been developed for the optimization of cardiac function [8,12-15]. These new techniques aim to decrease the degree of atrial and/or ventricular electromechanical asynchrony by modifying the pathways of depolarization provided by standard pacemakers [6]. Multichamber pacing may become useful in a variety of conditions to achieve either hemodynamic or antiarrhythmic results. Pacing from both the right and left ventricles (or the atria) is often called biventricular (or biatrial) pacing [5]. While biatrial or biventricular pacing is proposed to be effective in the prevention of special arrhythmias, implantable cardioverter defibrillators (ICDs) are accepted in the therapy of a wide range of arrhythmias.

Management of Atrial Fibrillation: Prevention and Therapy

Up to 50 % of patients treated with antiarrhythmic drugs for converting atrial fibrillation (AF) and maintaining sinus rhythm experienced a recurrence during the long-term treatment [18]. In addition, the proarrhythmic effects of these agents limited their widespread use, especially in patients with poor ventricular function [11,17]. The limited efficacy and proarrhythmic risks of antiarrhythmic drug therapy has led to the exploration of nonpharmacologic therapeutic approaches [41].

The first implantable cardioverter defibrillator for atrial application consisted of a three-lead system with right atrial and distal coronary sinus shock coils and a ventricular lead to allow R-wave synchronization and

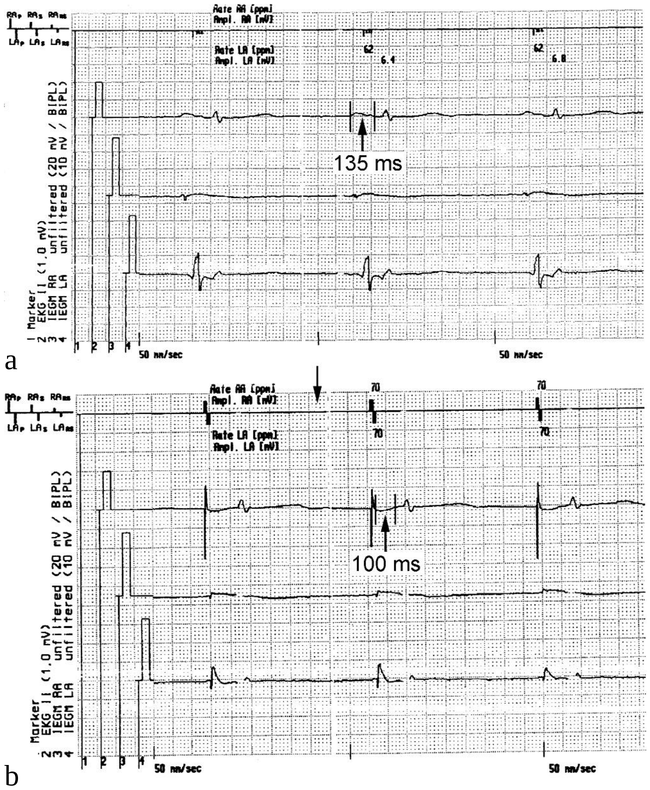


Figure 1. Effect of biatrial pacing on P-wave duration. Intracardiac electrograms: a) spontaneous rhythm b) during biatrial pacing P-wave duration is abbreviated.

post shock ventricular pacing. Right atrial pacing has been shown to reduce recurrences of AF when compared with ventricular demand pacing in observational and controlled clinical trials [3-4]. More recently, multisite atrial pacing modes have been reported to be effective in the prevention of AF including biatrial pacing and dual-site right atrial pacing [25-26,28-29]. Saksena [28-29] and Prakash [24] demonstrated that multi-site atrial pacing trended to be superior to single right atrial pacing in the prevention of recurrent AF. Biatrial pacing has been similarly effective in patients with AF and advanced interatrial block [12]. The mechanism of antiarrhyhmic benefit of these modes of atrial pacing is not completely understood [24].

The use of several modalities of treatment in a single patient with AF may provide additional benefits beyond any single therapy. The concept of hybrid therapy may take the form of varying combinations of ablation, pacing (including preventive and antitachycardia pacing), atrial defibrillators, and drugs. Certain combinations may prove to be synergistic for specific types of AF [33].

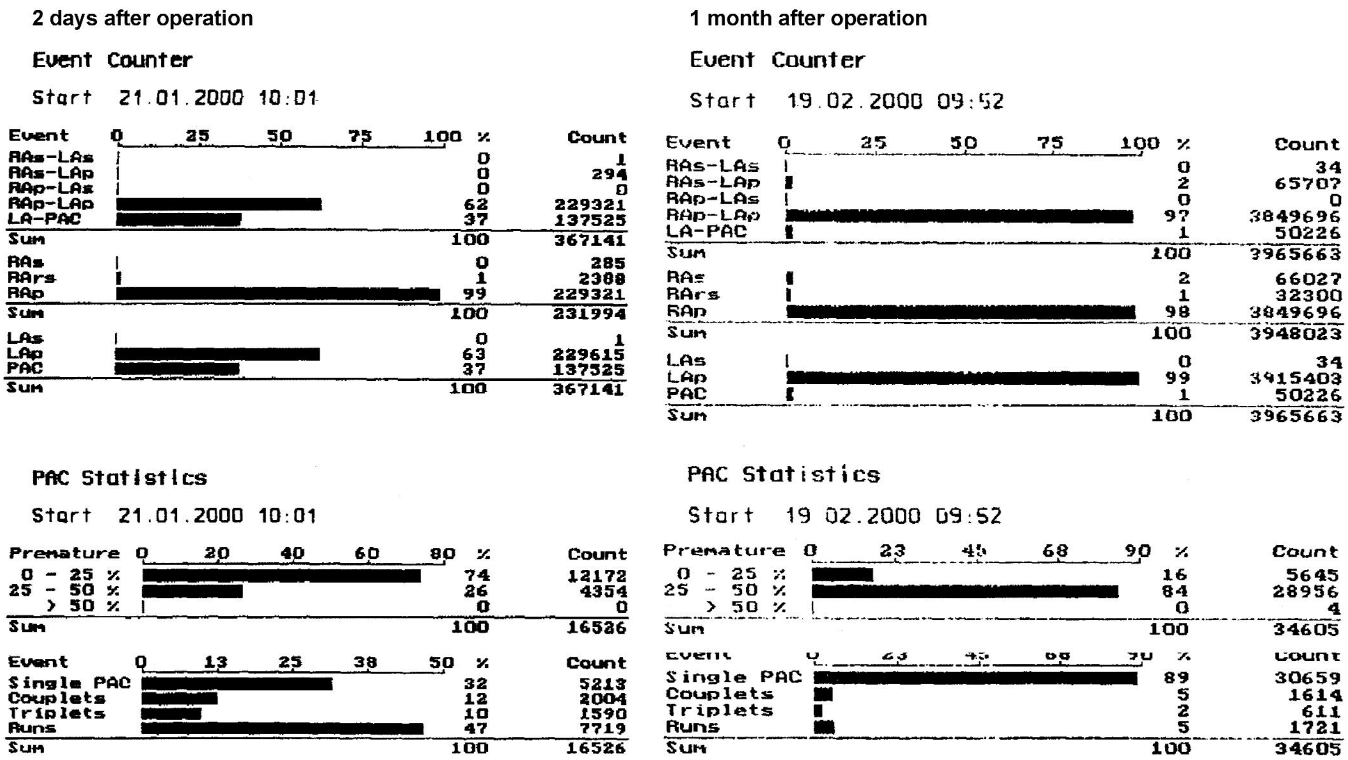
Biatrial Pacing and ICD

The antiarrhythmic mechanisms of multisite atrial pacing are unknown but could be related to altered electrophysiologic parameters (atrial resynchronization) and improved hemodynamics as the left atrioventricular interval is decreased [10]. Interatrial conduction block with retrograde activation of the left atrium was reported to be associated with a high incidence of atrial tachyarrhythmias [21]. Biatrial pacing resynchronizes the electrical activity of the atria, expressed as normalization of P-wave morphology and duration in contrast to single right atrial or coronary sinus pacing [15] (Figure 1). Prakash et al. [24] observed that single-site pacing was associated with an increase in P-wave duration as well as regional activation times, suggesting a true prolongation of global atrial activation. Dual-site right atrial and biatrial pacing resulted in its abbrevation, which reflects improved global conduction.

There is preliminary evidence that simultaneous right and left atrial pacing increases atrial refractoriness and decreases the intra-atrial conduction delay after a low right atrial ectopic beat [32]. Previous studies have demonstrated that dispersion of refractoriness and anisotropic conduction were two essential elements for sustaining of atrial arrhythmia [1,36]. Biatrial pacing might change the dispersion of refractoriness or anisotropic conduction; thus, it could prevent recurrence of AF. Wood et al. [46] showed that dispersion of atrial repolarization could be minimized by left atrial pacing only or by biatrial pacing in the isolated rabbit heart. By homogenizing atrial repolarization, dispersion of refractoriness will also be decreased.

For many patients, the natural history of paroxysmal AF is a process of degeneration to the chronic form of the disease [20]. Since "AF begets AF", recurrences of AF may lead to a pathologic process of electrical remodeling and/or structural changes, which is thought to promote the persistence of the arrhythmia and make maintenance of sinus rhythm more difficult [37,44]. AF reduces the wavelength of the impulse by reducing the refractory period; therefore, more and more simultaneous reentry circuit development is possible.

The possible role of inhibiting atrial remodeling in the antiarrhythmic mechanism could also be taken into account. By reducing the number of atrial premature beats, the trigger of AF will be eliminated (reentry and focal activity) and the progressive electrophysiological



a b

Figure 2. Reduction of the number of atrial premature beats using biatrial stimulation. Event counter and premature atrial contraction (PAC) statistics. a) 2 days after implantation; b) 1 month after implantation.

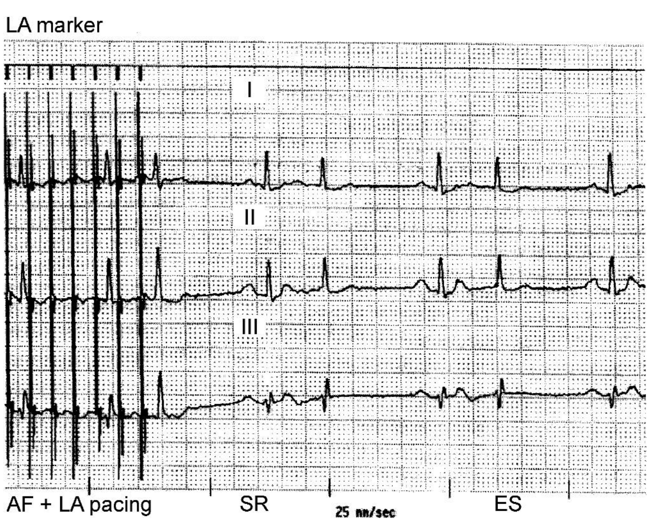


Figure 3. Termination of atrial fibrillation using left atrial burst stimulation. LA = left atrial; AF = atrial fibrillation; SR = sinus rhythm; ES = extrasystole.

and/or structural atrial remodeling will be limited (Figure 2). Premature beats may enhance the inhomogenity of atrial refractoriness. There is a complex situation in AF with multiple, ever-changing wavelets and a marked functional inhomogeneity of the atrial tissue [30]. Regional control of atrial tissue by rapid pacing is feasible during AF, and, through a multisite approach, this pacing modality might lead to a situation where the remaining nonentrained atrial tissue can no longer reaches critical mass [30]. Interestingly, rapid pacing (with bursts) may be effective in the termination of AF or atrial flutter in some cases in not only in the right but also in the left atrium, depending on the origin of the tachyarrhythmia (Figure 3).

Up to 30 % of ICD patients have paroxysmal AF. Special multichamber cardioverter defibrillators such as Tachos MSA (Biotronik, Germany) give us the possibility for both synchroneous dual chamber and biatrial pacing along with dual chamber tachyarrhythmia detection and therapy. Thus, the duration and possibly also the number of AF episodes are reduced [27]. A high frequency burst and a low energy cardioversion using a coronary sinus shock coil can reduce the duration of AF. Shortening the attacks of AF may exert an antiarrhythmic effect by limiting electrical, anatomical, and neurohumoral remodeling [38]. Serial increase in post-shock sinus rhythm duration has been seen in some patients treated with repeated endocardial defibrillation [34]. Therefore, sinus rhythm should be restored as rapidly as possible to avoid adverse electrophysiological remodeling.

Biventricular Pacing

Biventricular pacing has recently been proposed for treating patients with drug refractory heart failure associated with severe left ventricular systolic dysfunction and intraventricular conduction delay [9]. The rationale of multisite biventricular pacing in advanced heart failure is based on the high incidence and gradual deterioration of conduction disorders, especially intraventricular conduction delay [45,47]. These conduction disorders are responsible for major electromechanical abnormalities that mainly affect left atrioventricular (AV) synchrony and the ventricular contraction/relaxation sequence [48]. The purpose of multisite, biventricular pacing is to restore ventricular relaxation and contraction sequences by simultaneously pacing both ventricles at specific sites [2].

The potential interest in biventricular pacing to treat refractory heart failure was first investigated in studies of acute hemodynamics using temporary leads. Some investigators were able to find significant improvement in hemodynamic parameters (increased cardiac output, lower pulmonary capillary wedge pressure (PCWP) and V-wave) in patients with advanced heart failure and left ventricular systolic dysfunction under biventricular pacing, relative to intrinsic conduction or single-site DDD right ventricular pacing [14]. Cazeau et al. demonstrated that this acute hemodynamic improvement was independent of AV delay optimization [9]. Biventricular pacing decreased mitral valve regurgitation, which was confirmed by scintigraphic and echo-Doppler examinations. Most of the examined patients showed an abnormal activation sequence during standard pacing, which was corrected by biventricular pacing. Therefore, biventricular pacing improved not only the electrical, but also the mechanical activation sequence.

The results of one study demonstrated that the long-term benefits of biventricular pacing were correlated with the quality of ventricular resynchronization, as assessed from shorter QRS duration and the tendency for QRS axis normalization [2]. However, other experiences are conflicting. The results of one clinical study demonstrated [7] that the reduction of QRS duration did not predict the best hemodynamic results, which was also strongly supported by our experiences with biventricular pacing. Our results suggest that decreasing mitral regurgitation and PCWP are important factors. Figure 5 shows the intracardiac electrogram with a QRS duration of 120 ms with biventricular pacing, which is profoundly shorter in comparison to the 180 ms QRS duration for the patient without pacing.

In patients with end-stage heart failure, multisite pacing may be associated with a rapid and sustained hemodynamic improvement. In this way, arrhythmogenic factors may also be attenuated. Slight overdrive pacing could have an antiarrhythmic effect on ventricular arrhythmias based on a triggered or reentry mechanism.

A randomized crossover study investigated the effects of biventricular pacing on ventricular arrhythmogenesis [43]. The investigators concluded that biventricular pacing significantly decreased the 24-hour ventricular ectopic count and the ventricular salve count, as measured by Holter monitoring, without altering mean daily heart rate when compared to no pacing. Ventricular extrasystoles can trigger ventricular tachycardia based on different mechanisms. This has important indications concerning the potential safety and antiarrhythmic potential of this novel therapy.

Biventricular Pacing and ICD

A leading cause of death in patients suffering from severe heart failure is sudden death mediated by a malignant ventricular arrhythmia [19]. Antiarrhythmic drug therapies have failed to influence this risk [35], whereas ICDs have been shown to be beneficial for the prevention of arrhythmic sudden death in certain patient groups [23]. Therefore, the use of an ICD is increasingly accepted as a standard therapy for patients with heart failure who are at high risk of sudden death [22]. In addition to their poor prognosis, heart failure patients also suffer from a poor quality of life [16]. ICD implantation does not alter this impaired quality of life, whereas biventricular pacing has been advocated for the symptomatic management of medically refractory New York Heart Association (NYHA) Class III-IV heart failure. There is no evidence that this pacing technique will affect the prognosis in this patient group. It is increasingly likely that heart failure

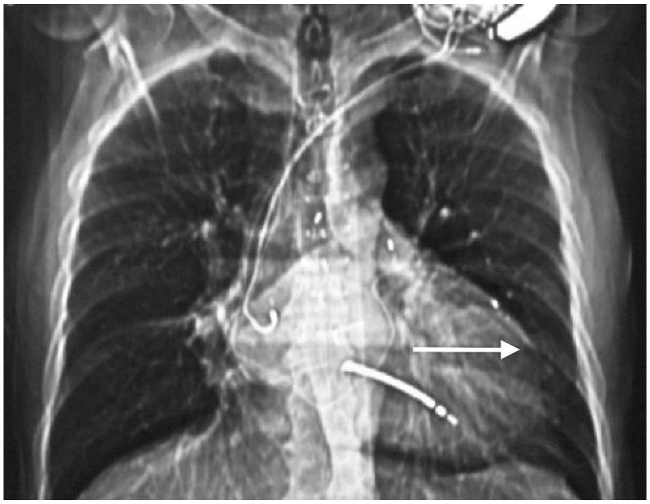


Figure 4. Biventricular ICD with right atrial, right ventricular, and coronary sinus electrodes. Arrow shows the distal end of coronary sinus electrode (Computer tomograph image).

patients with poor functional status and at high risk of sudden death will be considered for both an ICD and a biventricular pacemaker [39]. Figure 4 shows a biventricular ICD with right atrial and ventricular leads, whereas the left ventricle is paced by a lead that is inserted in a coronary sinus tributary vein.

Walker et al. reported their preliminary experiences with the combined use of an ICD and a biventricular pacemaker in six patients with heart failure and a malignant ventricular arrhythmia [42]. Four patients underwent both ICD and biventricular pacemaker implantation, while only two patients underwent a single device implantation. They concluded that implantation of both devices may be feasible with currently available pacing technology.

One study evaluated the number of ICD patients (n = 360) presenting a biventricular pacing indication [31]. These investigators predefined possible indications for biventricular pacing as follows: complete bundle branch block, left ventricular ejection fraction < 35 %, and NYHA-class > II. They concluded that about 10 %

Figure 5. Reduction of QRS duration using biventricular pacing (right panel).

Patient number	Age, gender	Underlying heart diseae	Arrythmia	NYHA	EF (%)	LV diameter (mm)	PQ-intervall (ms)	QRS-intervall (ms)	Drugs
1	56 years, male	Post MI, post CABG, congestive HF, MI II, LV aneurysm	Sustained VT 210/min, VF	NYHA III (BiV: NYHA II)	30	D: 70, S: 61	100	200	ACE-inhibitor β-blocker, diuretics, amiodaron
2	61 years, female	Post MI, congestive HF, MI II-III, LV aneurysm	Nonsustained VT and syncope	NYHA IV (BiV: NYHA II)	23	D: 75, S: 67	140	200	ACE-inhibitor β-blocker, diuretics, amiodaron
3	46 years, male	DCM, MI II-III	Nonsustained VT and syncope	NYHA IV (BiV: NYHA II)	15	D: 93, S: 80	100	240	Digitalis, ACE-inhibitor, diuretics
4	63 years, male	Post MI, congestive HF	Sustained VT, paroxysmal AF	NYHA III (BiV: NYHA II)	26	D: 72, S: 63	160	150	Digitalis, ACE-inhibitor, diuretics
5	59 years, male	Post MI, post CABG, congestive HF, MI II	Sustained VT, paroxysmal AF	NYHA III (BiV: NYHA II)	30	D: 73, S: 61	150	150	ACE-inhibitor, β-blocker, diuretics amiodaron

Table 1. Patient data. All patients were in sinus rhythm during ECG evaluation and presented with left bundle branch block. Post MI = post myocardial infarction; CABG = coronary artery bypass graft; HF = heart failure; MI = mitral insufficiency; LV = left ventricular; DCM = dilated cardiomyopathy; VT = ventricular tachycardia; VF = ventricular fibrillation; AF = atrial fibrillation; BiV = biventricular pacing; EF = ejection fraction; D = end-diastolic; S =end-systolic.

of their ICD patients had an indication for biventricular pacing at the time of implantation. During the mean follow-up of 34 months, 16 % of all patients presented an indication for biventricular pacing. Furthermore, patients with an indication for biventricular pacing had a higher mortality rate and more frequent AF than patients without such pacing [31].

Since July 1999, Vogt et al. implanted new cardioverter defibrillator systems with the option for transvenous bi- or univentricular stimulation in eight patients (EF 20 % ± 5 %, QRS duration 181 ± 20 ms) [40]. 4 weeks after the institution of AV-delay optimized pacing, heart failure symptoms and functional parameters improved markedly. They concluded that electric resynchronization in ICD patients with advanced chronic heart failure and left bundle branch block leads to a striking improvement of symptoms and functional parameters shortly after implantation. ICD candidates with left bundle branch block and ventricular tachycardia/fibrillation should be considered for a biventricular system. A long-term follow-up of these patients will prove whether life-threatening arrhythmias decrease.

From July to November 2000, we implanted biventricular ICDs (Tachos MSV, Biotronik) in five patients (57 ± 6.67 years, four male/one female). All of the patients, suffering from drug refractory heart failure (either congestive heart failure or dilated cardiomyopathy, NYHA III-IV), had a very low ejection fraction (EF < 30 %) and a wide QRS (QRS > 150 ms) with a left bundle branch block morphology. In the medical history of these patients, sustained ventricular tachycardia (VT) and ventricular fibrillation, sustained VT, and nonsustained VT combined with syncope were present in 1, 2 and 2 cases, respectively (Table 1).

Patient number	Right ventricular amplitude (mV)	Right ventricular threshold (V)	Left ventricular amplitude (mV)	Left ventricular threshold (V)	Right atrial amplitude (mV)	Right atrial threshold (V)	Defibrillation threshold (J)	QRS-intervall sponaneous (ms)	QRS-intervall BiV (ms)
1	7	0.4	30	0.4	3.1	0.3	20	200	130
2	12	0.4	12	0.5	2.1	0.5	12	200	160
3	36	0.4	12	0.7	1.8	0.7	20	240	140
4	9	0.5	11	1.2	2.2	1.0	10	150	135
5	12	0.3	14	1.6	3.5	0.4	8	150	130

Table 2. Electrophysiological parameters in study patients.

Table 2 shows the electrophysiological parameters. In one case, an epicardial, screw-in, left ventricular electrode was implanted. The QRS duration decreased significantly (mean change: 49 ± 35.7 ms) using biventricular stimulation in all of the patients; moreover, the NYHA functional class also improved (Table 1). In the mean follow-up period (3.5 ± 1.7 months), two episodes of ventricular arrhythmias were observed in one patient.

The future potential for the combination of these devices is of importance since medically refractory heart failure is associated with a poor prognosis and an impaired quality of life, and there are no other therapies with widespread availibility that address both of these problems. Potential benefits include long-term left ventricular remodeling (secondary to biventricular pacing) with a resulting reduction in arrhythmogenesis, a further improvement in patients' quality of life, and a reduction in the long-term risk of mortality. Prospective randomized trials investigating the effect of a biventricular ICD on the reduction of morbidity and mortality, the cost-effectiveness ratio, and the exact indication are required before this technique can achieve widespread acceptance [42].

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