Improvement of Interventricular Activation Time Using Biphasic Pacing Pulses at Different Sites on Right Ventricle Septal Wall

A. P. RAVAZZI, C. PRIOLO, F. P. PROVERA, P. DIOTALLEVI, R. AUDOGLIO*
Division of Cardiology, Osp. Civile, Alessandria, Italy, *SRA, Pavia, Italy

Summary

Natural kinetics of systole is substantially altered by pacing performed at the apex of right ventricle (RVA) which generates an antidromic activation. Moreover, an additional delay of left ventricular (LV) activation is induced that may generate consistently a loss of V-V and A-V coordination. Conventional ventricular pacing subverts the contractile function and contraction dynamics of the heart. In 18 patients (pts), all affected by II or III deg. AV block, a temporary decapolar pacing lead was positioned in the right ventricular apex and fixed in contact with septal wall. Stimulation was performed through various dipoles using five different pulse shapes: cathodic (considered as REFERENCE) and anodic monophasic, -/+ and +/- biphasic and overlapping biphasic (OLBI). QRS duration and morphology were measured and evaluated by means of an high resolution ECG averager/analyzer. In 10/18 pts an "extended" evoked QRS duration (range 190-240 ms) was observed when pacing with reference pulses at RVA. In these pts a consistent reduction (form 9% up to 29%) in the evoked QRS duration was observed using biphasic and OLBI pulses and moving dipole position from apex to outflow tract. The best improvement was achieved, in all pacing positions, using the OLBI pulse morphology. No statistically significant variations in evoked QRS duration were observed in the 8/18 pts showing an evoked QRS duration in the range of 130-150 ms when paced with reference pulses at RVA. In all pts, the QRS morphology changed significantly with different pulse morphologies and at pacing sites. Conventional pacing in RVA induced in 55% of our pts an additional V-V delay, that could only be partially shortened moving pacing site from apex to outflow tract. Almost never, in these pts the negative square pulse is the best one. Pulses with an anodic content (biphasic and OLBI) showed better performance. The best improvement in V-V activation time and the lowest pacing thresholds were achieved using OLBI configuration. These preliminary results show that biphasic pulses, at different septal sites, will substantially influence both, V-V conduction time and pathways.

Key Words

Inter-ventricular activation time, biphasic stimulation, OLBI stimulation, septal pacing

Introduction

During the last decade, the major challenge was to achieve a physiological pacing capable to restore the heart rhythm complying or miming basic functions that contribute to create the natural cardiac dynamic.
Dual chamber DDD pacing performed in standard pacing sites, i.e. atrial appendage and ventricular apex, seems to have reached this aim since it does not only preserve the life of the patient, but improves its quality as well. Restoration of atrio-ventricular synchronization adapts the cardiac rate to the patients needs and, moreover, it seems to be able to maintain the hemodynamic function by the contribution of the preserved atrial systole, which improves ventricular filling. Thus, it is a common opinion that all pacing modes guided by the atrial activity, spontaneous or artificially provoked, should be considered as physiologic [1].
In reality, at least in our opinion, these pacing approaches only preserve the dynamics of cardiac systole, but not its kinetic. This means that they cannot be considered truly physiologic [1-5].
Pacing performed at the apex of the RV substantially alters the natural kinetics of the systole, since it:

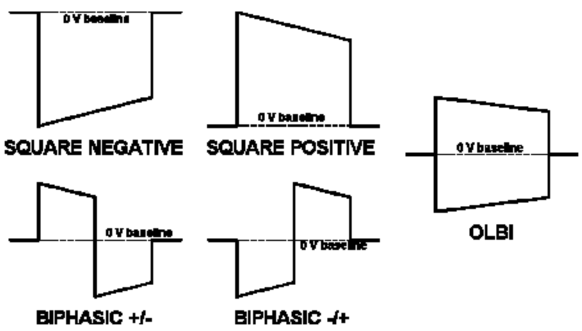

Figure 1. Pulse morphologies used within the study.

- generates considerable loss of V-V and A-V coordination inducing a left ventricular activation delay, which may lead to a reduction of the left ventricular contractile function [2, 3, 4, 6];
- causes a non-physiologic contraction generating in the ventricular muscle an antidromic activation from apex to base.

Accordingly, a substantial subversion of the cardiac contractile function and dynamics occurs [5, 7, 8, 9].

Recent literature reports of several cases in which the stimulation of interventricular septum or of right ventricular outflow tract have reduced the degree of the LBB block [10, 11].

An additional element, little known and insufficiently investigated, is the rule played by the morphology of the stimulus. Till now, the square cathodic morphology, which do not correspond to any physiological signal, is considered the "standard" configuration of the pacing pulse.

Therefore, we decided to investigate the influence, in terms of delay in left ventricular activation, of the stimulation site and of the pulse morphology in right ventricle compared to classic pacing with a standard pulse delivered at the ventricular apex.

Material and Methods

During pacemaker implantation in 18 patients (pts), 8 males and 10 females, with mean age of 68.6 years (range 52-78), an endocavitary electrophysiologic study (EPS) was performed. All pts were suffering from II or III deg. AV Block, whose etiology was: ischemia in 5 pts, degenerative myocardosclerosis in 10 pts and ipokinetic cardiomyophaty of unknown origin in 1 pt.

A temporary pacing lead (Medtronic, Inc. model Cardio-Rhythm TORQR CS Decapolar), with 10 electrodes equally spaced by 0.8 cm, was implanted in right ventricular apex through the right femoral access. The distal portion of the lead was carefully applied to the septal wall in order to maintain each electrode in contact with the myocardium. For investigation purposes an identification number was attributed to each electrode, from 1 (distal tip) up to 10 (most proximal ring).

Five different pulse morphologies were used in the study (Figure 1): square negative, square positive, biphasic +/-, biphasic -/+ and Overlapping biphasic (OLBI) [12]. For each pulse, a total pulse duration of 0.5 ms and a 50% duty cycle for bipolar pulses was chosen. Pulse amplitudes were measured peak to peak. Data collected with square negative pulses at the distal dipole (electrode dipole 1-2) were taken as "reference" (REF) to evaluate variations in the other site of pacing and with other pulse shapes.

An adhesive cutaneous pad for external defibrillation was placed in the left pectoral area of each pt to allow OLBI pacing and simulate the pulse generator case. The good contact of the pad was assessed measuring the unipolar pacing impedance, which was kept in the range of 350-500 Ohm to be acceptable. A pulse former/ threshold analyzer (Biotronik, Germany, mod. ERA B-20) was combined to a dual chamber Pacing System Analyzer (Biotronik, Germany, mod. ERA 300) in order to generate all required pulse shapes.

The pts were then connected to a 12 lead polygraphic ECG recorder (Manta mod. Trace-Master 34/2) and to an high resolution analyzer (HRA) for ECG averaging (Cardiomedica mod. ELP 3 Analyzer). Figure 2 depicts the measuring system connected to the pt.

For each pacing site and pulse morphology 300 consecutive evoked QRS were stored in the HRA ECG recording system. The high resolution averaged QRS signals (HRAS) were then evaluated in time domain, using the Simpson method with a bandpass filtering of 40 - 250 Hz, to perform the measurement of surface QRS complex duration.

All durations of the evoked HRAS were measured using the pacing pulse marker as starting point. This procedure is not correct, but, since the error was repeated in all measures, it does not affect the sense of final results.

The duration of the evoked HRAS measured at REF pacing conditions allowed to distinguish two separate

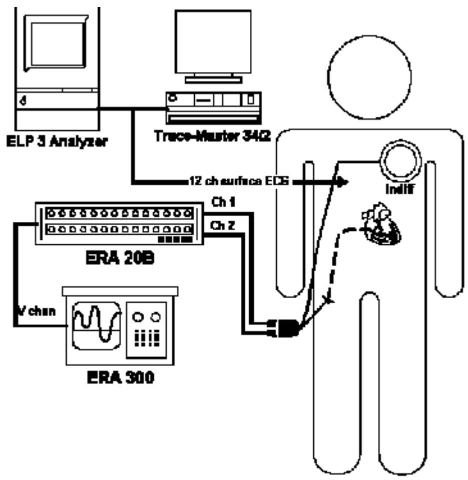

Figure 2. Measuring system connected to the pt during the study.

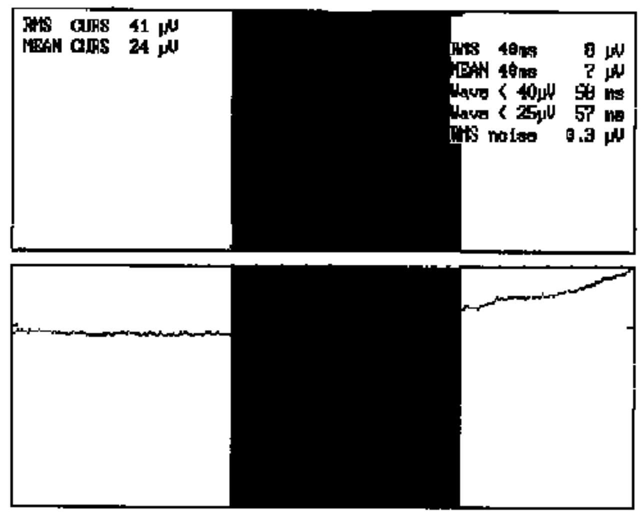

Figure 3. Typical HRA (top) and surface (bottom) QRS of pts with an evoked QRS duration < 150 ms.

groups of pts:

- in the first group (8 pts) the QRS duration was shorter (<) than 150 ms (range 130-150).
- in the second (10 pts) the QRS duration was longer (>) than 190 ms (range 190-240).

Results

Since no significant differences in QRS duration and morphology at basal condition was evidenced between pts in the whole, we should conclude that in the second group of pts (QRS>180 ms) an additional interventricular conduction delay was induced by the non-physiological stimulation at REF condition.

Typical HRAS analysis of the averaged signal, at REF pacing pulse, of pts with evoked QRS duration <150 ms and >190 ms are depicted in Figure 3 and 4 respectively (as shown by the ELP 3 Analyzer).

Significant differences in QRS duration and pacing threshold were indicated by the two groups of pts for each pulse morphology applied at different septal pacing sites.

Figure 5 shows the percentage of variation of the QRS duration when the five pulse morphologies were applied to five consecutive dipoles of the catheter along the septal wall in the first group of pts (QRS<150 ms). The same pulses were also applied to a long (6.4 cm - electrode 1-10) dipole and to one with half of that length (3.2 cm - electrode 1-5).

In all cases but one, the change in pulse shape and site of pacing moderately increase the QRS duration. Only the biphasic +/- pulse, when applied at dipole 9-10 in sub-valvular position, showed a very modest (1.5%) and not significant reduction of QRS duration. Data demonstrate that, in this group of pts, the pacing in apical position with square negative pulses seems to be the best, in other sites and with different pulse shapes the QRS duration is slightly pronged (up to 5%) or remains unchanged.

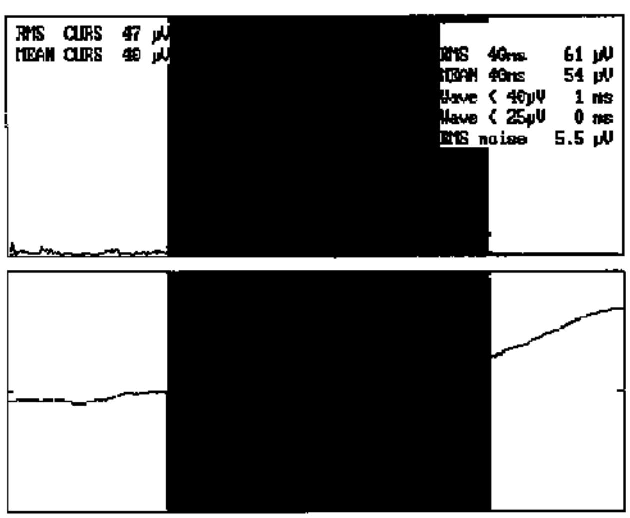

Figure 4. Typical HRA (top) and surface (bottom) QRS of pts with an evoked QRS duration >190 ms.

In Figure 6, the percentage of variation of evoked QRS

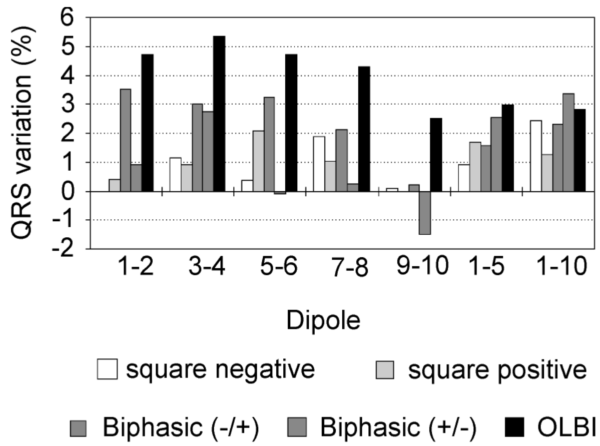

Figure 5. Variation (%) of the QRS duration vs. pulse morphology and pacing site in pts with evoked QRS<150 ms at REF.

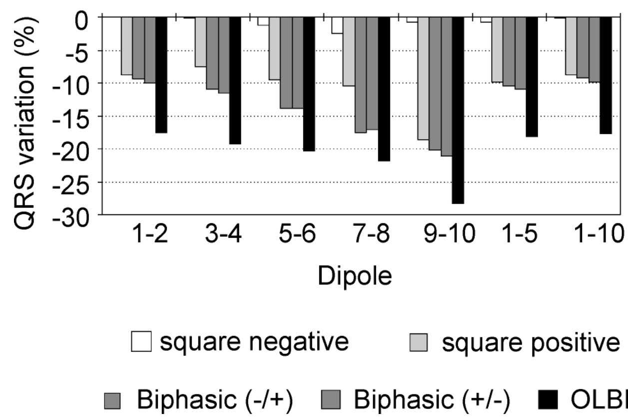

Figure 6. Variation (%) of the QRS duration vs. pulse morphology and pacing site in pts with evoked QRS>190 ms at REF.

duration, at the condition previously described, in the group of pts with QRS>190 ms is shown. In all pts of this group, a significant shortening of the QRS complex was achieved with all but square negative pulses, and when pacing site was moving from apical to subvalvular position along the septal wall. The shortening was in the order of 7% to 18% for square positive pulses, from 10% to 20% for biphasic -/+ and +/- pulses and reached a range of 17% to 28% with OLBI pulses, depending on pacing site.

In these pts, with regard to the pacing site only, without taking care of pulse morphology, we can see that the interventricular conduction time substantially improves when pacing is performed at sites close to the outflow tract (9 to 11% shortening). This is indicated by the parabolic trend from dipole 1-2 to dipole 9-10 shown in Figure 6. The length of the dipole has no influence on QRS shortening since dipoles 1-2, 1-5 and 1-10 showed similar values. Our data are confirmed by previous studies performed by several investigators and reported in literature.

Different considerations should be made when QRS shortening is related to pulse morphology. Looking to Figure 6, we can see that the QRS shortening, pacing the apex (dipole 1-2), was 8% with square positive pulse, 9 to 10% with biphasic pulses and reached 17% with OLBI pulse configuration. This basic improvement was substantially maintained when stimulation site was moved from apex to outflow tract. The sole characteristic in common to all pulse morphologies inducing shortening in QRS duration is the "anodic" component. The difference in yield may be attributed to the configuration of each pulse: square positive does not have any cathodic component; both biphasic have cathodic components, but its duration is short (0.25 ms) and is not simultaneous with the anodic one, in OLBI, which shows the best results, both anodic and cathodic components have the same duration and are generated simultaneously.

In order to understand the reason why OLBI performs better than other pulses, it is important to point out that the nature of this stimulation technique is not bipolar as all others used in this study. OLBI acts as a "double unipolar" pacing, since it delivers, simultaneously, one square negative and one square positive pulse from each active endocavitary electrode with reference to an indifferent electrode, that, in our case, is represented by the cutaneous pad applied on the chest of the pt. The spatial distribution of the electric field generated by OLBI stimulation is more orthogonal to the myocardium fibers than that originated by a bipolar configuration and, next to the electrode couple, it is more intense as well. This simply means that a larger amount of active myocardium is involved by the OLBI stimulation field, as it can be seen in Figure 7. The figure shows the HRAS time domain analysis of spontaneous and evoked QRS complexes recorded from the same pt, at the same pacing site (apex), but with different pulse morphologies.

In order to simply understand the graphic representation of the HRAS analysis in time domain, it is sufficient to know that the gray zone represents the duration

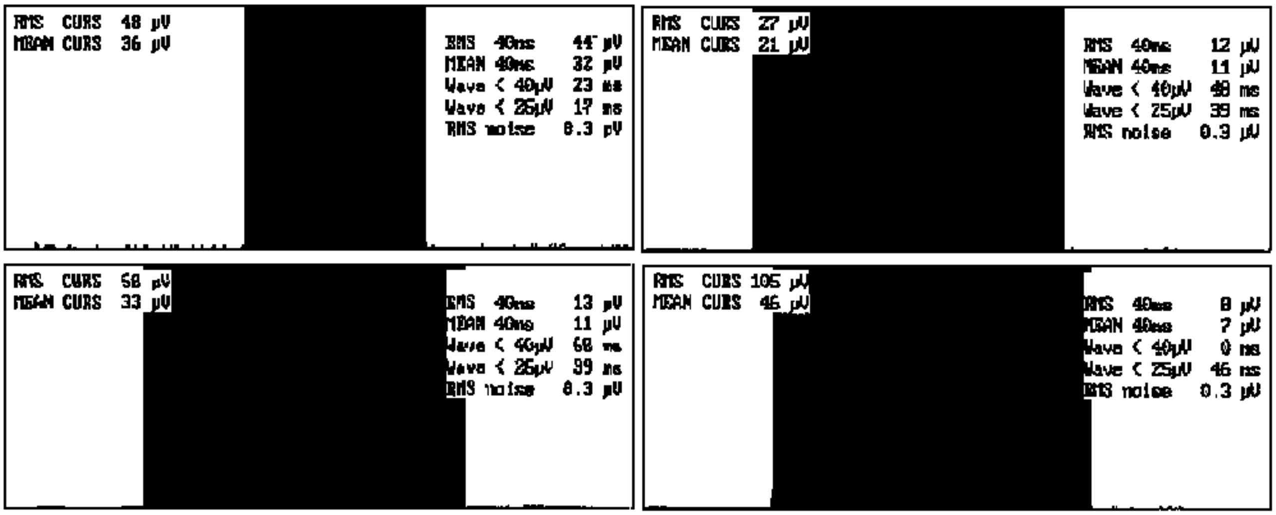

Figure 7. HRAS time domain analysis of surface QRS complexes recorded from the same pt. a) basal conditions, b) pacing at apical dipole with square pulses (no difference between positive and negative polarity), c) pacing at apical dipole with biphasic pulses (no difference between +/- and -/+ pulse configuration), d) pacing at apical dipole with OLBI pulses.

of the QRS complex. The amplitude of each peak is proportional to the amount of cardiac cells depolarizing at same time.

Figure 7a) shows the depolarization process at basal conditions. We can see that the largest amount of myocardium depolarizes between 40% to 80% of the total duration of the QRS complex, confirming the serious pathology of conduction pathways.

Figure 7b) shows the depolarization process during pacing with square pulses. Several portions of myocardium are sequentially involved in the depolarization process without any relevant predominance. Despite expectances coming from results in QRS shortening shown in Figure 6, no significative differences in the depolarization sequence were observed between analysis of signals generated by negative and positive square pulses.

In Figure 7c), the depolarization process during pacing with biphasic pulses is shown. A large portion of myocardium depolarizes immediately after the emission of the stimulus, then, several other portions sequentially depolarizes with a course similar to that shown by square pulses. In this case, the absence of significative differences between different phases of the biphasic pulse were predicted by results in QRS shortening shown in Figure 6.

Finally, Figure 7d) depicts the depolarization process with OLBI stimulation. More than the 80% of entire myocardial mass depolarizes immediately after the emission of the stimulating pulse. Only small portions of myocardium reacts late.

From HRAS analysis it is impossible to define which portion of myocardium depolarizes in a definite time interval but only the amount of it. Results obtained by HRAS analysis of OLBI evoked QRS demonstrates that at least a major portion of LV mass depolarizes synchronously with RV.

Discussion

Square and biphasic pulses showed an increase of ventricular pacing thresholds (VPTs) moving the pacing site from apex to upper septal sites and in lengthening the dipole. But differences between values should be mostly attributed to the distance between electrodes and active tissue than to a real difference in the excitability of myocardial cells at the different sites. Differences in VPT showed by different pulse morphologies but OLBI were minimal, quite stable and statistically not significant. Only the OLBI pulse, in all sites and dipole lengths, showed a threshold from 32% to 48% lower than bipolar and unipolar configuration respectively. This characteristic was less evident for medium and long dipoles since tissues involved by the OLBI "dual unipolar" stimulation were far each other and then the major benefit of this approach was minimized. The OLBI stimulation was also less influenced by distance from electrodes to myocardium giving, by consequence, more stable threshold values.

Looking at the data achieved in this study, we may try to advance the following hypothesis (to be supported by additional extensive investigations). Pts showing a long evoked QRS may have developed structural alterations in the intraventricular conductive pathways which causes a secondary additional delay in the activation of the left ventricle. These alterations seem to be refractory to cathodic potentials but they react when an anodic potential is applied. Since the course of these pathways moves from left to right ventricle and from the base to the apex inside the septum, pacing at the right sites close to the outflow tract using pulse morphologies more effective, as OLBI configuration, may avoid the secondary additional delay and improve interventricular activation.

Anyhow, the preliminary results obtained during this stage of the study are limited by the relatively small population of pts and do not allow to reach any definitive conclusion.

Collected data can only drive to few considerations:

- Traditional pacing in right ventricular apex using square negative pulses induces an additional and relevant interventricular delay in several pts.
- This delay can only be partially shortened moving the pacing site in a more favorable area of the right septal wall.
- Almost never, the negative pulse is the best one. Nearly always pulse morphologies with an anodic content showed better performance, at least in pts that participated this study.
- The OLBI stimulation, that depolarizes a larger amount of myocardium, shows the best results improving both interventricular conduction and pacing threshold.

OLBI stimulation, combined to uncommon pacing approaches, is a very attractive tool that needs additional and extensive investigations, since it may let to open a new way in the still partially unexplored field of cardiac pacing.

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