REVIEW

Noninvasive Assessment of the Biventricular Pacing System

Jonathan S. Steinberg, M.D.,* Parimal B. Maniar, M.D.,* Steven L. Higgins, M.D.,† Sherie L. Whiting, R.N.,† David B. Meyer, M.D.,† Sergio Dubner, M.D.,§ Abrar H. Shah, M.D.,¶ David T. Huang, M.D.,¶ and Leslie A. Saxon, M.D.‡

*From the *Division of Cardiology and Arrhythmia Service, St. Luke's-Roosevelt Hospital Center and Columbia University, New York; †Scripps Hospital, La Jolla, California; ¶Division of Cardiology, University of Rochester, Rochester, New York; §Clinica Y Maternidad Suizo Argentina, Buenos Aires, Argentina; and ‡Division of Cardiology, University of Southern California, Los Angeles, California*

Cardiac resynchronization using biventricular (BiV) pacing systems has been introduced for the treatment of symptomatic heart failure in patients with bundle branch block or prolonged QRS duration. Recent controlled clinical trials^{1,2} have concluded and the results indicate that the majority of carefully selected patients will experience clinical improvement. The Food and Drug Administration has recently approved BiV pacing systems for implantation in patients with NYHA class III-IV heart failure despite optimal medical therapy when the QRS duration is >130 ms.

The BiV pacing system differs from the conventional permanent pacemaker by incorporating a third lead that is positioned on the epicardial surface of the left ventricle (LV) via the coronary venous system. Simultaneous stimulation of the right ventricle (RV) (via a conventional endocardial lead) and the LV accomplishes BiV pacing and "resynchronizes" ventricular activation. This non-traditional format of ventricular stimulation may present new challenges in the assessment of pacing function, and will necessitate a greater understanding of basic and complex features of BiV pacing and its effect on noninvasive modalities such as the electrocardiogram (ECG) and intracardiac recordings on the pacemaker programmers. Initial systems utilized a conventional pulse generator with a modified header where LV and RV signals and output were linked; systems with separate ports for the LV and RV are now available.

Many variables, in addition to the basic lead configuration, can influence accurate assessment of BiV pacer function, including LV and RV lead position, consistency of capture, differences in impedance between the ventricular leads, conduction velocity and patterns, relative timing of stimulation between the ventricular channels, and fusion with intrinsic activation. New and unusual sensing problems can arise creating complications such as pacemaker-mediated tachycardia or inappropriate inhibition. Pacemaker programming also involves issues unrelated to combating bradycardia.

This review will focus on performing a noninvasive assessment of the BiV pacing system using the 12-lead ECG and intracardiac electrograms, analyses of sensing and capture functions, and general programming recommendations.

TWELVE-LEAD ECG

The ECG is the most readily available tool to ascertain whether BiV pacing has been successfully accomplished, and whether sensing or capture problems exist. The ECG can provide a permanent template of capture configurations (e.g., no pacing, RV, LV, BiV) for easy and reliable troubleshooting. Current BiV systems usually pace BiV via a unipolar LV lead as a common anode attached to the RV tip versus a ring or proximal shared electrode also on the RV lead. They may also pace in a unipolar

Address for reprints: Jonathan S. Steinberg, M.D., Division of Cardiology, St. Luke's-Roosevelt Hospital Center, 1111 Amsterdam Avenue, New York, NY 10025. Fax: (212) 523-3915; E-mail: jss7@columbia.edu

mode from both tips to the pacemaker can. Rarely, both leads may be bipolar.

At implant, it is important to create capture templates of four modes: intrinsic rhythm (by definition, with an interventricular conduction delay), RV pacing only, LV pacing only, and BiV pacing. Individual chamber pacing can be accomplished manually by connecting only specifically needed electrodes, in a unipolar format, to a pacemaker analyzer. A 12-lead ECG template for each pacing configuration should be recorded and stored for reference when needed.

The 12-lead ECG will vary in configuration between the different pacing modes, although not always in consistent patterns, or even predictable patterns if limited leads are examined. Because the vector of activation will, by definition, differ between the various possible capture modes, it has been possible to develop some simple and logical ECG algorithms that can predict the presence of BiV, LV, or RV capture. The need to confirm these patterns is evident for testing capture threshold of the individual lead components of the system, and very importantly, to be confident of a fully functioning system during the clinical care of the heart failure patient. In addition, the LV lead system is less stable and consistent than traditional RV leads.

The electrical axis on ECG reflects the sum of propagating wavefronts generated by the pacing leads. Even if there is no stereotypical ECG pattern of BiV capture, loss of capture in any component of the system will result in a change in QRS axis. Leads that are perpendicular to the direction of axis shift will demonstrate the most dramatic change.

Yong and Duby tested this concept in a training set of 63 patients undergoing BiV device implantation.³ The mean QRS axis during three modes of

pacing, was $-103^\circ \pm 19^\circ$ for BiV, $-75^\circ \pm 15^\circ$ for RV, and $-177^\circ \pm 50^\circ$ for LV (Fig. 1). Transitions of pacing from BiV to RV was predicted to be associated with a clockwise axis shift, from BiV to LV with a counterclockwise axis shift, RV to LV with a counterclockwise shift, and LV to RV with a clockwise shift. Concentrating on the most likely and important scenarios, the authors selected the lead perpendicular to the axis shifts to facilitate the detection of loss of capture. Thus loss of capture from BiV to RV was predicted to be most apparent in lead I and from BiV to LV in lead III. Figure 2 illustrates examples of these patterns. Simply put, BiV pacing was usually associated with a right superior axis, RV pacing with left superior axis, and LV pacing with a right inferior axis. Thus, transition from BiV to RV pacing generated an increase in the QRS amplitude in lead I, and from BiV to LV generated an increase in the QRS amplitude in lead III. These changes are relative and not absolute and require comparison to an alternate paced configuration. When tested prospectively in 38 patients, all transitions performed well with sensitivity and specificity in excess of 90%.³

Hart et al. described a simple algorithm to quickly and accurately identified loss of BiV capture during threshold testing.⁴ They performed a detailed analysis of 12-lead ECGs obtained in each pacing configuration at the implant of BiV pacemaker in 27 patients from the Post Atrioventricular Node Ablation Evaluation (PAVE) Study. The nature of this study eliminated any issues related to fusion. The results indicated that increment of R wave/dimution of S wave amplitude in lead II and/or no change in bundle branch morphology in lead V₁ accurately identified loss of RV capture. Conversely, deepening of S wave in lead II and/or

Figure 1. Mean axes associated with BiV, left ventricular and right ventricular pacing. (Reprinted with permission from PACE³).

Figure 2. Transition from BiV to (a) right ventricular pacing, (b) left ventricular pacing. (Reprinted with permission from PACE³).

change in bundle branch morphology in V_1 accurately predicted a loss of LV capture (Table 1).

These and any other algorithms assume complete or near-complete capture of ventricular chambers without fusion or pseudo-fusion. These ECG differences are maximized by using short atrioventricular (AV) delays in the DDD or PV delays in the VDD modes. In addition, it may be necessary to begin capture threshold testing at maximal amplitude to ensure capture at all sites, and testing at varying

pulse widths to ensure that RV and LV sites do not fortuitously have the identical threshold. Atrial fibrillation presents a number of obstacles, particularly related to variable intrinsic AV conduction and thus fusion.

The LV lead position may vary due to technical and anatomic considerations, but unfortunately the final lead position does not produce changes in ECG configurations sufficient to help in management.⁵ When delivering pacing in a bipolar mode, using the shared common ring on the RV lead, especially at higher outputs necessary for testing of capture of LV leads, it is possible to exceed the anodal capture threshold and identify four capture patterns, with the addition of RV anodal capture to the usual sites. The ECG will demonstrate changes consistent with more dominant RV capture, and should not be mistaken, in the transition QRS patterns, for loss of capture of RV or LV. It can be recognized by assessing the marker of ventricular electrogram channels.

QRS Duration

In patients with an intrinsic intraventricular conduction delay, the QRS duration usually shortens with BiV pacing compared to intrinsic conduction. However, the change is variable and unpredictable and thus, cannot guide assessment of successful capture. Cardiac resynchronization therapy (CRT) on average shortened QRS duration by 12–20 ms. Alonso et al. studied QRS durations in 26 patients with CRT with BiV pacing. QRS duration was 154 ± 17 versus 177 ± 26 ms ($P = 0.016$) in responder versus nonresponder, respectively.⁶ They suggested that the optimal positions of the right and left ventricular leads would be those that could induce the greatest shortening of QRS duration. But, other studies showed that hemodynamic improvement with pacing appears to be more closely related to homogenization of the LV contraction than to QRS narrowing;^{7,8} therefore, the criteria best suited to guide the intraoperative selection of optimal LV pacing site are yet to be determined.

INTRACARDIAC ELECTROGRAM INTERPRETATION

Linking right and left ventricular leads have resulted in new challenges in the interpretation of device function, whether pacemaker or implantable cardioverter defibrillator (ICD). Since the currently

Table 1. Positive and Negative Predictive Value of Two Major ECG Criteria Described to Accurately Identify Loss of BiV Capture by Hart et al.⁴

	Positive Predictive Value (%)	Negative Predictive Value (%)
Transition from BiV to LV pacing		
1. Increment in R or diminution in S wave in lead II	96	93
2. No change in BB morphology in lead V ₁	71	89
Criterion 1 and 2	100	93
Criterion 1 or 2	100	100
Transition from BiV to RV pacing		
1. Deepening of S wave in lead II	93	96
2. Change in BB morphology in lead V ₁	89	71
Criterion 1 and 2	100	73
Criterion 1 or 2	100	100

BiV = biventricular, LV = left ventricular, RV = right ventricular, and BB = bundle branch.

available first-generation systems do not permit independent ventricular channel analysis, care must be taken in both demonstration of appropriate sensing and BiV capture. In addition, two leads yoked together can result in potential interactions that warrant special diagnostic evaluation for troubleshooting. In the above section, the value of 12-lead EKG analyses in discriminating right and left ventricular pacemaker function is described. In this section, we will review the additive value of intracardiac electrogram analysis.

Threshold Determination

Although surface lead analysis is generally adequate for determining right or left ventricular loss of capture, intracardiac electrograms provide additional valuable information. As demonstrated in Figure 3, the combined intracardiac rate lead electrogram can serve as the "13th lead" in the evaluation of loss of capture. In the example shown, BiV pacing results in a narrow surface QRS and in-

tracardiac electrogram. As left ventricular capture is lost (at 0.6 V), the surface lead and intracardiac electrograms widen, and are clearly distinguishable from the third electrogram morphology with complete loss of capture (at 0.4 V) and return of sinus rhythm.

Practically, a 12-lead EKG is not easily available in all clinical situations. Typically, device programmers can display only one to three surface leads though they do provide capability for rate sensing intracardiac electrogram display. For routine threshold determination, this channel alone can demonstrate independent chamber loss of capture. Since the channel displays a filtered electrogram from the extended bipole of right and left ventricular unipolar leads, no determination of the specific chamber of first capture loss (left or, less commonly, right) can be ascertained. For this, independent intracardiac channels are needed or a surface electrogram. Nevertheless, a reproducible change in electrogram morphology is a reliable demonstration of univentricular loss of capture.

Troubleshooting

Intracardiac electrogram analysis is a valuable tool in troubleshooting device-related problems. For traditional rhythm discrimination, the combined ventricular electrogram provides similar information to that from the single right ventricular pacing/ICD lead.^{9,10} However, the ability to independently pace or sense from two far-field ventricular locations provides additional challenges.

Much attention has been drawn to the potential for "double-counting" of BiV pacing signals. To avoid these issues, most current devices sense

Figure 3. Recordings from a BiV pacemaker/ICD during threshold determination. The top channel is surface lead I, middle, the intracardiac electrogram from the combined left and right ventricular leads and the bottom, the shock lead electrogram. See text for discussion.

from the right ventricular channel alone yet provide BiV stimulation. Theoretically, the lack of left ventricular sensing poses the risk of undersensing of left ventricular events and thus inappropriate pacing, such as arrhythmia induction from the "R on T" phenomenon. Practically, this is exceedingly rare and regardless, should be promptly terminated when the BiV device is an ICD and not a pacemaker alone.

There have been clinical situations of double counting resulting in inappropriate or accelerated therapy, initially presented as isolated case reports.^{11,12} Figure 4a and b shows an interesting example of a patient with double counting of ventricular electrograms in sinus rhythm resulting in inappropriate antitachycardia pacing (ATP) therapy accelerating the patient to ventricular fibrillation corrected by an appropriate device shock. This patient had an epicardial lead system though these problems have been reported with coronary sinus (CS) leads as well, in both approved and so-called "off-label" systems. Generally, off-label systems utilize approved pacing leads inserted into the CS for left ventricular pacing which is Y-connected to a right ventricular pacing lead which is then connected to the ICD or pacemakers ventricular rate sensing port.

Kanagaratnam and colleagues recently reviewed their experience with 21 off-label BiV transvenous leads attached to a standard Medtronic ICD.¹³

Figure 4. All panels show atrial (above) and shock electrograms. Panel A shows the initiation of double counting in sinus rhythm with BiV pacing not present. The double counting results in inappropriate ATP therapy, which initiates ventricular fibrillation (VF). In Panel B, the VF is terminated with appropriate shock therapy and BiV pacing resumes without double counting.

They found that 36% of patients had inappropriate shocks during a mean 13 months of follow-up. Inappropriate therapies have included ventricular fibrillation therapy for relatively slow ventricular tachycardia in two patients, tachycardia therapy for sinus rhythm or premature atrial contractions in five patients and in one patient, tachycardia therapy for AV nodal tachycardia at a rate below the device cut-off but exceeding that cut-off due to the double counting.

It has been suggested that double counting is more common in off-label ICD systems, since the components were not designed for BiV use. Now that approved systems are available, double-counting issues may be less common. For example, in the Guidant Contak CD trial, oversensing was reported to occur in less than 6% of cases with 4% receiving an inappropriate shock. These episodes occurred predominantly when BiV pacing was programmed off allowing sensing of the wider intrinsic electrogram. In the Medtronic Insync ICD trial, the occurrence of double counting was not reported. In BiV pacemaker systems, the incidence is uncommon as the ventricular refractory periods are programmable unlike that in ICDs. In addition, newer devices that sense univentricular (RV) minimize the potential for double counting.

There have been several corrective measures suggested for the avoidance of this double-counting issue. At implantation, a careful review of the intracardiac electrograms is necessary. Typically, any lead position that results in a right ventricular to left ventricular (V-V) electrogram separation of 135 ms or less should avoid this problem. In Figure 5, an electrogram width of 137 ms resulted in double counting, rectified at implant by minor repositioning of the left ventricular lead. If this is not possible, the addition of a separate right ventricular rate-sensing lead placed in the RV outflow tract can also resolve the problem. When the problem is encountered postoperatively, other potential corrective measures utilized more commonly include ablation of the AV node and/or pharmacologic therapy to slow AV nodal conduction, thus avoiding the ability to double-count sinus or supraventricular tachycardia.

Postoperatively, reprogramming of the device may be all that is necessary to resolve the double-counting issue. Although the ventricular sensed refractory window is not programmable in most ICDs, programming to confirm appropriate pacing of both chambers should result in a narrow

Figure 5. A single beat viewed by surface (top), atrial intracardiac (middle), and ventricular electrograms (bottom) at 50 mm/s paper speed. Double counting of the ventricular signal occurs when the electrogram width exceeds 135 ms.

ventricular electrogram. Thus, the issue is more commonly observed when BiV pacing is intentionally programmed off, a situation more commonly encountered in the research setting. In addition, double counting can be a clue to an elevated ventricular capture threshold when only one ventricular chamber is captured with pacing and the second chamber is sensed with resultant prolonged V-V timing. We have observed one situation where a finding of double counting of the paced ventricular electrogram resulted in documentation of an elevated left ventricular capture threshold. This patient required CS lead repositioning to again achieve cardiac resynchronization and clinical improvement.

There are other opportunities to noninvasively reprogram a device to avoid double-counting issues. Most obviously, the tachyarrhythmia zones can be programmed to avoid inappropriate shock

therapy. For example, if double counting is observed in sinus tachycardia at 92 beats per minute (bpm), programming the first zone of antitachycardia therapy to include the rate double this (184 bpm) should result in ATP therapy, rather than a shock. Often, the ATP will resolve the issue, Figure 5 notwithstanding. Some have advocated predischARGE treadmill testing to survey for these issues.¹⁴

Future Advances

The first generation of BiV pacing systems has resulted in a tremendous clinical advance for indicated heart failure patients.^{15,16} However, with this new therapy, new problems have arisen both in regard to diagnosis and therapy. Future generation devices will rectify many of these problems. For example, recently released in the United States are BiV pacing systems with independent ventricular channel programming capability. The next generation devices will have independent right and left ventricular electrograms that should remarkably simplify troubleshooting. Obviously, the ability to independently record and program ventricular channel features should rectify many of the problems noted above. Of course, this future advance will bring new challenges for intracardiac electrogram analysis, particularly when RV-LV timing becomes programmable.

Thus, BiV electrograms provide a new tool for the analysis of resynchronization therapy in BiV pacing systems. These electrograms are useful for documentation of appropriate device function and for troubleshooting of BiV capture issues. Future advances should provide even better tools useful in tailoring CRT for heart failure management.

BIVENTRICULAR DEVICE SENSING

Left ventricular pacemaker lead technology is evolving and different types of pacemaker lead have been used. Sensing has changed along with this evolution, starting with initial experience that utilized epicardial left ventricular pacing through leads positioned at limited thoracotomy.¹⁷ The more recent experiences have used a lead specifically designed for left atrial pacing via the CS. This tine-free lead has a bipolar, coaxial polyurethane coating with a 5.8-mm nonsteroid eluting canted electrode tip.¹⁸⁻²⁰

Right atrial bipolar lead

RA connector (IS-1)

Right ventricular bipolar lead

RV connector (IS-1, DF-1)

LV unipolar (IS-1)

CS connector (programmable)

Figure 6. The different positions and polarities of atrial and left and right ventricular leads.

Another advance was a tine-free unipolar polyurethane coated coaxial lead designed specifically for left ventricular pacing via the CS (Fig. 6). To aid with CS cannulation, a guiding sheath with specific design was used. This sheath is preshaped to facilitate CS entry, thus allowing LV pacemaker lead placement through its lumen. After the LV pacemaker lead positioning, the sheath can be pulled back and split externally along its entire length to allow separation from the underlying pacing lead.^{21,22} In addition the lead used was of a novel design with a terminal adaptation allowing lead passage over a prepositioned guidewire (side-wire pacing leads).²³

Although at the present time, most of the pacemaker generators have a three-lumen head (with different types of sensing functions), the initial experience was with a standard dual chamber device where the left ventricular lead was connected to the atrial port of the device and the right ventricular lead was connected to the ventricular port. By setting the AV delay to its minimum, near-simultaneous BiV capture could be achieved. Unipolar or bipolar pacing and sensing could be used dependent on the pacemaker lead utilized.²⁰ Another step was the use of a Y connection for right and left ventricular leads in a dual chamber pacemaker, with simultaneous pacing and sensing in both ventricles.

Presently, three chamber pacemakers with three-lumen heads are available and sensing varies among different models. All of them have bipolar (programmable to unipolar if required) sensing in right atrium; but some of them have unipolar sensing at the LV independent of the RV sensing (usually bipolar). Some also have bipolar sensing

Table 2. Sensing Options in Different Biventricular Pacemaker Models

Manufacturer	Model	Sensing
BIOTRONIK	Tachos MSV	RV-only sensing
ELA	Talent MSP 313	RV-only sensing
GUIDANT	Contak CD	Simultaneous LV + RV sensing
	Renewal	Independent LV and RV sensing
MEDTRONIC	InSync	RV-only sensing
St. JUDE	Frontier	Simultaneous LV + RV sensing

RV = right ventricle; LV = left ventricle.

between the RV and the LV lead tip and some of them have RV-only sensing, as shown in Table 2.

Sensitivity

If a cardiac signal of sufficient amplitude and morphology occurs during the sensing period, the pacemaker output will be inhibited or triggered depending upon the mode selected. The sensing circuit is specially designed to reject extraneous signals while sensing P waves or R waves.

Sensitivity determines the minimum intracardiac signal that the device can detect when intrinsic atrial or ventricular events occur. The higher the millivoltage (mV) value, the lower the sensitivity. When sensitivity is programmed to a very sensitive setting (a low mV value) the device may detect signals unrelated to cardiac depolarization (oversensing, e.g., sensing of myopotentials). When sensitivity is programmed to a less sensitive setting (a higher mV value) the device may not detect the cardiac depolarization signal (undersensing). Sensitivity must be programmed to a value that prevents sensing of extraneous signals, but ensures accurate sensing of intrinsic cardiac signals. Intrinsic atrial signals are typically of lower amplitude than ventricular signals, thus lower sensitivity settings are typically programmed for the atrium. Left ventricular signals are typically of lower amplitude than right ventricular signals. In some devices, this is an independent value but in others the measurement is a combination of signals from the left and RV and the ventricular signal may be attenuated. So, sensitivity settings should be programmed accordingly.

Whether selecting sensing parameters at implant or verifying sensing at follow-up, the same considerations apply: (1) select sensing polarity for leads;

(2) determine sensing thresholds; and (3) select appropriate sensitivity settings.

Bipolar RV/LV Sensing Polarity

In the unipolar LV lead, the electrical activity will be sensed between the LV lead tip and the RV lead ring. The distance traveled by the stimulus between the LV lead tip and the RV lead ring will be affected by the size of the heart. The greater the distance, the more prone the device is to sensing myopotentials.

Determining Sensing Threshold at Implant

Before connecting a lead, the implanting physician should measure the sensing potentials in the unipolar and the bipolar configurations. Adequate intracardiac signal should be present in both configurations to ensure proper sensing in either.

Verifying Sensing Threshold at Follow-Up

Intracardiac signal amplitudes decrease during the lead maturation process. Most programmers provide an automatic sensitivity test that allows the follow-up clinician to verify a patient's sensitivity settings. The automatic test provides for atrial or ventricular monitoring. The test provides the sensitivity setting just above and below the point at which P waves or R waves are sensed.

The cardiac signal presented to the stimulator by the ventricular two-lead system is a composite signal from the parallel combination of both ventricular leads in some devices. The sensing test treats this signal as a single input with measurable amplitude that can be used to determine an appropriate setting for ventricular sensitivity. Usually this signal may be attenuated in the BiV configuration. Conducting the sensing test for the ventricular two-lead system does not require any special considerations.

Pitfalls and Solutions

Sensing RV only, or in both ventricles, together or separately, during pacing or in sinus rhythm should modify the response of the system. The differences between these situations, as well as double counting of T waves and farfield noise, should be addressed.

A system that senses RV-only may not detect an ectopic beat that originated in the LV and may stim-

ulate during the refractory period. On the other hand, any intrinsic ventricular action inhibits delivery of a ventricular pulse in the DDD mode. The ventricles are not brought into synchrony with each other.

A system that senses both the RV and LV leads in the presence of a QRS > 130 ms may double sense a sinus rhythm event. This situation is true only when the patient's P-R interval is shorter than the programmed AV delay, and/or there are no pacing beats at the ventricles. A similar situation could be seen if the sensing delay of both ventricles is greater than the ventricular refractory period.

Although optimal performance of a BiV devices' sensing has yet to be determined, some manufacturers have modified the sensing system to avoid these problems and others have introduced the DDT(R)/V mode and the LV protection period.

The DDT(R)/V mode has been specially designed to ensure BiV synchronization. It is a permanent rate-adaptive pacing mode that represents a combination of the DDDR mode with a VVT mode. In DDT(R)/V mode, the pacemaker triggers a ventricular pace when the AV interval is completed without sensing an intrinsic ventricular event (Fig. 7). Furthermore, intrinsic right and left

DDT(R)/V-Mode

Figure 7. The first beat shows an atrial and ventricular pacing without sensing an intrinsic ventricular beat; the second beat shows a P wave sensed followed by an intrinsic ventricular beat that triggers a BiV pace within 10 ms.

ventricular senses trigger a BiV pace within 10 ms. Thus, the pacemaker response in the ventricular channel corresponds to a VVT mode, and its atrial or AV-sequential behavior is analogous to a DDD mode. The clinical benefit of the DDT(R)/V mode is based on the ability to resynchronize both ventricles even during ventricular sense events.

Sensing on the LV channel, as well as the RV, could help avoid a pace during the refractory period after a premature ventricular beat (PVC). The following example could help to understand the case: in the presence of PVC originated in the lateral wall of the LV, if the device senses only the RV, it may not see the PVC and will pace the RV and the LV (possibly during the vulnerable period). To avoid this situation, some devices sense the LV and allow you to program the refractory period during which there is no chance to stimulate the LV if there was a sensed activity.

PACING AND CAPTURE FUNCTION OF THE BIVENTRICULAR PACEMAKER

Left Ventricle Lead Capture

The success rate of implanting transvenous BiV pacing devices in major studies is approaching 80–92%^{18,24} and complication rates related to the procedure are within acceptable range. In a recent study, only 4% patients had CS dissection and 2% had a cardiac vein or CS perforation.² Complete heart block and cardiac arrest occurred in 1.2% of patients. Early lead dislodgment requiring repositioning occurs in 5% patients.¹⁸ The left ventricular lead may also become dislodged and is reported to occur in 4–6% of patients.^{2,25}

Capture Thresholds

Long-term pacing thresholds in reported studies are less than 2 volts with a mean impedance of 694 ± 243 Ohms and sensing mean amplitude of 11 mV.¹⁸ Acceptable capture threshold can be achieved in most cases with reported mean pacing threshold of around 1 V/0.5 ms at the time of implantation and increased slightly up to <2 V/0.5 ms during follow-up.^{20,26} LV pacing thresholds of epicardial leads placed through the CS venous structures are usually greater than RV pacing thresholds. In some BiV cases it is difficult to find a LV pacing site below 3.0 V. An acute LV pacing threshold of greater than 3.0 V is considered too high for a

chronic system implant. Recent study has shown that chronic CRT may actually lead to a decrease in ventricular capture thresholds over time. The etiology for this cannot be explained by improving inflammation at the implant site but may be due to a direct result of CRT. In the MIRACLE study the threshold increased from 2.09 ± 1.43 to 2.27 ± 1.17 volts in a patient randomized to no BiV pacing and reduced from 2.00 ± 1.65 to 1.74 ± 0.78 volt in a patient with BiV pacing.²⁷ Delivering electrical current to two pacing leads with different impedances connected in parallel does not result in a clinically significant increase in pacing threshold in one small study when compared to the pacing thresholds measured from each lead individually.²⁸

The surface of the RV (+) electrode has an important effect on the LV (–) capture. The larger the anode, the lower the LV(–) pacing threshold. As a consideration, the pacing threshold of a LV (–) unipolar lead can be minimized by using the distal shocking coil as the RV anode (+) in ICD systems.²⁹

CRT to date has been delivered mostly via simultaneous BiV pacing pulses, using tied outputs. Newer BiV devices have independent programmable outputs for both right and LV. Aside from potential hemodynamic advantages of programmable differential timing of right and left ventricular pacing, there may be electrotonic advantages as well. If both pacing pulses are delivered simultaneously from capacitive coupled outputs programmed to different pacing voltages, this will create unexpected output-to-output current pathways, and may increase capture thresholds. Capture thresholds of two sites during simultaneous BiV pacing can be higher than the capture thresholds of those same sites paced individually. Separating the simultaneous pacing pulses by 1 ms avoids complex intersite current pathways and keeps capture thresholds to their individual lowest levels.³⁰

LV and RV Pacing Sites

Pacing the midlateral area or posterior area of the LV in patients with left bundle branch block (LBBB) leads to greater improvements in pulse pressure and dP/dt than pacing anterior or apical LV sites.³¹ The superior anterior septum can be paced from the anterior interventricular vein, the LV lateral free wall from the left marginal vein, and the posteroinferior portion of the LV from the left posterior vein. In 75% of patients the septal RV pacing QRS duration is shorter than the apical RV pacing

QRS duration for a given LV pacing site. Therefore, if only one RV site is to be selected for a BiV system, the mid-RV septum or outflow tract is preferable whenever possible.^{32,33}

Anodal Capture

In second-generation devices with independent ventricular outputs the RV ring electrode can be included in both LV and RV pacing configurations. Stimulation initiated at the RV ring electrode (i.e., anodal capture) has been observed. Steinhaus et al. evaluated the RV lead ring effects on anodal capture.³⁴ They showed that multiple RV lead types exhibit anodal capture and therefore loss of sequential pacing can occur with all lead types. They found no statistical significance in anodal capture threshold between ring types or fixation types. Collectively there is no statistical significance in anodal capture threshold for the RV lead positions studied. According to their data, the majority of patients can be programmed $> 2 \times$ safety margin chronically without anodal capture.

Diaphragmatic Stimulation

Optimal BiV pacing requires insertion of a lead in a posterior, posterolateral, or lateral coronary vein. Their epicardial position and proximity to the diaphragm and left phrenic nerve make diaphragmatic stimulation more likely than with conventional pacing. Clinically, diaphragmatic stimulation is posture dependent, particularly in left decubitus position, while the LV capture threshold does not change significantly according to body positions.³⁵ Because it is often position dependent, diaphragmatic stimulation can occur clinically even after negative intraoperative supine testing. A low LV capture threshold is thus important to allow safe reprogramming if unexpected diaphragmatic stimulation develops.

Pacing and Capturing Complications

Left ventricular pacing lead through the CS has higher dislodgment rate as compared to right ventricular pacing lead. Loss of LV pacing capture should be ruled out in patients with worsening of congestive heart failure. Patients with a higher initial LV pacing threshold are more likely to experience dislodgment. Dislodgment is 1.5 times more likely to occur in patients with a posterior lead position.³⁶ Perforation of the CS lead should also be

considered in any patient with an acute increase in left ventricular pacing threshold or loss of left ventricular pacing capture.

Exit block at the CS lead may limit the efficacy of ventricular resynchronization therapy. Despite programmed safety margin of the stimulation parameters, exit block occurs in a high percentage of patients in early studies with BiV pacemaker systems.³⁷ With the availability of separate programming of the left and right ventricle output in BiV devices the difficulty of exit block can be overcome.

PROGRAMMING THE BIVENTRICULAR DEVICE: ATRIAL VENTRICULAR TIMING

Acute Optimization of the AV Interval

The majority of acute benefit resulting from CRT is on measures of systolic response and is independent of the programmed AV interval. Yet, left-sided AV timing is clearly an important consideration in the programming of resynchronization devices. Appropriate AV interval timing can maximize the benefit of CRT and if programmed poorly, has the potential to curtail the beneficial effects. Unfortunately, there are no prospectively tested criteria that define the best methods of measuring or assessing the effects of AV interval programming. The most widely used measures are acute hemodynamic measures of forward output and echo/Doppler assessments.^{38–45}

The goals of AV interval programming during CRT are to select the AV interval that optimizes both left ventricular filling and forward stroke volume (Figs. 8, 9). In Figure 8, three mitral inflow Doppler profiles are shown. In the top panel, during baseline sinus rhythm with at a prolonged PR interval of 240 ms, mitral E and A waves are fused. This is due to atrial contraction beginning in early diastole resulting in atrial contraction becoming superimposed upon the early left ventricular filling phase. This causes curtailed ventricular filling. If atrial relaxation then occurs when left ventricular end-diastolic pressure rises, so that it exceeds left atrial pressure, diastolic mitral regurgitation may be observed. The lower left panel illustrates a very short programmed AV interval of 80 ms. In this instance atrial contraction occurs at the onset of ventricular systole, against a closed mitral valve. Programming the AV interval to 150 ms results in

Figure 8. Doppler profile mitral inflow: effects of varying AV interval during resynchronization therapy.

separation of the early filling and atrial contraction phases, normalizing the filling pattern as shown in the bottom right panel. Figure 9 demonstrates that forward output, as assessed by aortic valve velocity time integral, also improves with the AV interval that maximizes filling.⁴³

Currently, most implanting physicians place the right atrial lead in the right atrial appendage or high right atrium for sensing and pacing. However, timing of mechanical left atrial to left ventricular events during CRT may differ markedly depending upon whether the atrium is sensed or paced. The presence of discrete atrial conducting pathways, in close relation to the sinus node, facilitates conduc-

Figure 9. Doppler profile aortic valve flow: effects of varying AV interval during resynchronization therapy.

tion from the right to the left atria during sinus rhythm. Pacing at a distance from these pathways, at a location such as the right atrial appendage, results in a slower conduction through atrial myocardial tissue. This can lead to marked conduction delays to the left atrium. This is a particularly important concern during CRT with intact AV nodal conduction, due to the need to provide the resynchronization therapy in advance of native ventricular depolarization. It is unclear if the benefit of CRT is fully achieved if fusion is present between native conduction with bundle branch block and BiV stimulation. In addition to these considerations, the optimal AV interval determined for BiV stimulation may differ from the optimal AV interval to achieve resynchronization with LV stimulation alone. The AV interval programming issues become even more complex if the patient is expected to alternate between atrial sensed and paced events. Table 3 summarizes some of the key considerations in AV interval programming.³⁸⁻⁴⁶

Data from the PATH CHF and PATH II European trials of CRT evaluated acute AV interval optimization by hemodynamic measures. These studies determined the optimal AV interval by assessing pulse pressure and dP/dt measures. There was no complete agreement between these measures on the optimal AV delay. Using maximum pulse pressure as an endpoint, the data show that programming the AV interval to correspond to the point of peak atrial pressure is optimal. Using dP/dt as an endpoint, a programmed AV interval at 50% of the PR interval was optimal in the presence of a QRS duration >150 ms. A programmed AV interval at 70% of the PR interval or even longer produced the greatest increase in dP/dt in those patients with shorter QRS duration, and interestingly, resulted in native and paced QRS fusion.⁴³

In clinical trials performed in United States, echo/Doppler measures are the most common

Table 3. Summary of Considerations in AV Interval Programming

Right atrial lead location?
Is the atrium sensed or paced?
Resynchronization achieved BiV or LV stimulation?
Endpoint assessment invasive hemodynamic or non-invasive echo/Doppler measures?
Supine rest vs. exercise AV interval?
Need for chronic reassessment and AV interval programming?

Figure 10. Noninvasive: "Ritter's Equation"; Ritter et al., PACE 1995 (abstract).

method used to determine AV interval programming. One Doppler method used in the MIRACLE studies is the Ritter method or equation. The Ritter equation is complex, but seeks to maximize trans-mitral inflow, prolong diastolic filling time and prevent early closure of the mitral valve. This method does not assess forward output (Fig. 10).⁴²

There are no published data relating Doppler-derived measures of acute hemodynamic measures of pulse pressure or dP/dt. Use of other technologies such as phonocardiography and noninvasive surrogates for pulse pressure are under investigation.

Chronic Optimization of the AV Interval

Most physicians following resynchronization devices do not attempt to provide chronic optimization of the AV interval either at rest or with activity. It is unknown if the acute AV interval programmed by whatever method at implantation remains optimal during follow-up. Data from the MIRACLE trial of CRT with BiV stimulation performed in the VDD mode used the Ritter method to optimize AV interval programming. Patients underwent AV interval optimization at predischarge, 3 and 6 months of follow-up. An AV delay averaging 100 ms was optimal in the majority of patients and remained stable over time.⁴⁴

In a further study, MIRACLE III, of resynchronization, right and left ventricular timing offsets were also studied. Atrial-ventricular interval optimization was performed according to the Ritter

method and then fixed. Alterations of V-V timing were performed and forward flow or stroke volume assessed. Interestingly, unlike AV interval programming, there was marked variability in the optimal V-V timing interval over time.⁴⁶

There are no chronic data available that provide insight into the best measures or endpoints for determining the optimal AV interval during activity states. Standard device features such as dynamic AV delay, have not been tested with chronic CRT. In the CONTAK CD trial of CRT, the AV interval was programmed short enough to insure complete BiV capture on treadmill testing, but these values were not correlated with echocardiographic measures.

REFERENCES

1. Cazeau S, Leclercq C, Lavergne T, et al. Effects of multisite biventricular pacing in patients with heart failure and intra-ventricular conduction delay. *N Engl J Med* 2001;344:873-880.
2. Abraham WT, Fisher WG, Smith AL, et al. Cardiac resynchronization in chronic heart failure. *N Engl J Med* 2002;346:1845-1853.
3. Yong P, Duby C. A new and reliable method of individual ventricular capture identification during biventricular pacing threshold testing. *Pacing Clin Electrophysiol* 2000;23:1735-1737.
4. Hart D, Luiza P, Arshad R, et al. Assessment of ventricular capture in patients with cardiac resynchronization devices: A simple surface electrocardiographic algorithm. *PACE* 2003;26:1083.
5. Ricci R, Ansalone G, Toscano S, et al. Cardiac resynchronization: Materials, technique and results. The InSync Italian registry. *Eur Heart J* 2000;2(Suppl. J):J6-J15.
6. Alonso C, Leclercq C, Victor F, et al. Electrocardiographic predictive factors of long-term clinical improvement with multisite biventricular pacing in advanced heart failure. *Am J Cardiol* 1999;84:1417-1421.
7. Kass DA, Chen CH, Curry C, et al. Improved left ventricular mechanics from acute VDD pacing in patients with dilated cardiomyopathy and ventricular conduction delay. *Circulation* 1999;99:1567-1573.
8. Leclercq C, Cazeau S, Le Breton H, et al. Acute hemodynamic effects of biventricular DDD pacing in patients with end-stage heart failure. *J Am Coll Cardiol* 1998;32:1825-1831.
9. Guidant Physician's System Manual Contak CD CRT-D 1823. Guidant Corporation, 2002.
10. Higgins S. The Implantable Cardioverter Defibrillator, A videotape and manual. Armonk, NY: Futura Publishing Co., Inc, 1997.
11. Betts TR, Allen S, Roberts PR, et al. Inappropriate shock therapy in a heart failure defibrillator. *Pacing Clin Electrophysiol* 2001;24:238-240.
12. Garcia-Moran E, Mont L, Brugada J. Inappropriate tachycardia detection by a biventricular implantable cardioverter defibrillator. *Pacing Clin Electrophysiol* 2002;25:123-124.
13. Kanagaratnam L, Pavia S, Schweikert R, et al. Matching approved "nondedicated" hardware to obtain biventricular

- pacing and defibrillation: Feasibility and troubleshooting. *Pacing Clin Electrophysiol* 2002;25:1066-1071.
14. Winters SL, Packer DL, Marchlinski FE, et al. Consensus statement on indications, guidelines for use, and recommendations for follow-up of implantable cardioverter defibrillators. North American Society of Electrophysiology and Pacing. *Pacing Clin Electrophysiol* 2001;24:262-269.
15. Higgins SL, Hummel JD, Niazi IK, et al. Cardiac resynchronization therapy for the treatment of heart failure in patients with intraventricular conduction delay and malignant ventricular tachyarrhythmias. *J Am Coll Cardiol* 2003;In press.
16. Auricchio A, Stellbrink C, Sack S, et al. Long-term clinical effect of hemodynamically optimized cardiac resynchronization therapy in patients with heart failure and ventricular conduction delay. *J Am Coll Cardiol* 2002;39:2026-2033.
17. Cazeau S, Ritter P, Lazarus A, et al. Multisite pacing for end-stage heart failure: Early experience. *Pacing Clin Electrophysiol* 1996;19:1748-1757.
18. Daubert JC, Ritter P, Le Breton H, et al. Permanent left ventricular pacing with transvenous leads inserted into the coronary veins. *Pacing Clin Electrophysiol* 1998;21:239-245.
19. Jais P, Douard H, Shah DC, et al. Endocardial biventricular pacing. *Pacing Clin Electrophysiol* 1998;21:2128-2131.
20. Walker S, Levy T, Rex S, et al. Initial United Kingdom experience with the use of permanent, biventricular pacemakers: Implantation procedure and technical considerations. *Europace* 2000;2:233-239.
21. Walker S, Levy T, Brant S, et al. Simultaneous utilization of an implantable automatic defibrillator in a patient with previously implanted bi-ventricular pacemaker for end-stage heart failure. *Arch Mal Coeur Vaiss* 1999;92:1795-1799.
22. Walker S, Levy T, Rex S, et al. Preliminary results with the simultaneous use of implantable cardioverter defibrillators and permanent biventricular pacemakers: Implications for device interaction and development. *Pacing Clin Electrophysiol* 2000;23:365-372.
23. Walker S, Levy T, Rex S, et al. Initial results with left ventricular pacemaker lead implantation using a preformed "peel-away" guiding sheath and "side-wire" left ventricular pacing lead. *Pacing Clin Electrophysiol* 2000;23:985-990.
24. Blanc JJ, Benditt DG, Gilard M, et al. A method for permanent transvenous left ventricular pacing. *Pacing Clin Electrophysiol* 1998;21:2249-2255.
25. Gras D, Mabo P, Tang T, et al. Multisite pacing as a supplemental treatment of congestive heart failure: Preliminary results of the Medtronic Inc. InSync Study. *Pacing Clin Electrophysiol* 1998;21:2249-2255.
26. Alonso C, Leclercq C, d'Allonnes FR, et al. Six year experience of transvenous left ventricular lead implantation for permanent biventricular pacing in patients with advanced heart failure: Technical aspects. *Heart* 2001;86:405-410.
27. Greenberg JM, Ransom S, DeLurgio DB, et al. Left ventricular remodeling during cardiac resynchronization therapy: Effect on ventricular dimension and stimulation threshold chronically after biventricular pacing. *J Am Coll Cardiol* 2002;39(5 Suppl. A):107A.
28. Alvarez LG, Gilligan DM, Knight BP, et al. Delivering current simultaneously to two pacing leads with different impedances does not result in increased pacing thresholds. *J Am Coll Cardiol* 2001;37(2 Suppl. I):106A.
29. Worley SJ, Gohn DC, Mandalakas NJ, et al. Biventricular pacing: The size of the anode is critical for successful capture of the LV. *Pacing Clin Electrophysiol* 2001;24(4 Suppl. II):618.
30. Stahmann J, Belalcazar A, Spinelli JC, et al. Staggered pacing pulses are required to maintain low individual site capture thresholds during simultaneous independent output biventricular stimulation. *Pacing Clin Electrophysiol* 2001;24(4 Suppl. II):623.
31. Auricchio A, Klein H, Tockman B, et al. Transvenous biventricular pacing for heart failure: Can the obstacles be overcome? *Am J Cardiol* 1999;83(Suppl. 5B):136D-142D.
32. Worley SJ, Gohn DC, Mandalakas NJ, et al. Biventricular pacing: For deducing the biventricular paced QRS duration, an LV + mid septal RV position is superior to an LV + RV apex position. *Pacing Clin Electrophysiol* 2001;24(4 Suppl. II):642.
33. Mortensen PT, Sogaard P, Jensen HK, et al. QRS prolongation during biventricular pacing predict a nonfavourable response to cardiac resynchronization and is most often seen in combination with an apical right ventricular pacing site. *Pacing Clin Electrophysiol* 2001;24(4 Suppl. II):56.
34. Steinhaus D, Suleman A, Vlach K, et al. Right ventricular anodal capture in biventricular stimulation for heart failure. *J Am Coll Cardiol* 2002;39(5 Suppl. A):107A.
35. Haw JM, Pinski SL, Murphy JK, et al. Diaphragmatic stimulation with biventricular pacing is frequent and often posture dependent. *Pacing Clin Electrophysiol* 2002;24(4 Suppl. II):551.
36. Giudici M, Payne V, Mester S, et al. Factors that predict dislodgment of a coronary venous lead designed for left ventricular function. *Pacing Clin Electrophysiol* 2002;24(4 Suppl. II):548.
37. Weretka S, Michaelsen J, Hilbel T, et al. Incidence of coronary sinus exit block in biventricular pacemaker systems: A prospective Holter study. *Pacing Clin Electrophysiol* 2002;24(4 Suppl. II):647.
38. Nelson GS, Curry CW, Wyman BT, et al. Predictors of systolic augmentation from left ventricular preexcitation in patients with dilated cardiomyopathy and intraventricular conduction delay. *Circulation* 2000;101:2703-2709.
39. Auricchio A, Ding J, Spinelli JC, et al. Cardiac resynchronization therapy restores optimal atrioventricular mechanical timing in heart failure patients with ventricular conduction delay. *J Am Coll Cardiol* 2002;39:1163-1169.
40. Stellbrink C, Breithardt OA, Franke A, et al. Impact of cardiac resynchronization therapy using hemodynamically optimized pacing on left ventricular remodeling in patients with congestive heart failure and ventricular conduction disturbances. *J Am Coll Cardiol* 2001;38:1957-1965.
41. Saxon LA, Hourigan L, Guerra P, et al. Influence of programmed AV delay on left ventricular performance in biventricular pacing systems for treatment of heart failure. *J Am Coll Cardiol* 2000;35(2A):116A.
42. Ritter P, Dib JC, Mahaux V, et al. New method for determining the optimal atrio-ventricular delay in patients paced in DDD mode for complete atrioventricular block (abstract). *Pacing Clin Electrophysiol* 1995;18(4 Suppl. II):237.
43. Auricchio A, Kramer A, Spinelli JC, et al. for the PATH CHF I & II Investigator Groups. Can the optimum dosage of resynchronization therapy be derived from the intracardiac electrogram? *J Am Coll Cardiol* 2002;39(5 Suppl. A):878-874.
44. Delurgio D. NASPE Consensus Conference, 2002.
45. Nelson GS, Berger RD, Fetis BJ, et al. Left ventricular or biventricular pacing improves cardiac function at diminished energy cost in patients with dilated cardiomyopathy and left bundle-branch block. *Circulation* 2000;102:3053-3059.
46. Leclercq C, Faris O, Tunin R, et al. Systolic improvement and mechanical resynchronization does not require electrical synchrony in the dilated failing heart with left bundle-branch block. *Circulation* 2002;106:1760-1763.