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Mini-review:

Pacing technology: advances in pacing threshold management

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Abstract: Over the last five decades, pacemaker therapy has undergone remarkable technological advances with increasing sophistication of pacemaker features. However, device longevity has remained one of the major issues in pacemaker design ever since the first endocardial pacing lead implantation in 1958. In addition to various hardware design to enhance device longevity, software-based solutions to minimize pacing energy and yet with good safety margin have also been developed. Together with desire and need of fully automatic pacing system in increasingly busy pacemaker clinic, several manufacturers have introduced different automatic threshold management algorithm. This article summarizes the current state-of-the-art management in pacing threshold in the modern pacemakers.

Key words: Pacemaker, Threshold management, Autocapture
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1 Introduction

With the aging population, there has been an increasing trend in cardiac pacemaker implantation worldwide. In the United States, up to 2.25 million electronic pacemakers were implanted in the period from 1990 to 2002, and the annual implantation rate increased almost 3-fold (Maisel, 2006). Despite remarkable technologic advances of the pacemaker therapy as reflected by the increase in the number of circuitry components from 2–3 transistors in early pacemakers to about one million components in modern systems (Ohm and Danilovic, 1997), the need and desire to lengthen device longevity have remained one of the major issues in pacemaker design ever since the first endocardial pacing lead implantation in 1958. Hardware improvements to improve device longevity, including high-energy density battery, high impedance, and low threshold leads, have been developed. Likewise, software-based solutions to pace the cardiac chamber of interest with the lowest feasbile energy and good safety margin have also been developed. This article reviews the current state-of-the-art management in pacing threshold in the modern pacemakers.

2 Pacing threshold management

Pacing threshold exhibits significant inter-individual variations. Even in an individual, pacing threshold may vary over time because of spontaneous threshold rise after implantation, microdislodgment of pacemaker lead, diurnal changes, and changes secondary to drugs and/or myocardial ischemia (Schaldach *et al.*, 1990; Curtis *et al.*, 1991). However, these variations in pacing thresholds may narrow the safety margin of pacing stimulation, thus rasing potential safety issues. On the other hand, the unnecessary high pacing output adversely shortens battery life of pulse generator. Thereby, the ability to automatically track threshold and to adjust the pacing outputs accordingly will maximize patient safety and minimize battery drain for pacing. Table 1 lists the reasons for automatic pacing threshold management. Several manufacturers have developed algorithms to detect pacing thresholds based on either evoked response (ER) or impedance. The threshold data can be used (1) on a beat-by-beat basis to ensure a paced response or (2) intermittently to adjust output parameters.

Table 1 Potential benefits of capture management*

Potential benefits
Increase in battery drain (e.g., sensors, electrogram monitoring, and multisite pacing)
Increase in battery longevity
Two-third of patients will be alive at the time of battery replacement
Pacing for populations such as those with AF and after atrioventricular nodal ablation
Reduction in battery size
Physiologic/medical variation in threshold
Reduction in time for pacemaker programming

* Adapted from Lau and Siu (2010)

2.1 Beat-by-beat pacing threshold management

St. Jude Medical first introduced the Autocapture™ pacing system in a single chamber Microny™ pacemaker in 1995. It verifies a response (capture or myocardial depolarization) to each pacing stimulus and automatically adjusts the pacing output accordingly. Specifically, the algorithm opens an ER detection window after a ventricular pacing stimulus for 46 ms after a 14-ms blanking period, and the detection of an ER is used to diagnose capture (Fig. 1). When an ER is not detected (loss of capture), a high energy back-up pulse of 4.5 V will be discharged 100 ms after the ventricular pacing stimulus in order to avoid long pauses. If two consecutive high energy back-up pulses have been delivered, a stimulation threshold search will initiate with increasing output voltage until two consecutive captures ensue. After detection of threshold, safety margin of 0.3 V is added. For single chamber devices (Microny and Regency SR), automatic threshold search is performed once every 8 h in order to avoid pacing at high output due to diurnal fluctuation in threshold. In dual chamber devices, ventricular stimulation threshold search is performed with a shortened A-V interval (50 ms (Ap) or 25 ms (As)) to ensure overdrive of intrinsic ventricular rhythm.

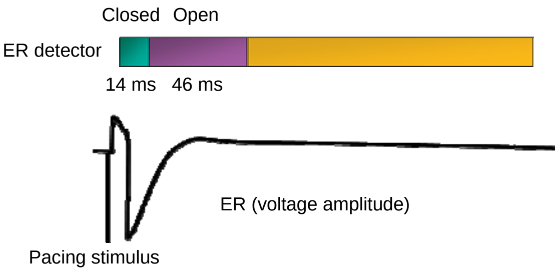

Fig. 1 Evoked response (ER) detection

After a ventricular pacing stimulus, the algorithm opens an ER detection window for 46 ms after a 14-ms blanking period, and the detection of an ER (voltage) is used to diagnose capture

Table 2 Factors affecting capture detection*

Factors
Electrode polarization
Fusion beats (false negative)
Ventricular capture intrinsic beat
Pseudofusion beats (false positive)
Pacing spike (and failure of capture) intrinsic beat
Algorithm related: unipolar pacing, bipolar sensing
Adequate ER
Other applications: atrial, epicardial, and left ventricle

* Adapted from Lau and Siu (2010)

The efficacy as well as the safety of the capture management alogrithm depends very much on accuracy of detection of ER. Table 2 lists factors that affect ER detection. One major challenge is the difficulty to discriminate the ER signal from the pace-induced after potential. For instance, a large electrode polarization artifact relative to size of ER can adversely affect ER detection. The use of low polarization electrodes (made possible by increasing the microscopic electrode-tissue interface area) (Schaldach *et al.*, 1990), as well as a biphasic waveform (comprises a fast precharge followed by a negative postcharge to minimize polarization effect) (Curtis *et al.*, 1991), can reduce the problem and enhance accuracy of ER detection. In fact, it has been shown in 45 patients using a modified fast prepulse on Autocapture™ algorithm with leads from two manufacturers (Medtronic 4024 Cap Sure, and Pacesetter 1450 K/T and 1470 T leads) that although ER was not affected by the type of pacing pulse, the polarization artifact was significantly less during the modified pulse compared with the conventional pacing pulse, thus improving the efficacy of the Autocapture™ algorithm (94% vs. 71% successful ER detection) (Provenier *et al*., 2000). For safety issue, it is recommended that an ER amplitude >2.5 mV is needed to activate the Autocapture™ algorithm. Although majority of patients (93% of 60 patients in one study) (Schuchert *et al.*, 2000) have ER amplitude large enough for the activation of this algorithm, no clinical or conventional electrical parameters could accurately predict the size of the ER signal. Recently, a new ER algorithm (ACP™ confirm from St. Jude Medical) measuring the depolarization integral (area) instead of ER signal amplitudes (voltage) to determine ER has enhanced the accuracy of capture verification; in fact, the algorithm allows ER determination even with old high-polarization bipolar leads (Fig. 2). Because of the enhanced sensitivity, discrimination of small atrial ER from pace-induced afterpotential has become possible. This is particularly in the extension of automatic capture management in atrial pacing as the small atrial electrical signals pose sigificant difficulties in the discrimination between ER signal and pace-induced afterpotential. In fact, the beat-to-beat capture verification has recently been extened to atrial stimulation in Zephyr pacemaker using this new algorithm.

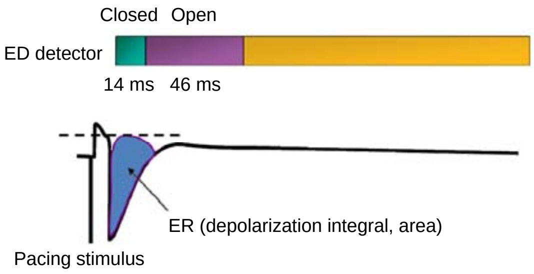

Fig. 2 Evoked response (ER) detection with depolarization integral (area) to determine ER

The one-year stability of the algorithm has been tested in a multicenter study in 113 patients implanted with Pacesetter Microny SR+ (Clarke *et al.*, 1998). ER was satisfactory for Autocapture™ algorithm in 90% of patients. While the ER remained stable over time, it correlated poorly with the R wave at implantation. Nonetheless, the chronic pacing thresholds measured at the clinic correlated well with that derived from Autocapture™ algorithm (Clarke *et al.*, 1998). More importantly, there was no failed ventricular capture, and back-up pulses were used in 1.1% of all paced beats as verified with 24 h electrocardiograph (ECG) monitoring (fusion or pseudofusion beats (87%), undersensing of either R wave or ER (4.6%), and loss of capture (7%)) (Clarke *et al.*, 1998). Consistent results from the Autocapture™ algorithm in medium term for safety and efficacy have also been published (Gelvan *et al.*, 2003; Medtronic AT500 Technical Manual). In comparson with the factory-set pacemaker setting (5 V), Autocapture™ algorithm reduced the energy drain in the Microny SR+ (with 0.35 A·h), which was translated into an increased device longevity by 53%. For the Regency SR+ with a larger battery (0.79 A·h), the increase in device longevity was more remarkable (245%). However, when the conventional output was reduced to 2.5 V, the benefit of Autocapture™ algorithm on battery life was less impressive (Love *et al.*, 1997; Leung *et al.*, 1998).

In addition to the algorithm from St. Jude Medical, the automatic capture algorithm from Boston Scientific also provides a beat-to-beat verification of myocadial capture based on the ventricular ER. The ventricular voltage output was automatically adjusted to 0.5 V above the measured threshold. In case of loss of capture, a back-up pacing pulse 1.5 V higher than the measured threshold is delivered 100 ms after the primary stimulus. When loss of capture is confirmed for two cycles out of four beats, automatic threshold test will be initated to check for the new threshold.

The main benefit of any automatic capture management algorithm is patient safety by ensuring effective capture upon threshold changes in different physiological and pathological conditions. In addition, simplification of threshold programming could be anticipated as the Autocapture™ threshold is well correlated with bedside threshold assessment. In patients with chronic high pacing threshold, the energy saving would be more important. However, fusion/pseudofusion beats remain the main limitation in terms of limiting battery energy reduction and erroneous threshold determination (Savelieva and Camm, 2000).

2.2 Intermittent pacing threshold management

In addition to beat-to-beat pacing threshold management, pacing threshold can be detected intermittently, accompanied with pacing output adjustment. The Kappa 700 pacemakers from Medtronic are equiped with an ER-based threshold assessment: the pacing threshold search (ambulatory) and capture management threshold test (bedside). During the threshold test, the threshold at the rheobase is determined at 1 ms by progressively decreasing amplitude until loss of capture, followed by amplitude increment until capture confirmed. The chronaxie is then determined by doubling the programmed amplitude, and decreasing the pulse width (followed by increasing amplitude to capture). According to this data, a recommended pacing setting could then be determined. The physician can choose the ambulatory threshold data to automatically adjust the threshold (adaptive), or to use for monitoring only, or the algorithm can be turned off. The ventricular capture management can be programmed to activate every 15 min for 42 d; however, it is not a beat-by-beat threshold tracking algorithm. According to a predictive estimation of the device longevity of Medtronic Kappa 700 series pacemakers featuring three automatic algorithms including Capture management, Sinus Preference, and Search AV in 22 patients, the estimated overal longevity with all three features was (106.3±8.4) months with (8.1±5.8) months longer than that without Capture management and Search AV (Gelvan *et al.*, 2003).

Likewise, the Logos pacemakers from Biotronik interrmittenly measure the ER signals from several successful capture beats to generate a reference curve for pacing output determination (Guilleman *et al.*, 1999; Novak *et al.*, 1999). Although there are no back-up pacing pulses, persistent loss of capture results in an increase of pulse output in 2-V steps. After a programmable period of time, the output is reduced to the programmed value. This algorithm ensures patient safety through beat-by-beat capture verification.

3 Summary

The increased sophistication in pacemaker technology has led to pacemaker features that average pacemaker implanters may not have the time either to understand or to program appropriately, as well as prolonged pacemaker interrogation time during regular follow-up (Seidl *et al*., 1998). The automaticity of the optimization of many pacing parameters has significantly faciliated daily clincal management. In fact, programming of threshold can be simplified as the algorithm-determined threshold was significantly correlated with conventional threshold assessment. The main benefit of automatic pacing threshold algorithm is to maintain effective capture during threshold changes, to prolong device longevitym and to ensure patient safety. These algorithms have been demonstrated to be safe and useful for prolonging device longevity (Guilleman *et al.*, 1999; Israel *et al.*, 2000; Gelvan *et al.*, 2003).

References

Clarke, M., Liu, B., Schüller, H., Binner, L., Kennergren, C., Guerola, M., Weinmann, P., Ohm, O.J., 1998. Automatic adjustment of pacemaker stimulation output correlated with continuously monitored capture thresholds: a multicenter study. European Microny Study Group. *Pacing and Clinical Electrophysiology*, **21**(8):1567-1575. [doi:10.1111/j.1540-8159.1998.tb00244.x]

Curtis, A.B., Vance, F., Miller, K., 1991. Automatic reduction of stimulus polarization artifact for accurate evaluation of ventricular evoked responses. *Pacing and Clinical Electrophysiology*, **14**(4 Pt 1):529-537. [doi:10.1111/j.1540-8159.1991.tb02825.x]

Gelvan, D., Crystal, E., Dokumaci, B., Goldshmid, Y., Ovsyshcher, I.E., 2003. Effect of modern pacing algorithms on generator longevity: a predictive analysis. *Pacing and Clinical Electrophysiology*, **26**(9):1796-1802. [doi:10.1046/j.1460-9592.2003.t01-1-00272.x]

Guilleman, D., Bussillet, H., Scanu, P., Raguin, D., Aisenfarb, J.C., Bienvenu, P., Meunier, J.F., Canot, N., 1999. Output adjustment with the DDD pacemaker with automatic capture-control algorithm. *Progress in Biomedical Research*, **4**:291-294.

Israel, C.W., Gascon, D., Nowak, B., Campanale, G., Pascotto, P., Hartung, W., Lellouche, D., Pulsar/Selute Picotip VDD Study Group, 2000. Diagnostic value of stored electrograms in single-lead VDD systems. *Pacing and Clinical Electrophysiology*, **23**(11 Pt 2):1801-1803.

Lau, C.P., Siu, C.W., 2010. Pacing Technology and Its Indications: Advances in Threshold Management, Automatic Mode Switching, and Sensors. *In*: Saksena, S., Camm, A.J., Boyden, P.A., Dorian, P., Goldschlager, N. (Eds.), Electrophysiological Disorders of the Heart. Elsevier/Churchill Livingstone, Philadelphia, USA.

Leung, S.K., Lau, C.P., Lam, C.T., Tse, H.F., Tang, M.O., Chung, F., Ayers, G., 1998. Programmed atrial sensitivity: a critical determinant in atrial fibrillation detection and optimal automatic mode switching. *Pacing and Clinical Electrophysiology*, **21**(11 Pt 2):2214-2219. [doi:10.1111/j.1540-8159.1998.tb01155.x]

Love, C.J., Wilkoff, B.L., Hoggs, K.S., 1997. Incidence of mode switch in a general pacemaker population. *Pacing and Clinical Electrophysiology*, **20**:1137.

Maisel, W.H., 2006. Pacemaker and ICD generator reliability: meta-analysis of device registries. *The Journal of the American Medical Association*, **295**(16):1929-1934. [doi:10.1001/jama.295.16.1929]

Medtronic AT500 Technical Manual. Medtronic, Minn., USA.

Novak, M., Kamaryt, P., Haeuser, T., Mach, P., 1999. Simplifying pacemaker follow-up using automatic threshold determination in ventricle. *Progress in Biomedical Research*, **4**:287-290.

Ohm, O.J., Danilovic, D., 1997. Improvements in pacemaker energy consumption and functional capability: four decades of progress. *Pacing and Clinical Electrophysiology*, **20**(1 Pt 1):2-9. [doi:10.1111/j.1540-8159.1997.tb04805.x]

Provenier, F., Germonpre, E., de Wagter, X., 2000. Improved differentiation of the ventricular evoked response from polarization by modification of the pacemaker impulse. *Pacing and Clinical Electrophysiology*, **23**(12):2073-2077. [doi:10.1111/j.1540-8159.2000.tb00779.x]

Savelieva, I., Camm, A.J., 2000. Clinical relevance of silent atrial fibrillation: prevalence, prognosis, quality of life, and management. *Journal of Interventional Cardiac Electrophysiology*, **4**(2):369-382. [doi:10.1023/A:1009823001707]

Schaldach, M., Hubmann, M., Weikl, A., Hardt, R., 1990. Sputter-deposited TiN electrode coatings for superior sensing and pacing performance. *Pacing and Clinical Electrophysiology*, **13**(12 Pt 2):1891-1895. [doi:10.1111/j.1540-8159.1990.tb06911.x]

Schuchert, A., Ventura, R., Meinertz, T., 2000. Automatic threshold tracking activation without the intraoperative evaluation of the evoked response amplitude. AUTOCAP Investigators. *Pacing and Clinical Electrophysiology*, **23**(3):321-324. [doi:10.1111/j.1540-8159.2000.tb06756.x]

Seidl, K., Meisel, E., Vanagt, E., Ottenhoff, F., Hess, M., Hauer, B., Zahn, R., Senges, J., 1998. Is the atrial high rate episode diagnostic feature reliable in detecting paroxysmal episodes of atrial tachyarrhythmias? *Pacing and Clinical Electrophysiology*, **21**(4 Pt 1):694-700. [doi:10.1111/j.1540-8159.1998.tb00125.x]
