Int J Clin Exp Med 2015;8(4):6079-6084
www.ijcem.com /ISSN:1940-5901/IJCEM0005972

Original Article

Clinical observation of atrial threshold monitoring algorithm: a single center experience

Jianqing She[1,2], Jing Zhou[4], Zhan Hu[3], Yulong Xia[4]

[1]Department of Cardiovascular, First Affiliated Hospital of Medical College, Xi'an Jiaotong University, Xi'an, PR China; [2]Key Laboratory of Environment and Genes Related to Diseases, Ministry of Education, Xi'an, PR China; [3]Peking Union Medical College Hospital, Beijing, PR China; [4]Department of Cardiovascular Medicine, First Hospital of Peking University, Beijing, PR China

Received January 15, 2015; Accepted March 24, 2015; Epub April 15, 2015; Published April 30, 2015

Abstract: Objective: To observe the atrial capture management in an atrial threshold monitoring algorithm. By calculating the enabling rate of the atrial threshold monitoring algorithm and comparing atrial thresholds measured automatically and manually, we evaluate its safety, reliability and applicability in clinical practice. Methods and results: Data were collected at implant, start of atrial threshold monitoring, visits scheduled 1 month, 2 months and 4 months thereafter, and upon notification of adverse events. Atrial threshold monitoring algorithm was enabled in 94 patients, while in 38 not, indicating an enabling rate of 71.2%. Causes of the unsuccessful attempts to enable automatic atrial threshold include tachycardia (2, 5.3%), and atrial safety margin not met (36, 94.7%). A total of 88 pairs of atrial thresholds measured automatically and manually were gained. The auto threshold was 0.528 ± 0.270 V, and the manual threshold was 0.580 ± 0.223 V. There is a strict correlation between the automatic measurements and those conducted manually by the physician with a $P < 0.05$. No significant differences were observed during the 1-month, 2-month and 4-month follow-up. Conclusion: Atrial threshold monitoring algorithm is safe, reliable and applicable over time. Atrial threshold monitoring tested atrial threshold was demonstrated to be clinically equivalent to the manual atrial threshold test. The addition of atrial threshold monitoring will benefit the patients by reducing energy cost and enhancing pacemaker safety.

Keywords: Pacemaker, atrial capture management, ACap™Confirm

Introduction

Modern pacemakers have made automatic assessment of pacing threshold possible. By automatically testing and adjusting pacing threshold, we can minimize battery depletion, improve patient safety and increase pacemaker longevity.

Automatic detection of ventricular capture already exists and has been used in medical practice for a long time [1-3]. However, automatic atrial threshold monitoring has been proved difficult because P wave is relatively small and is prone to evoke response undersensing [4].

EnPulse™ (Medtronic Inc., MN, USA) and Zephyr® (St. Jude Medical, MN, USA) are two major kinds of pacemakers that can process automatic atrial threshold measurement. The automatic threshold of EnPulse™ implantable pacemaker has already been widely studied and used in clinical practice [5-8]; however, the automatic atrial threshold measurement of Zephyr®, defined as ACap™Confirm, is lack of formal published clinical studies. Our study aims to test the clinical safety and applicability of this atrial threshold monitoring algorithm and try to find predictors of enabling rate of ACap™Confirm.

Methods

Study protocol

The purpose of atrial threshold monitoring clinical study was to evaluate the atrial threshold monitoring algorithm. The primary objective was to access the clinical equivalence of auto-

Table 1. Patient characteristics

Age	70 ± 7
Male gender (n, %)	56/132 (42)
Hypertension (n, %)	112/132 (85)
Structeral heart disease (n, %)	36/132 (27.3)
Heart failure (n, %)	8/132 (6)
Diabetes (n, %)	20/132 (15)
Sick sinus syndrome (n, %)	112/132 (85)
Atrial ventricular block (n, %)	20/132 (15)
Atrial fibrillation (n, %)	28/132 (21)
β-blockers (n, %)	32/132 (24)
Amiodarone (n, %)	4/132 (3)
Propafenone (n, %)	16/132 (12)

matic and manual threshold measurements at different follow-up visits.

Patients with class I or II indications for dual-chamber pacing received a Zephyr® DDDR pacemaker. Devices were implanted in nonrandomized manner according to clinical profile and device availability. Patients in the study gave written informed consent.

A total of 132 patients were enrolled in the study. Data were collected at implant, start of atrial threshold monitoring, visits scheduled 1 month, 2 months and 4 months thereafter. A manual measurement threshold using atrial amplitude auto-decrement test with a voltage step of 0.25 V was compared with the atrial pacing threshold assessed by atrial threshold monitoring algorithm test using the same pulse width (0.4 ms) and an amplitude auto-decrement with a 0.25 voltage step. Clinical equivalence was defined as a difference in mean value that lies between -0.25 and +0.5 V. It was calculated that 20 successful measurements would be needed to show 95% clinical equivalence. The operating physician was allowed to perform the manual test but not the automatic setup, so that they were blinded to the equivalence results. The atrial threshold monitoring test results were available in the device memory.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation range, while categorical data were expressed as the frequency and percentage of subjects. After checking the normality of distributions by means of the Kolmogorov-Smirnov test, comparisons between continuous variables were made by t-test or nonparametric test for independent or paired samples. Correlation between manually and automatically measured threshold values was evaluated by Spearman's test for pooled data. Predicted values of probability were used to evaluate the influencing factors of enabling atrial threshold monitoring algorithm.

Description of the atrial threshold monitoring algorithm

The Zephyr® automatic threshold monitoring algorithm is defined as ACap™Confirm. As mentioned earlier, owing to the small amplitude of atrial-evoked response, atrial captures are prone to be undersensed. As a result, ACap™Confirm use pacing depolarization integral to calculate atrial-evoked response [9], in order to decrease the influence of artifact during measurement. The atrial threshold monitoring algorithm measures the atrial pacing threshold automatically on a beat-to-beat basis.

Before starting this function, initializing test must be done. When atrial-evoked response/artifact is bigger than 2:1, and the safety margin is in accordance with the initial output, atrial threshold monitoring algorithm is recommended enabled and automatic measurement of atrial threshold begins. Measuring output will be either 3.875 V when pacing output is above 3.875 V, or the present output when pacing output is below 3.875 V. The output decrease by 0.125 V per measurement, until three exactly same outputs confirm loss of capture and back-up pulse is released. Tested threshold plus additional 0.125 V will remain the final output until the next follow-up. Atrial threshold monitoring algorithm will be unable if the atrial output is inhibited at the follow-up. The atrial pacing threshold is recorded and stored in the device memory, and atrial pacing outputs are adjusted based on the measurement. As the test is realized with bipolar pulse, atrial bipolar leads are necessary.

Results

Patient demographics

132 patients were enrolled in the study and all underwent pacemaker implantation. All had

Table 2. Average manual threshold, lead impedance, and sensitivity for ACap™Confirm

	Enabled group	Not enabled group	P
Manual threshold (V)	0.61 ± 0.21	0.63 ± 0.22	> 0.05
Lead impedance (Ω)	486.4 ± 94.1	437.8 ± 72.0	> 0.05
Sensitivity (mV)	3.58 ± 1.16	3.50 ± 1.41	> 0.05

Table 3. Summary of all obtained automatic and manual threshold measurements

	Manual thresholds	Automatic thresholds	Difference
	(Mean ± SD)	(Mean ± SD)	(Mean ± SD)
Pooled data	0.528 ± 0.270	0.580 ± 0.223	0.085 ± 0.060
1st month	0.550 ± 0.194	0.517 ± 0.226	0.083 ± 0.061
2rd month	0.500 ± 0.000	0.417 ± 0.072	0.083 ± 0.072
4th month	0.708 ± 0.577	0.750 ± 0.433	0.125 ± 0.000

endocardia bipolar atrial leads. All newly implanted leads were steroid-eluding. Indications for pacemaker implantation include Sick Sinus Syndrome and Atrial Ventricular Block; The average percentage of atrial pacing is 72 ± 6% in the patients with Sick Sinus Syndrome and 14 ± 4% in the patients with Atrial Ventricular Block. Clinical characteristics of the patients are reported in **Table 1**.

Applicability of atrial threshold monitoring algorithm

Applicability of atrial threshold monitoring algorithm is defined as the percentage of patients who had atrial threshold monitoring enabled. The atrial threshold monitoring measurement were achieved in 94 patients out of 132 patients who had pacemaker implantation, which means the enabling rate of atrial threshold monitoring algorithm is 71.2%. In the remaining 38 patients, atrial threshold monitoring algorithm failed because of ongoing supraventricular tachycardia in 2, and safety margin not meet in 36. The average manual threshold, lead impedance, and sensitivity for atrial threshold monitoring enabled and not enabled groups are showed in **Table 2**.

Clinical equivalence of atrial threshold monitoring algorithm

For patients suitable for enabling atrial threshold monitoring algorithm, we measured their automatic and manual threshold at 1 month, 2 months and 4 months follow-up. A total of 88 pairs of automatic and manual atrial thresholds were achieved. The atrial threshold monitoring algorithm demonstrated an automatic threshold of 0.528 ± 0.270 V vs. a manual test of 0.580 ± 0.223 V. The mean difference was 0.085V ± 0.060 V. A significant correlation was observed between thresholds measured manually and automatically (Spearman's Test, Rho = 0.539, P < 0.05). Clinical equivalence of automatic and manual threshold was defined prospectively as a difference in the mean value that lies with 95% confidence between -0.25 V and 0.5 V. The 95% interval was (0.025, 0.145) and the threshold differences were never outside of the range of clinical equivalence. **Table 3** and **Figure 1** summarize the automatic and manual threshold measurements at 1 month, 2 months and 4 months follow-up. Neither pacemaker-mediated tachycardia nor atrial arrhythmia was induced during the stimulation required to measure the threshold.

Predictors of atrial threshold monitoring success

A statistical model in **Table 4** was developed to detect factors predictive of successful atrial threshold monitoring performance. However, it seems that the atrial threshold monitoring success rate is independent of history of hypertension, atrial ventricular block, sick sinus syndrome, implantation time of the pacemaker, pulse width, manual threshold, lead impedance and sensitivity.

Discussion

This report observes the atrial threshold monitoring algorithm, ACap™Confirm. The data offers useful clues for clinical performance, equivalence, and applicability of the atrial threshold monitoring algorithm in Zephyr@ pacemaker.

ACap™Confirm reliability

In this study, a significant correlation is observed between thresholds measured manually and automatically. Differences between

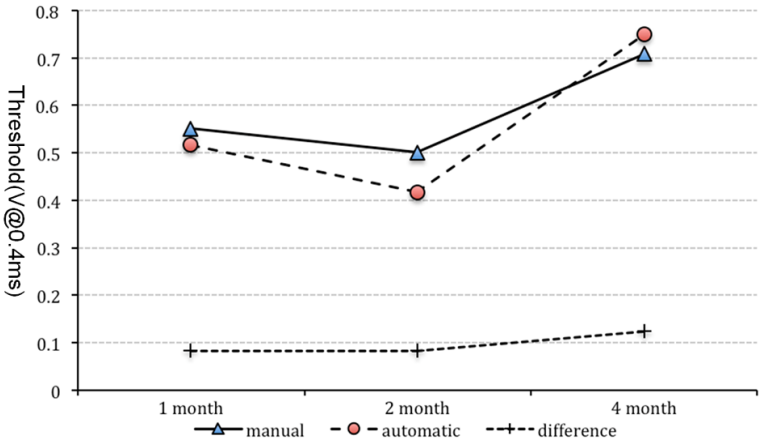

Figure 1. Automatically and manually measured atrial thresholds over the first 4 months post implantation.

Table 4. Predictors of ACap™Comfirm success

	P-value	OR	95% CI
Pulse width*	0.037	0.065	0.005-0.852
Hypertension	0.364		
Atrial fibrillation	0.55		
AVB	1.072		
SSS	0.06		
Implatation time	0.672		
Mannual threshold	1.131		
Lead impedence	0.57		
Sensitivity	0.896		

*Hosmer-Lemeshow test: 0.012.

automatic and manual atrial thresholds absolute values are equal to zero in 31.8% of patients and 0.125 V in 68.2%. The results demonstrate that ACap™Confirm determined thresholds are clinically equivalent to manual threshold tests at a pulse width setting of 0.4 ms. No clinically significant difference between automatic and manual threshold is observed for any patient and no adverse arrhythmia is observed during ACap™Confirm test. ACap™Confirm is clinically safe and reliable in automatic assessment of atrial threshold.

ACap™Confirm appilicability

ACap™Confirm enabling rate is 71.2%, and causes of unsuccessful attempts to perform automatic atrial threshold measurement include ongoing supraventricular tachycardia in 2 and safety margin not meet in 36.

For the ongoing tachycardia patient, the ACap™Confirm was processed successfully in the post-6-month follow-up. During the ACap™Confirm setup test, heart rate should be kept below 120 bpm. Heart rate more than 120 bpm is considered ongoing supraventricular tachycardia or atrial fibrillation by pacemaker programmer, which makes automatic atrial threshold management useless. As a result, for this patient, ACap™Confirm was possible 6 months later when heart rate returned normal.

The major obstacle to enable ACap™Confirm is safety margin not meet. In order to further explore the underlying problem, we developed a statistical model to detect factors predictive of successful ACap™Confirm performance. Unfortunately, it seems that the enabling rate of ACap™Confirm has little relation with history of hypertension, atrial ventricular block, sick sinus syndrome, implantation time of the pacemaker, pulse width, manual threshold, lead impedance and sensitivity. However, more factors should be considered and repeated statistical analysis should be done to exclude other influencing factors in further follow-up tests.

Potential benefit of ACap™Confirm

Previous studies [5] demonstrated that atrial capture management of EnPulse™ does not test on a beat-to-beat basis, and relies on either stable sinus rate or AV conduction. Therefore, for patients without stable sinus rate or AV conduction, atrial capture management is not possible. However, the atrial threshold monitoring method, ACap™Confirm, can process atrial capture management on a beat-to-beat basis. Therefore, this algorithm is able to realize automatic atrial threshold monitoring despite complete pacemaker dependence and unstable sinus rate or AV conduction. Thus, more patients may benefit from the algorithm.

In addition, according to previous study by Boriani et al. [10] and Buffi et al. [11], application of automatic ventricular threshold assessment significantly increased pacing longevity by

lowering ventricular pacing output. Besides, our study validates that the automatic adjustment of atrial threshold can also lower the pacing output. As a result, we assume that pacing longevity may also be increased by ACap™Confirm. More study about actual pacemaker longevity of automatic atrial threshold management may be done in the future.

Particularity of this study

Our study focuses on the atrial threshold monitoring algorithm, ACap™Confirm. By processing atrial threshold management on a beat-to-beat basis, this algorithm can realize automatic atrial management despite unstable AV conduction or sinus rate.

The excellent correlation between automatic and atrial threshold further proves the validity of automatic atrial threshold assessment. Our study shows that ACap™Confirm is a safe, reliable and stable algorithm for future atrial threshold management.

Study limitations

It should be noted that, although ACap™Confirm is based on beat-to-beat tests, failure to enable ACap™Confirm may occur wen safety margin is not met. Further study is needed to advise clinician how to achieve more effective atrial output and realize maximum enabling rate of ACap™Confirm.

This study has only examined the safety, reliability and applicability of ACap™Confirm. Due to limited patients and follow-up period, influencing factors to enable ACap™Confirm cannot be effectively detected. n the future study, we need to increase patient number as well as follow-up time to point out what actually affect the maximum utilization of this function.

Conclusion

This study focuses on observation of the atrial threshold monitoring algorithm, ACap™Confirm. The study demonstrates that ACap™Confirm is safe, reliable and applicable over time. The ACap™Confirm in Zephyr® pacemaker will provide another option for atrial automatic threshold management. It is estimated that atrial capture management can benefit the patients by reducing energy cost and enhancing pacemaker safety.

Acknowledgements

Supported by “the Fundamental Research Funds for the Central Universities in China”. We thank Chengcheng Yu from St.Jude Medical, Inc., for the precious help for this study.

Disclosure of conflict of interest

None.

Address correspondence to: Jing Zhou, Department of Cardiovascular Medicine, First Hospital of Peking University, Beijing, PR China. E-mail: zhoujing-123@126.com

References

[1] Biffi M, Sperzel J, Martignani C, Branzi A, Boriani G. Evolution of pacing for braycardia: Autocapture. European Heart Journal Supplements 2007; 9: 123-132.

[2] Sperzel J, Nowak B, Himmrich E, Zhang G, König A, Willems R, Reister C, Sathaye A, Fröhlig G. Acute performance evaluation of a new ventricular automatic capture algorithm. Europace 2006; 8: 65-69.

[3] Bertini M, Biffi M, Ziacchi M, Valzania C, Saporito D, Boriani G. Automatic verification of ventricular stimulation: Fusion management algorithm. Pacing Clin Electrophysiol 2008; 31: 64-69.

[4] de Voogt WG, Vonk BF, Albers BA, Hintringer F. Understanding capture detection. Europace 2004; 6: 561-569.

[5] Sperzel J, Milasinovic G, Smith TV, Mead H, Brandt J, Haisty WK, Bailey JR, Roelke M, Simonson J, Englund J, Farges E, Compton S. Automatic Measurement of atrial pacing thresholds in dual chamber pacemakers: clinical experience with atrial capture management. Heart Rhythm 2005; 2: 1203-10.

[6] Biffi M, Spitali G, Silvetti MS, Argnani S, Rubino I, Fontana P, Barbato G, Mazzini E, De Santo T, Drago F, Boriani G. Atrial threshold variability: implications for automatic atrial stimulation algorithms. Pacing Clin Electrophysiol 2007; 30: 1445-54.

[7] Luc Rey J, Quenum S, Hero M. Automatic assessment of atrial pacing in current medical practice. Europace 2012; 14: 1615-19.

[8] Chen KP, Xu G, Wu S, Tang B, Wang L, Zhang S. Clinical evaluation of pacemaker automatic capture management and atrioventricular interval extension algorithm. Europace 2013; 15: 395-401.

[9] Lu RM, Dawson AK. The measurement of the paced depolarization integral using the braid-

ed endocardial lead. Pacing Clin Electrophysiol 1992; 15: 1996-9.

[10] Boriani G, Biffi M, Branzi A, Mininno A, Sigliano R. Benefits in projected pacemaker longevity and in pacing related costs conferred by automatic threshold tracking. Pacing Clin Electrophysiol 2000; 23: 1783-7.

[11] Biffi M, Bertini M, Saporito D, Ziacchi M, Martignani C, Diemberger I, Boriani G. Actual pacemaker longevity: the benefit of stimulation by automatic capture verification. Pacing Clin Electrophysiol 2010; 33: 873-81.