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Accelerometer-based atrioventricular synchronous pacing with a ventricular leadless pacemaker: Results from the Micra atrioventricular feasibility studies

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BACKGROUND Micra is a leadless pacemaker that is implanted in the right ventricle and provides rate response via a 3-axis accelerometer (ACC). Custom software was developed to detect atrial contraction using the ACC enabling atrioventricular (AV) synchronous pacing.

OBJECTIVE The purpose of this study was to sense atrial contractions from the Micra ACC signal and provide AV synchronous pacing.

METHODS The Micra Accelerometer Sensor Sub-Study (MASS) and MASS2 early feasibility studies showed intracardiac accelerations related to atrial contraction can be measured via ACC in the Micra leadless pacemaker. The Micra Atrial TRacking Using A Ventricular AccELerometer (MARVEL) study was a prospective multicenter study designed to characterize the closed-loop performance of an AV synchronous algorithm downloaded into previously implanted Micra devices. Atrioventricular synchrony (AVS) was measured during 30 minutes of rest and during VVI pacing. AVS was defined as a P wave visible on surface ECG followed by a ventricular event <300 ms.

RESULTS A total of 64 patients completed the MARVEL study procedure at 12 centers in 9 countries. Patients were implanted with a Micra for a median of 6.0 months (range 0–41.4). High-degree AV block was present in 33 patients, whereas 31 had predominantly intrinsic conduction during the study. Average AVS during AV algorithm pacing was 87.0% (95% confidence interval 81.8%–90.9%), 80.0% in high-degree block patients and 94.4% in patients with intrinsic conduction. AVS was significantly greater ($P < .001$) during AV algorithm pacing compared to VVI in high-degree block patients, whereas AVS was maintained in patients with intrinsic conduction.

CONCLUSION Accelerometer-based atrial sensing is feasible and significantly improves AVS in patients with AV block and a single-chamber leadless pacemaker implanted in the right ventricle.

KEYWORDS Accelerometer; Atrial contraction; Atrioventricular block; Atrioventricular synchronous pacing; Leadless pacemaker

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Introduction

The introduction of the transvenous pacemaker transformed the outcomes of patients with bradyarrhythmias. Since then, evolution in pacemaker technology has concentrated on device miniaturization and battery life extension. Yet, addressing the system size did not substantially affect the complication risk associated with transvenous systems, including infection, pneumothorax, hematoma, and lead dislodgment.[1,2] The recent introduction of the transcatheter leadless pacemaker has dramatically reduced the risk for major complications by >50%.[3,4] In the Micra Transcatheter Pacing Study, procedural success rate was 99.2%, and major complication rate was 4.0%; this low rate of complication was confirmed in the real-world setting.[3,5] Importantly, 1-year follow up of the Micra cohort demonstrated an 82% reduction in the need for system revision compared to transvenous systems.[6] With these promising results, there is increasing interest in expanding the utilization of leadless pacing. However, the use of single-chamber pacemakers is limited to 14% of pacemaker implantations.[7] This is largely because of the potential benefits of atrial pacing in patients with sinus node dysfunction (SND) as well as the recognized benefits of atrioventricular synchrony (AVS) in decreasing the incidence of pacemaker syndrome, improving stroke volume, and positively influencing functional status and quality of life in patients with atrioventricular block (AVB).[8–10] We conducted 3 clinical trials to develop and evaluate the performance of a novel downloadable algorithm for the Micra single-chamber ventricular leadless pacemaker, based on intracardiac accelerometer data. We report the development and performance of this algorithm in successfully achieving AVS in a large proportion of patients with high-grade AVB and an implanted Micra device.

Methods
Study design

The purpose of the Micra Accelerometer Sensor Sub-Study (MASS) and MASS2 studies were to characterize the intracardiac accelerometer signals from the implanted Micra device during various patient activities to assess the feasibility of sensing atrial contraction from the accelerometer. Both MASS and MASS2 were prospective nonrandomized, multicenter clinical feasibility studies.

The Micra Atrial TRacking Using A Ventricular AccELerometer (MARVEL) study was an acute, prospective, nonrandomized, multicenter clinical feasibility study. The primary aim of MARVEL was to test the feasibility of providing AVS pacing in patients with AVB using the algorithm developed from MASS and MASS2 studies.

Each study's protocol was approved by the ethics committee at each participating institution and associated national and local regulatory agencies where applicable. All patients provided written informed consent.

Algorithm description

Accelerometer signals collected from MASS/MASS2 patients demonstrated that 4 distinct segments of cardiac activity were seen in the accelerometer signal (Figure 1, bottom panel). These segments corresponded to isovolumic contraction and mitral/tricuspid valve closure (A1), aortic/pulmonic valve closure (A2), passive ventricular filling (A3), and atrial contraction (A4). The systolic components A1 and A2 have been previously reported.[11] Accelerometer segments A3 and A4 were associated with mitral valve flow E- and A-wave measurements. Based on these signals, an AV synchronous algorithm was developed to provide a VDD pacing mode. Specifically, blanking windows were manually set by the clinician to reject detection of signals in the accelerometer that were ventricular in origin (A1, A2). Atrial contraction was detected when the filtered and rectified accelerometer signal exceeded 1 of 2 programmable thresholds. Because the A3 and A4 signals can fuse, creating larger accelerometer signals at higher sinus rates >80 bpm, the algorithm includes 2 programmable thresholds: a larger A3 threshold to detect fused A3/A4 and a lower A4 threshold for detecting the A4 signal later in diastole.

If atrial contraction was detected (A4), an atrial marker (AS) was output via telemetry, and a programmable AV interval was initiated. Because of the electromechanical delay between the electrical P wave and the A4 signal on the accelerometer, the A4 VP was typically programmed to 10 ms. The algorithm incorporated a rate smoothing feature designed to maintain AVS during intermittent A4 undersensing. If an atrial contraction (A4) was not detected, a ventricular pace was delivered at a programmable rate smoothed interval (typically 100 ms) longer than the median R-R interval.

Patients and procedures

A substudy of the Micra Transcatheter Pacing Study, MASS included patients who had completed their 12-month follow-up. The MASS study consisted of a single in-office visit and an optional overnight Holter monitor recording period. After patient consent was obtained, software was downloaded into the patient's device allowing telemetry of the accelerometer signal and marker channel to a Holter monitor. The patient then performed a series of posture and maneuver tests while accelerometer signal was collected from each of Micra's 3 accelerometer vectors. After study participation, the downloadable software was removed.

Inclusion criteria for the MASS2 study were similar to the MASS study with the addition of an exclusion criterion that the patient was not in atrial fibrillation (AF). The MASS2 study procedures were similar to the MASS study procedures with the addition of echocardiographic recording after the posture and maneuver testing.

The MARVEL study enrolled patients ≥18 years of age with AVB and not in permanent atrial arrhythmia who were previously implanted with a Micra device. After
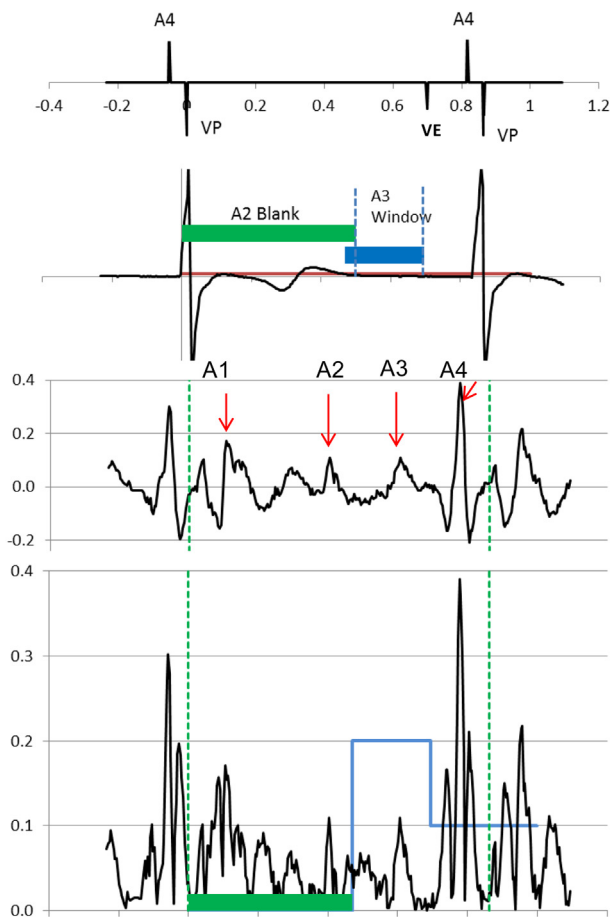
Figure 1 Overview of the atrioventricular synchronous algorithm developed from MASS/MASS2 accelerometer signals. **Top:** Device marker channel and programmable A2 and A3 blanking windows. VE = end of A3 window. **Middle:** Accelerometer signal in relation to the ventricular event (*dashed green vertical lines*) and A1, A2, A3, and A4 events. **Bottom:** Rectified accelerometer signal and A2 blanking period (*solid horizontal green bar*). Two programmable thresholds for A4 detection are indicated by the *light blue line*. The first programmable threshold is greater than the second, allowing for detection when the A3 and A4 signals fuse at higher heart rates.

consent was obtained and baseline procedures performed, an investigational software implementation of the AV synchronous algorithm was downloaded into the patient's implanted device and a Holter monitor placed. Algorithm parameters, including accelerometer vector, A2 blanking period, A3 end time, A3 threshold, and A4 threshold, were programmed to optimize A4 detection while the patient sat or laid still. After parameter optimization, the patient performed a series of posture maneuvers (supine, laying on left side, laying on right side, sitting, and standing) and exercises (walking at a normal and fast cadence). Additionally, each patient rested in a supine or sitting position for approximately 30 minutes. Echocardiography was performed while the AV synchronous algorithm was programmed to adaptive mode (VDD pacing) and monitor mode (VVI pacing). To assess stroke volume, the left ventricular outflow tract velocity–time integral (LVOT VTI) was measured in both modes. Patient participation in an overnight Holter recording period was optional.

Before study exit, the Holter and investigational software were removed.

Endpoints

For the MASS and MASS2 studies, the primary endpoint of interest was the A4 amplitude associated with atrial contraction for each cardiac cycle during each posture, maneuver, and vector combination.

For the MARVEL study, the primary endpoint was the rate of AVS during the 30-minute resting period. An additional endpoint was the rate of atrial detection (A4). In patients with intrinsic AV conduction, AVS will be high because of intact conduction, and the atrial detection provides a better indication of performance of the atrial sensing.

Statistical analysis

MASS/MASS2

There was no *a priori* statistical justification for the sample size in the MASS/MASS2 studies, as the primary goal of these studies was to collect accelerometer signals for algorithm development.

ECG, right ventricular electrogram, and intracardiac accelerometer waveform were extracted from each Holter data file and processed using custom MATLAB tools (Math-Works, Natick, MA). For each Holter recording and within each cardiac cycle, an A4 sensing window was identified. The peak-to-peak A4 amplitude was measured from this signal within the A4 sensing window. In patients with intrinsic conduction, the mean of the A4 amplitude was computed for each posture, maneuver, and vector combination. A mixed effects linear model with 2 fixed factors (vector and posture) and 1 random factor (patient) was used to determine the impact of vector and posture on A4 amplitude among patients with normal sinus function (intrinsic conduction) and infrequent pacing during the Holter recording period.

MARVEL

A sample size of 50 usable Holter files was postulated to allow the AVS percentage to be estimated with precision of 3.8% (ie, distance between lower and upper 95% confidence interval [CI]) during the 30-minute resting period based on the following assumptions: (1) average within patient AVS percentage was 90% with a standard deviation (SD) of 12% and (2) average patient heart rate was 65 ± 5 bpm.

Similar to the MASS/MASS2 studies, surface ECG, right ventricular electrogram, intracardiac accelerometer waveform, and device marker channel were extracted from each Holter data file. A technician (blinded to the device marker channel) identified P waves on the surface ECG signal. A custom MATLAB script collated the timing of each P wave, times corresponding to each posture and maneuver, and timing for each device marker channel relative to the beginning of the Holter recording. For each cardiac cycle, the primary endpoint of AVS was considered met if the
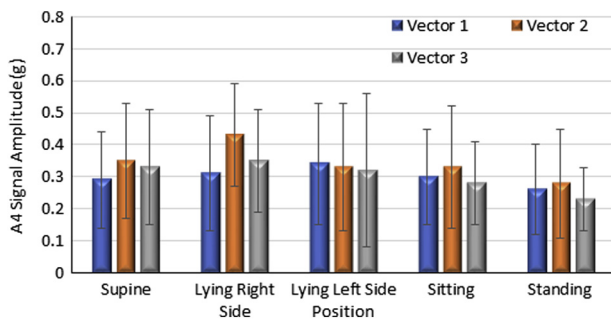
Figure 2 A4 signal amplitude from patients with normal sinus function and intrinsic conduction requiring infrequent pacing. Error bars represent standard deviation. Units (g) on the y-axis represent acceleration. N ranged from 22 in vector 3, left position, to 38 in vector 1, supine position.

timing of the ventricular marker was within 300 ms of the P wave. Similarly, the atrial contraction was considered detected if the AS marker was before the ventricular marker and within 300 ms of the P wave.

AVS percentage and atrial detection rates were computed within each patient and posture/maneuver combination by dividing the total number of cardiac cycles meeting each endpoint by the number of cardiac cycles. Logistic regression models using generalized estimating equations to account for correlation in algorithm performance within patient were used to estimate the performance of the AV synchronous algorithm across all patients within each posture/maneuver.

AVS percentage between VVI pacing (measured during echocardiogram in AV synchronous algorithm monitor mode) and the 30-minute resting period were also compared using logistic regression models utilizing generalized estimating equations among patients within each predominant heart rhythm observed (AVB or intrinsic conduction). Linear regression was used to characterize the association between time since device implant and AVS and A4 detection rates. A paired *t* test was used to compare LVOT VTI between AV algorithm and VVI pacing. Statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC) or R (www.r-project.org).

Results
Early feasibility results (MASS/MASS2)
Seventy-five patients were enrolled in the MASS/MASS2 studies, of whom 66 had normal sinus function and 9 were in AF. Mean age was 74 ± 12 years. Mean time since Micra implant was 13.6 months (range 0–35.5 months). Of these 75 patients, 39 had normal sinus function with intrinsic conduction and did not require frequent pacing during the monitoring period. Four distinct segments of cardiac activity were seen in the accelerometer signal (A1, A2, A3, and A4; Figure 1). Mean A4 amplitude varied across postures and vectors (Figure 2). Specifically, A4 amplitude for vector 2 (longitudinal to device body) was significantly larger than for vector 1 ($P <$.001) or vector 3 ($P <$.001) (both radial to device body). A4 amplitude was lowest in the standing position relative to the left side, right side, and supine positions

Table 1 Baseline and medical history of patients in MARVEL

Characteristics	Enrolled (n = 70)	Usable Holter (n = 64)
Age (years)		
Mean ± SD	71.3 ± 15.1	72.0 ± 14.4
Range	24–92	30–92
Female	24 (34)	20 (31)
Months from Micra implant		
Mean ± SD	11.6 ± 12.3	11.5 ± 12.4
Range	0–41.4	0–41.4
Comorbidities		
Hypertension	41 (59)	38 (59)
Paroxysmal atrial fibrillation	14 (20)	11 (17)
Diabetes	17 (24)	16 (25)
Coronary artery disease	16 (23)	15 (23)
Chronic obstructive pulmonary disease	5 (7)	5 (8)
Device location		
Apex	19 (27)	16 (25)
Septum	47 (67)	46 (72)
Right ventricular outflow tract	2 (3)	2 (3)
Not reported	2 (3)	0 (0)
Predominant rhythm during Holter recording		
2nd-/3rd-degree AVB	NA	33 (52)
Intrinsic AV conduction	NA	32 (48)

Values are n (%) unless otherwise indicated.
AVB = atrioventricular block; MARVEL = Micra Atrial TRacking Using A Ventricular AccELerometer study.

($P <$.05). These recordings from the MASS/MASS2 studies were used to develop an algorithm to provide AV synchronous pacing.

MARVEL results
A total of 70 patients at 12 centers in Malaysia, Europe, and the United States were enrolled in the MARVEL study. Of these patients, 64 (91%) had usable Holter recordings and were included in the analysis. Six patients were not included in the analyses: 2 exited the study before AV synchronous algorithm download, 2 had no visible P waves on Holter recordings, 1 was discovered to be in AF after download, and 1 exited before performing all study procedures. Of the 64 patients with usable Holter data, 1 was studied twice because that patient was willing to undergo procedures again at later follow-up (1 day postimplant and 3 months postimplant). The 2 Holter datasets from this patient were analyzed and reported separately, unless otherwise specified. Patients with usable Holter recordings were on average 72.0 ± 14.4 years old and had been implanted with their Micra device for 11.5 ± 12.4 months (range 0–41.4 months) (Table 1). The majority of patients (52%) had a predominant rhythm of 2nd- or 3rd-degree AVB during the Holter recording, whereas 48% had intrinsic conduction. Most of the patients with intrinsic conduction received their pacemaker for episodic AVB and did not demonstrate AVB during the study.

During the 30-minute resting period, 118,640 cardiac cycles were evaluated across the 64 usable Holter recordings.
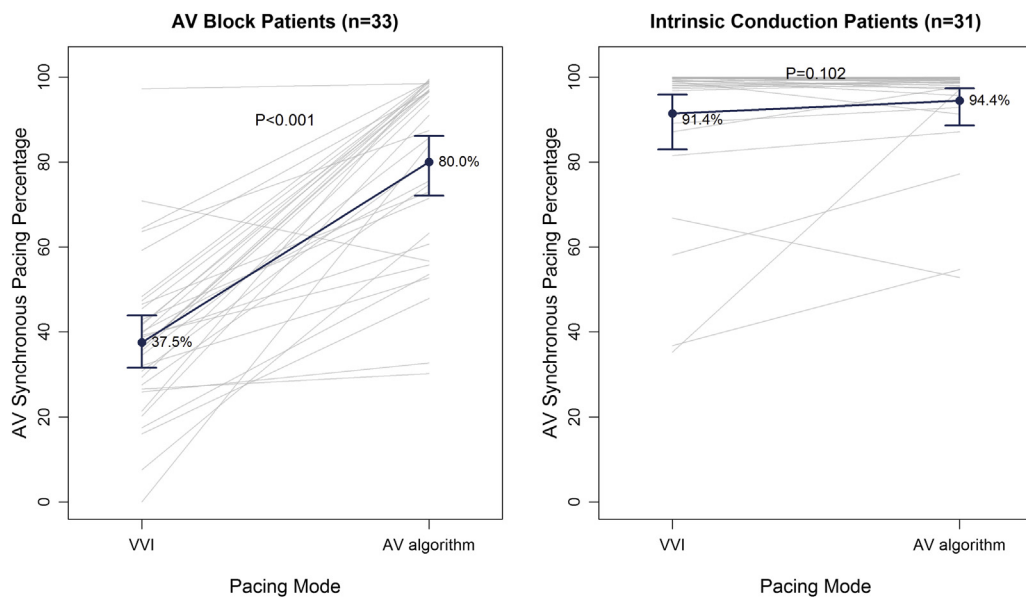
Figure 3   AV synchronous pacing percentage during AV algorithm pacing vs VVI mode by predominant rhythm during rest. *Gray lines* indicate individual patients. *Dark blue line* indicates average. Error bars represent 95% confidence intervals. AV = atrioventricular.

The AVS percentage across 64 patients was 87.0% (95% CI 81.8%–90.9%) and ranged from 30.2%–100% for individual patients, with 53 patients (83%) having an AVS percentage >70% (Supplemental Figure S1). During AV algorithm mode, patients with a predominant rhythm of AVB had a significant increase in AVS percentage while resting compared to VVI pacing (80.0% vs 37.5%; P <.001), whereas AVS was maintained in patients with intrinsic conduction (94.4% vs 91.4%; P = .102) (Figure 3). Eleven patients (9 with AVB and 2 with intrinsic conduction) had AVS percentages <70% during rest (Table 2). There was no statistical association between AVS percentage and time since implant among the 33 patients with AVB (P = .757) (Figure 4, left). Likewise, there was no association between the A4 detection

rate and time since implant among all 64 patients (P = .654) (Figure 4, right). However, the one patient studied twice had an AVS percentage of 98.9% (1 day postimplant), which decreased to 53.6% (3 months postimplant). At the second visit, the patient had a sinus rate <50 bpm and a lower A4 amplitude.

The rate smoothing operation of the AV algorithm improved AVS percentages during intermittent A4 undersensing in AVB patients, allowing AVS percentages to exceed the rate of A4 detection (80.0% vs 71.3%) (Supplemental Figure S2).

During posture testing, average AVS percentages in the 33 patients with AVB ranged from 62.7% during fast walking to 81.5% during sitting; in the 31 patients with intrinsic

Table 2   Reasons for AV synchrony rates <70% during rest

Patient	Predominant rhythm during Holter monitoring	Synchrony during rest (%)	Reason for low synchrony
0002950105	AVB	30.2	Low-amplitude A4
4192011007	AVB	32.7	Low-amplitude A4
4192011003	AVB	47.9	Conservative algorithm settings: tracked sinus rate 2:1
0002950104	AVB	52.8	Sinus rate <50 bpm
6100101002	Intrinsic AV conduction	52.8	SND: high sinus rate variability High PVC rate
4192011010	AVB	53.6	Low amplitude A4 Sinus rate <50 bpm
1480101004	Intrinsic AV conduction	54.7	High PVC rate
0042050101	AVB	55.8	Low-amplitude A4
1470101005	AVB	56.7	Low-amplitude A4
4192011008	AVB	60.7	Low-amplitude A4
6100101003	AVB	63.3	Sinus rate >120 bpm

AV = atrioventricular; AVB = atrioventricular block; PVC = premature ventricular complex; SND = sinus node dysfunction.
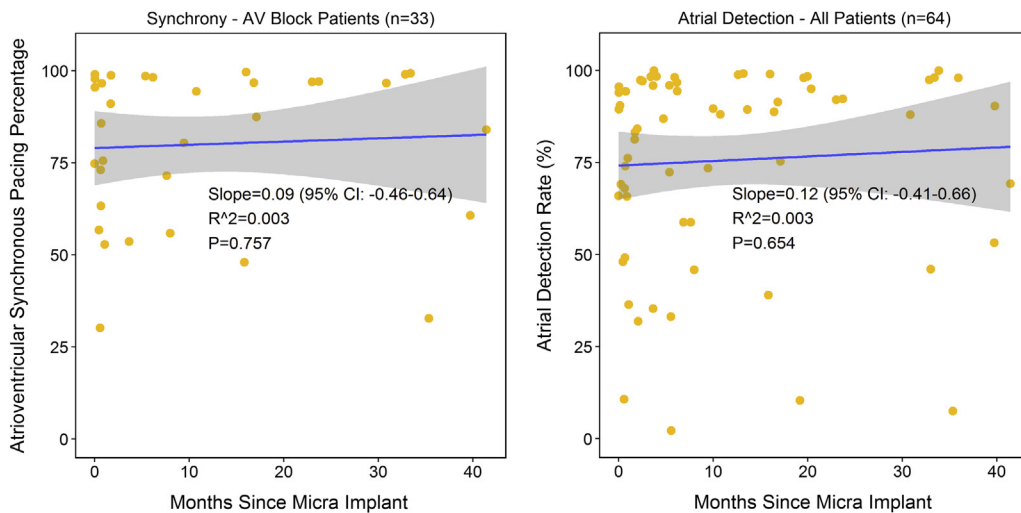
Figure 4 Relationship between time since implant and AV synchronous pacing percentage (**left**) and atrial detection rate (**right**). AV = atrioventricular; CI = confidence interval.

conduction, AVS percentages ranged from 84.0% (fast walking) to 94.4% (resting) (Figure 5). AVS percentages were lowest during maneuvers requiring activity, regardless of predominant heart rhythm.

Of the 33 patients with a predominant rhythm of AVB, 31 had an echocardiogram available for analysis during AV algorithm and VVI pacing. LVOT VTI was significantly higher during AV algorithm pacing compared to VVI pacing (23.9 vs 21.8 cm; $P = .004$) (Figure 6).

Evaluation of electrograms and ECGs in all 64 Holter datasets revealed no pauses and no instances of pacemaker-mediated tachycardia during AV algorithm pacing. Addition-

ally, no adverse events related to the device or AV algorithm pacing mode were reported during the study.

Discussion
The MARVEL study demonstrated the feasibility of tracking atrial contractions and providing AVS using a mechanical accelerometer-based sensor in the Micra ventricular pacemaker. Specifically, the average AVS percentage at rest was 87%. In patients with high-grade AVB, AVS improved from 37.5% to 80% when comparing VVI vs AV algorithm mode. The presence of the algorithm had no detrimental
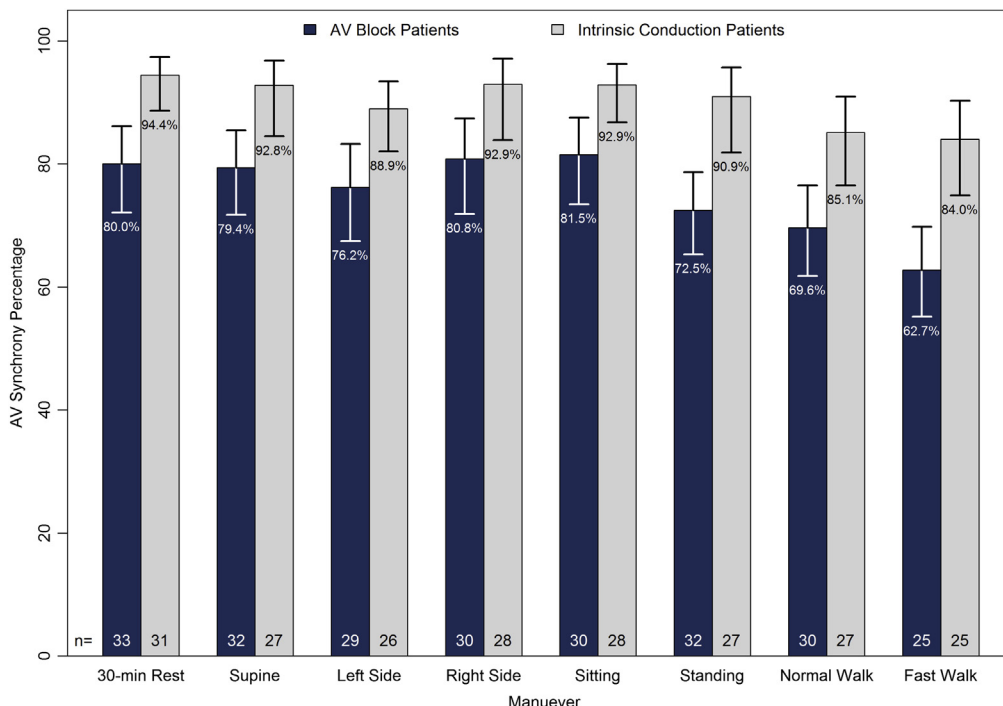

Figure 5 AV synchronous pacing percentage by maneuver. *Blue* indicates patients with a predominant rhythm of AV block during study. *White* indicates patients with a predominant rhythm of intrinsic conduction during study. Error bars represent 95% confidence intervals. AV = atrioventricular.
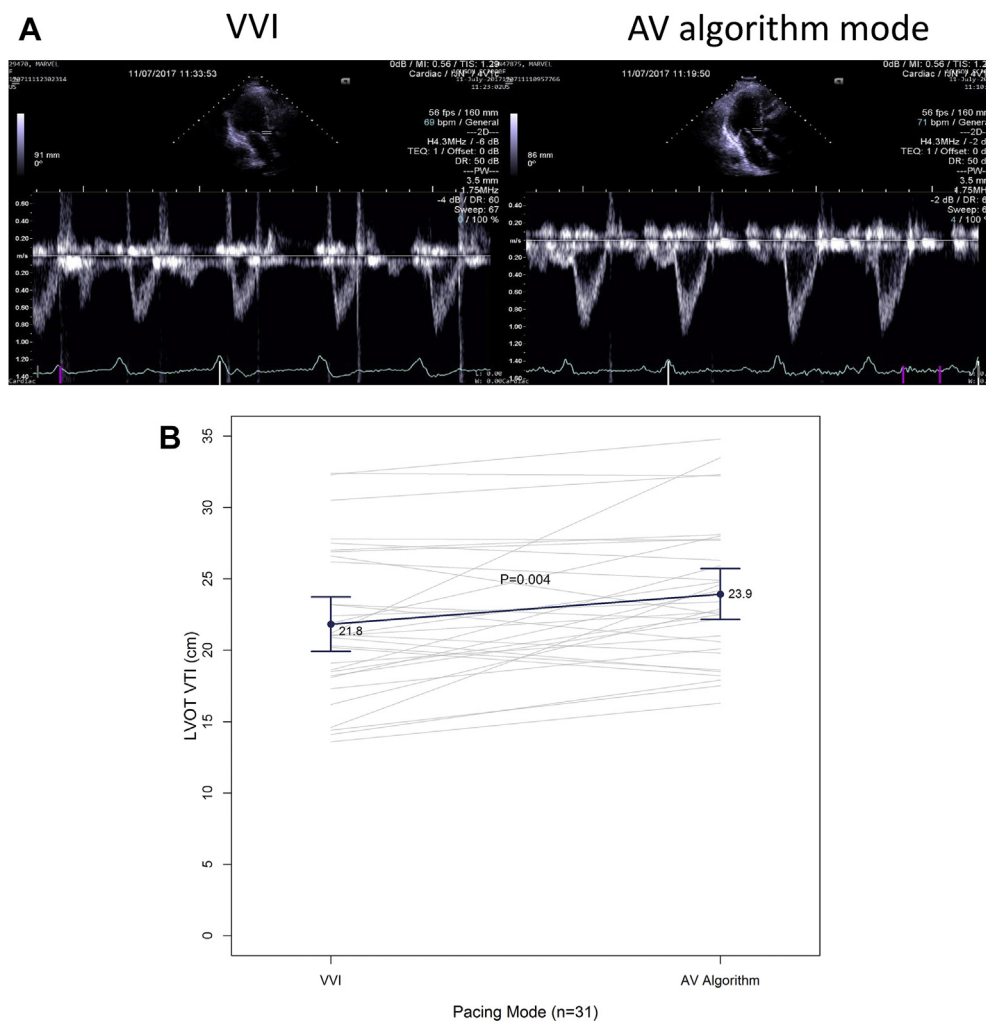
Figure 6   **A:** Example echo-Doppler LVOT showing VTI in a patient during VVI vs VDD pacing. **B:** LVOT VTI (cm) during VVI mode and AV algorithm pacing modes in 31 patients with AV block and paired echocardiogram. *Gray lines* indicate individual patients. *Dark blue line* indicates average. Error bars represent 95% confidence interval of mean. *P* value from paired *t* test. AV = atrioventricular; LVOT = left ventricular outflow tract; VTI = velocity–time integral.

impact on AVS in patients with intrinsic AV conduction. The achievement of AVS had a demonstrable effect on stroke volume as measured by VTI on echocardiography. As expected, SND, premature ventricular complexes, and low-amplitude signals contributed to a lack of synchrony, although this was evident in a relatively small number of patients.

The study demonstrated that AVS with this algorithm was impacted by activity. Detection of the atrial signal during activity decreased as the patient's heart rate increased, creating fusion of the atrial and ventricular components of the accelerometer signal, and acceleration due to motion superimposing on the signal. AVS was not impacted by changes in posture while at rest. In this circumstance, it is important to consider that the loss of atrial synchrony is compensated for by an increase in heart rate and ejection fraction during exercise, particularly in patients with preserved left ventricular systolic function.[12] In addition, the algorithm was designed to include a rate smoothing feature and programmable blanking periods that frequently allowed for the maintenance of AVS when A4 sensing was difficult or

intermittent. This feature improved the rate of AVS by approximately 9%.

The study included patients tested from the day after device implant to 41 months after implantation, and the data showed no association between the time of implant and the achievement of AVS or the ability to sense the A4 signal, although these were not paired tests. There were no instances of pacemaker-mediated tachycardia or significant interruption in ventricular pacing resulting in symptomatic pauses. All other safety issues were either minor or unrelated to the device.

The literature and published guidelines support use of single-chamber pacemakers in patients with AVB under certain circumstances.[13] These include infrequent need for pacing, vascular access issues, sedentary patients, and comorbidities likely to impact clinical outcomes. However, this does not preclude the benefit of AVS, if it can be achieved safely in this population of patients. This provides the opportunity for this patient population to benefit from AVS and increased stroke volume, reduction in pacemaker

syndrome incidence, and improvement in functional status and quality of life; however, this would require long-term evaluation.[14–16] The loss of AVS with increased levels of activity may be a limitation of the algorithm. However, this may be mitigated by the fact that cardiac output at higher rates has been shown to be more dependent on heart rate than AVS.[17] Thus, rate responsive pacing (ie, VVIR) may be an adequate option for patients when active. In addition, it has been demonstrated that the symptoms of "pacemaker syndrome" are usually seen at rest[18] and are mostly related to retrograde VA conduction, which primarily occurs when the ventricular rate is substantially higher than the atrial rate.[19]

Patients with lower AVS tended to have SND (manifesting primarily as sinus arrhythmia, sinus bradycardia, and sinus tachycardia) or had low-amplitude A4 signals. Clearly patients with persisting or permanent atrial arrhythmias would not benefit from implantation of these devices; furthermore, the A4 signal during AF will likely be low and not detected, resulting in pacing near the lower rate. Loss of AVS also occurred as a result of low-amplitude signals measured by the accelerometer. The signals obtained from the accelerometer can be complex, and setting up the algorithm will require knowledge of the cardiac components of the accelerometer signal. Although multiple accelerometer vectors were tested at the initial setup, some patients had consistently low-amplitude signals or experienced variations in A4 amplitude during the monitoring periods. It is conceivable that atrial contractility is a significant factor in sensing the A4 signal and achieving mechanical synchrony. It is also reasonable to speculate that patients with poor atrial contraction may not benefit from AVS and that rate responsive pacing alone is adequate for this population of patients with single-chamber leadless devices. It will be important to understand the factors creating an impediment to achieving AVS and aid the decision-making process for physicians contemplating the appropriateness of implanting these devices.

Study limitations
The limitations of this study are related to the acute manual download of the algorithm into patients already receiving VVI pacing by an implanted Micra device. Furthermore, the algorithm cannot be used chronically because new hardware will be required to efficiently process the accelerometer signal for AVS and provide adequate longevity. The device needs to be tested chronically on *de novo* patients throughout the life of the device. Paired individual patient data are not yet available to assess the maintenance of a high percentage of synchrony over time. Although the acute safety data are robust, long-term safety and individual patient tolerance to variable loss of AVS remain unknown. In addition, this study did not establish the percentage of AVS required to achieve anticipated benefits such as reduction in pacemaker syndrome, improvement in functional status and quality of life, and augmentation of cardiac function. Finally, although the

true safety of leadless pacemaker implantation is somewhat limited by the lack of a randomized trial, the available data strongly suggest that the elimination of morbidity associated with lead dislodgment, hematoma, prolonged hospitalizations, pneumothorax, and infections will remain most significant.

Conclusion
Accelerometer-based atrial sensing is feasible and significantly improves AVS in patients with AV block and a single-chamber leadless pacemaker implanted in the right ventricle.

Acknowledgments

Appendix
Supplementary data
Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.hrthm.2018.05.004.

References
1. Kirkfeldt RE, Johansen JB, Nohr EA, Jorgensen OD, Nielsen JC. Complications after cardiac implantable electronic device implantations: an analysis of a complete, nationwide cohort in Denmark. Eur Heart J 2014;35:1186–1194.
2. Udo EO, Zuithoff NP, van Hemel NM, de Cock CC, Hendriks T, Doevendans PA, Moons KG. Incidence and predictors of short- and long-term complications in pacemaker therapy: the FOLLOWPACE study. Heart Rhythm 2012;9:728–735.
3. Reynolds D, Duray GZ, Omar R, et al. A leadless intracardiac transcatheter pacing system. N Engl J Med 2016;374:533–541.
4. Reddy VY, Knops RE, Sperzel J, et al. Permanent leadless cardiac pacing: results of the LEADLESS trial. Circulation 2014;129:1466–1471.
5. Roberts PR, Clementy N, Al Samadi F, et al. A leadless pacemaker in the real-world setting: the Micra Transcatheter Pacing System Post-Approval Registry. Heart Rhythm 2017;14:1375–1379.
6. Duray GZ, Ritter P, El-Chami M, et al. Long-term performance of a transcatheter pacing system: 12-Month results from the Micra Transcatheter Pacing Study. Heart Rhythm 2017;14:702709.
7. Greenspon AJ, Patel JD, Lau E, Ochoa JA, Frisch DR, Ho RT, Pavri BB, Kurtz SM. Trends in permanent pacemaker implantation in the United States from 1993 to 2009: increasing complexity of patients and procedures. J Am Coll Cardiol 2012;60:1540–1545.
8. Lamas GA, Ellenbogen KA. Evidence base for pacemaker mode selection: from physiology to randomized trials. Circulation 2004;109:443–451.
9. Lamas GA, Orav EJ, Stambler BS, Ellenbogen KA, Sgarbossa EB, Huang SK, Marinchak RA, Estes NA 3rd, Mitchell GF, Lieberman EH, Mangione CM, Goldman L. Quality of life and clinical outcomes in elderly patients treated with ventricular pacing as compared with dual-chamber pacing. Pacemaker Selection in the Elderly Investigators. N Engl J Med 1998;338:1097–1104.
10. Nielsen JC, Andersen HR, Thomsen PE, Thuesen L, Mortensen PT, Vesterlund T, Pedersen AK. Heart failure and echocardiographic changes during long-term follow-up of patients with sick sinus syndrome randomized to single-chamber atrial or ventricular pacing. Circulation 1998;97:987–995.
11. Tassin A, Kobeissi A, Vitali L, Rouleau F, Ritter P, Gaggini G, Dupuis JM. Relationship between amplitude and timing of heart sounds and endocardial acceleration. Pacing Clin Electrophysiol 2009;32(Suppl 1):S101–S104.

12. Ausubel K, Steingart RM, Shimshi M, Klementowicz P, Furman S. Maintenance of exercise stroke volume during ventricular versus atrial synchronous pacing: role of contractility. Circulation 1985;72:1037–1043.

13. Gillis AM, Russo AM, Ellenbogen KA, et al. HRS/ACCF expert consensus statement on pacemaker device and mode selection. Developed in partnership between the Heart Rhythm Society (HRS) and the American College of Cardiology Foundation (ACCF) and in collaboration with the Society of Thoracic Surgeons. Heart Rhythm 2012;9:1344–1365.

14. Masuyama T, Kodama K, Uematsu M, Nanto S, Taniura K, Kitabatake A, Inoue M. Beneficial effects of atrioventricular sequential pacing on cardiac output and left ventricular filling assessed with pulsed Doppler echocardiography. Jpn Circ J 1986;50:799–807.

15. Ouali S, Neffeti E, Ghoul K, Hammas S, Kacem S, Gribaa R, Remedi F, Boughzela E. DDD versus VVIR pacing in patients, ages 70 and over, with complete heart block. Pacing Clin Electrophysiol 2010;33:583–589.

16. Toff WD, Camm AJ, Skehan JD, United Kingdom P, Cardiovascular Events Trial I. Single-chamber versus dual-chamber pacing for high-grade atrioventricular block. N Engl J Med 2005;353:145–155.

17. Benditt DG, Milstein S, Buetikofer J, Gornick CC, Mianulli M, Fetter J. Sensor-triggered, rate-variable cardiac pacing. Current technologies and clinical implications. Ann Intern Med 1987;107:714–724.

18. Griffin JC. VVIR or DDD(R): does it matter? Clin Cardiol 1991;14:257–260.

19. Farmer DM, Estes NA 3rd, Link MS. New concepts in pacemaker syndrome. Indian Pacing Electrophysiol J 2004;4:195–200.