Studie MARVEL (1, 2)

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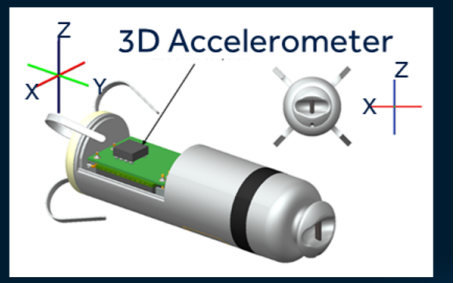
XXVII. VÝROČNÍ SJEZD ČESKÉ KARDIOLOGICKÉ SPOLEČNOSTI
MORAVA (pavilon A3) – úterý 14. 5. 2019

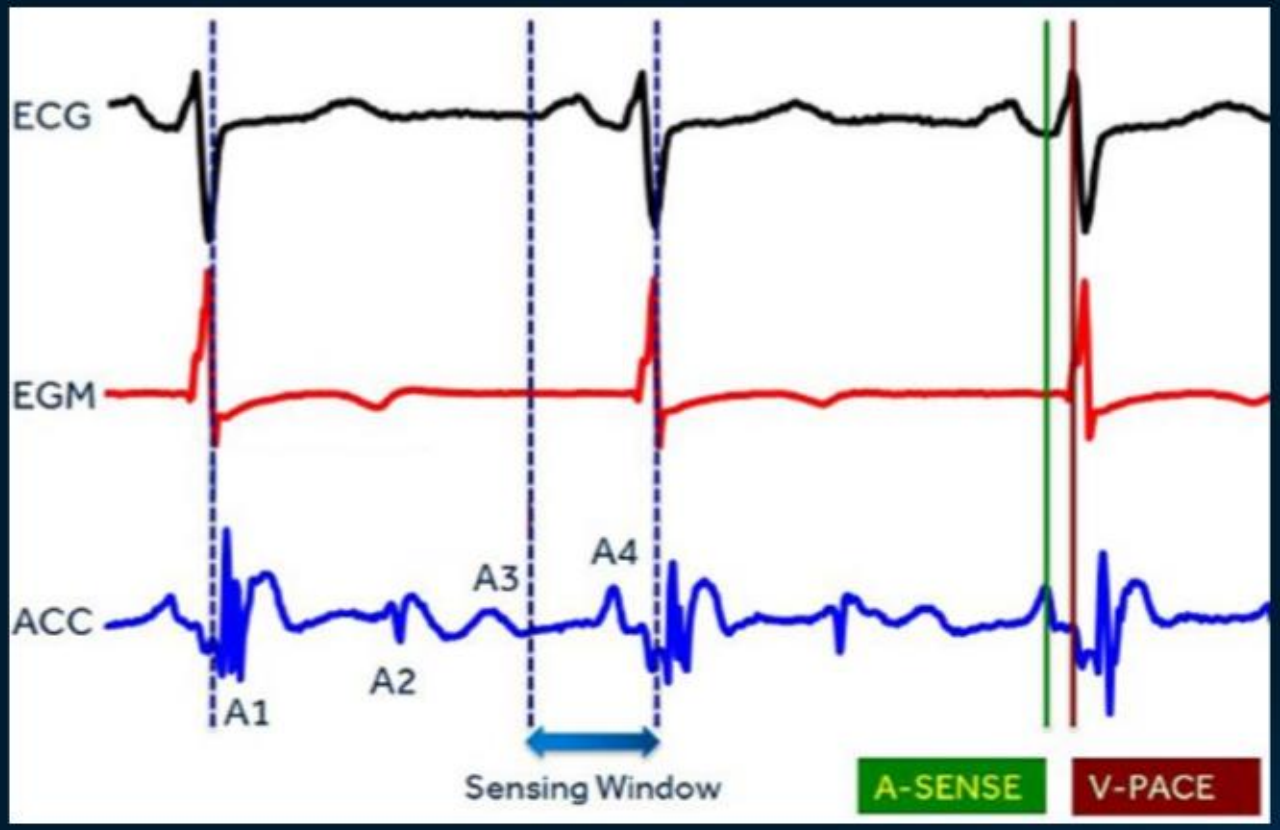
VDD režim ....

Micra Accelerometer Technology

- Sensing the atrial activity is necessary to provide AV synchrony
- Micra contains a 3 axis accelerometer
- Sensing the atrial contraction using the accelerometer may provide a signal for AV synchrony



Vector 1 = X direction
Vector 2 = Y direction
Vector 3 = Z direction



- **A1** – Isovolumic contraction and mitral/tricuspid valve closings
- **A2** – Aortic/pulmonic valve closing
- **A3** – Early passive ventricular filling
- **A4** – Atrial contraction generating active filling

Larry A. Chinitz, MD, FHRS, Heart Rhythm Scientific Sessions, May 2018, Boston

MARVEL

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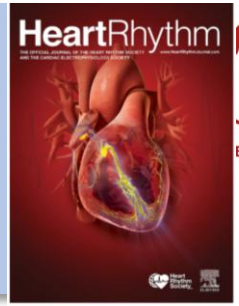
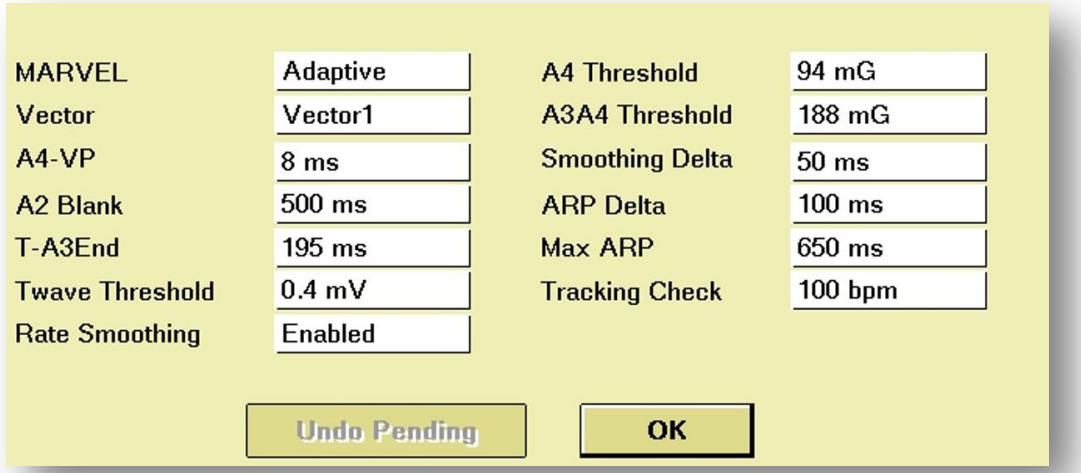


- Prospektivní, 12 center, 9 zemí (Evropa, USA, Malajsie)
- 70 pac. s AV blokem, bez perzistující FS
- 6 pacientů z NNH
- Primární cíl:
  - posoudit efektivitu nového algoritmu detekující síňovou aktivitu k docílení AV synchronie

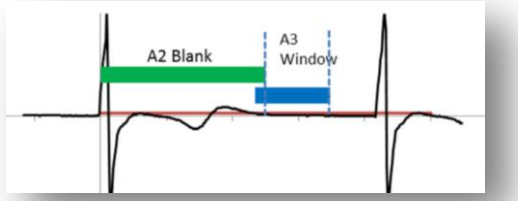
    (Definice AV synchronie: P vlna na EKG následována komorovou odpovědí do 300 ms)

- Sekundární cíle:
  - Charakteristiky detekce síňové aktivity, vlivy vektoru akcelerometru a polohy pacienta na schopnost detekce vlny P, echokardiografické změny VVI x VDD stimulace

Schéma aktivace softwaru a monitorace



- Manuální nastavení parametrů:
  - Snímací vektor, A2 blanking period, A3 end time, A3 threshold, A4 threshold (vsedě, vleže)
- **30 minut monitorace v klidu**
- Různé polohy (na zádech, pravý a levý bok, sed) a pohyb (rychlá/pomalá chůze)
- ECHO hodnocení VDD x VVI režim … LVOT VTI



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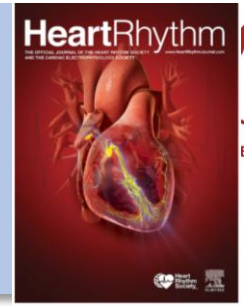

	Enrolled (n=70)	Usable Holter (n=64)
Age (years)	71.3 ± 15.1	72.0 ± 14.4
Time since implant (months)	11.6 ± 12.3 Range: 0 – 41.4	11.5 ± 12.4 Range: 0 – 41.4
Female	24 (34%)	20 (31%)
Hypertension	41 (59%)	38 (59%)
Paroxysmal AF	14 (20%)	11 (17%)
Diabetes	17 (24%)	16 (25%)
CAD	16 (23%)	15 (23%)
COPD	5 (7%)	5 (8%)
Predominant Rhythm on Holter		
• 2nd/3rd degree AV Block	NA	33 (52%)
• Intact AV conduction	NA	31 (48%)

- **64**/70 pacientů
- 3 pac. vystoupili ze studie
- 1 pac. měl fibrilaci síní
- u 2 pac. nebyly detekovatelné vlny P na holteru

- **33 (52%)** pac. S AV blokem vyššího stupně

	pohlaví	věk	implantace	studie	měsíce od implantace	24hod holter	EKG	důvod implantace
1	M	47	11.09.2017	02.10.2017	1	A	AVB 3	AVB 3 po ablaci
2	F	67	02.01.2015	02.10.2017	33	N	AVB 3	SSS, po ablacích FS
3	M	67	10.11.2016	03.10.2017	11	A	AVB 3	AVB 3, infekce, po extrakci
4	M	91	01.09.2017	03.10.2017	1	N	AVB 3	AVB 3, infekce, po extrakci
5	F	31	15.09.2017	03.10.2017	1	A	AVB 3	vrozený AV blok
6	M	70	27.12.2016	13.10.2017	10	N	AVB 3	AVB 2, infekce, po extrakci

Výsledky

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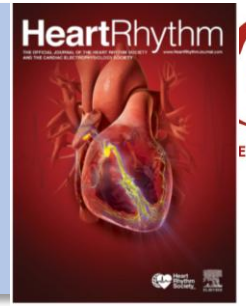
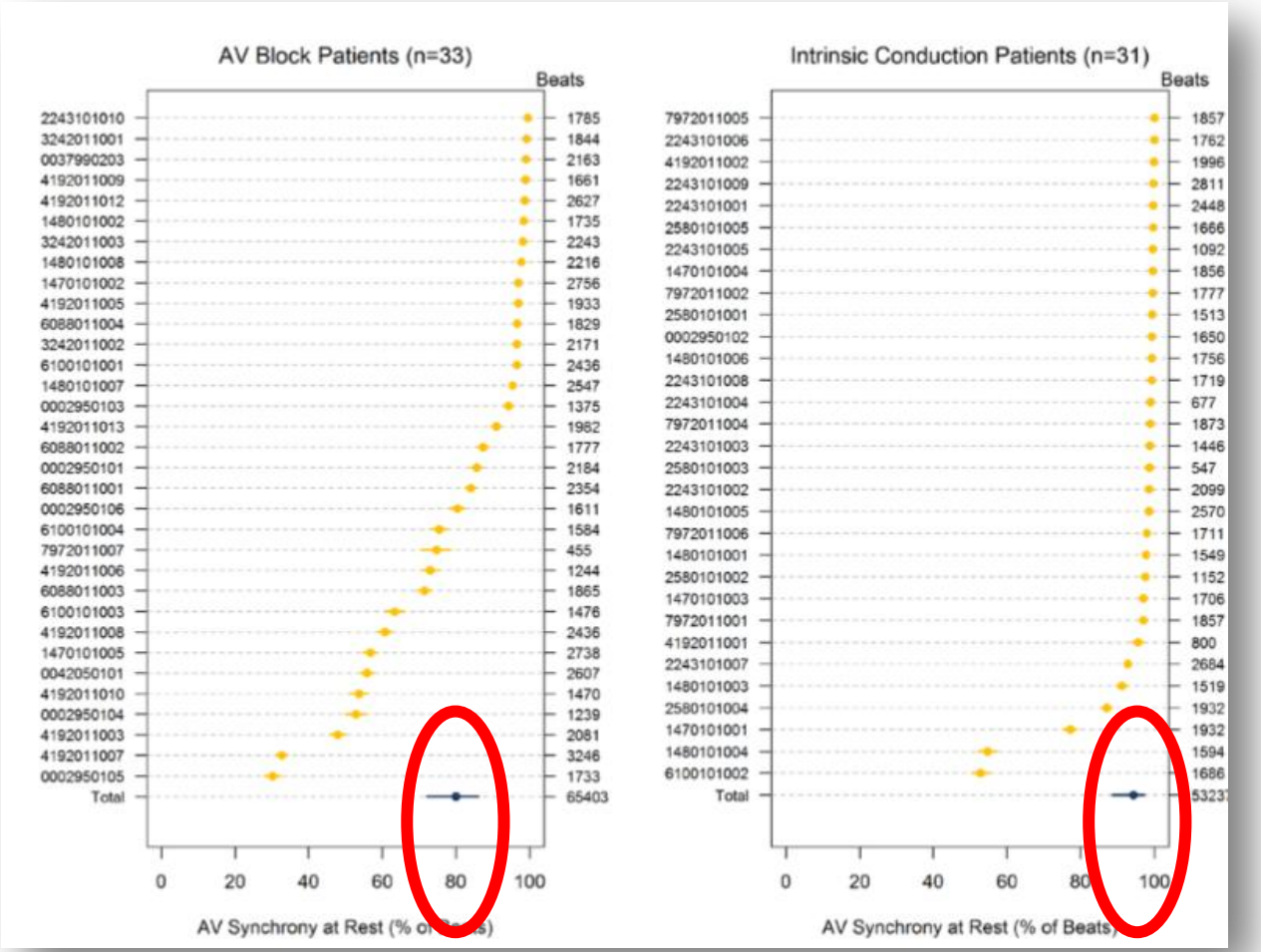


- Celkem hodnoceno 118640 srd. cyklů (30 min v klidu)
- AV synchronie: Ø **87.0%**
  (95% CI: 81.8%-90.9%)
- Rozmezí AVS: 30.2% - 100%
- 83% pac. mělo AVS ≥ 70%



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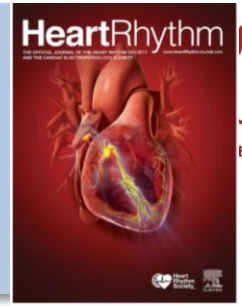

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- 83% pac. mělo AVS ≥ 70%

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

11 pacientů (9 AV blok)

1. Nízká amplituda vlny A4
2. Sinusová tachy/bradykardie
3. Komorová extrasystolie

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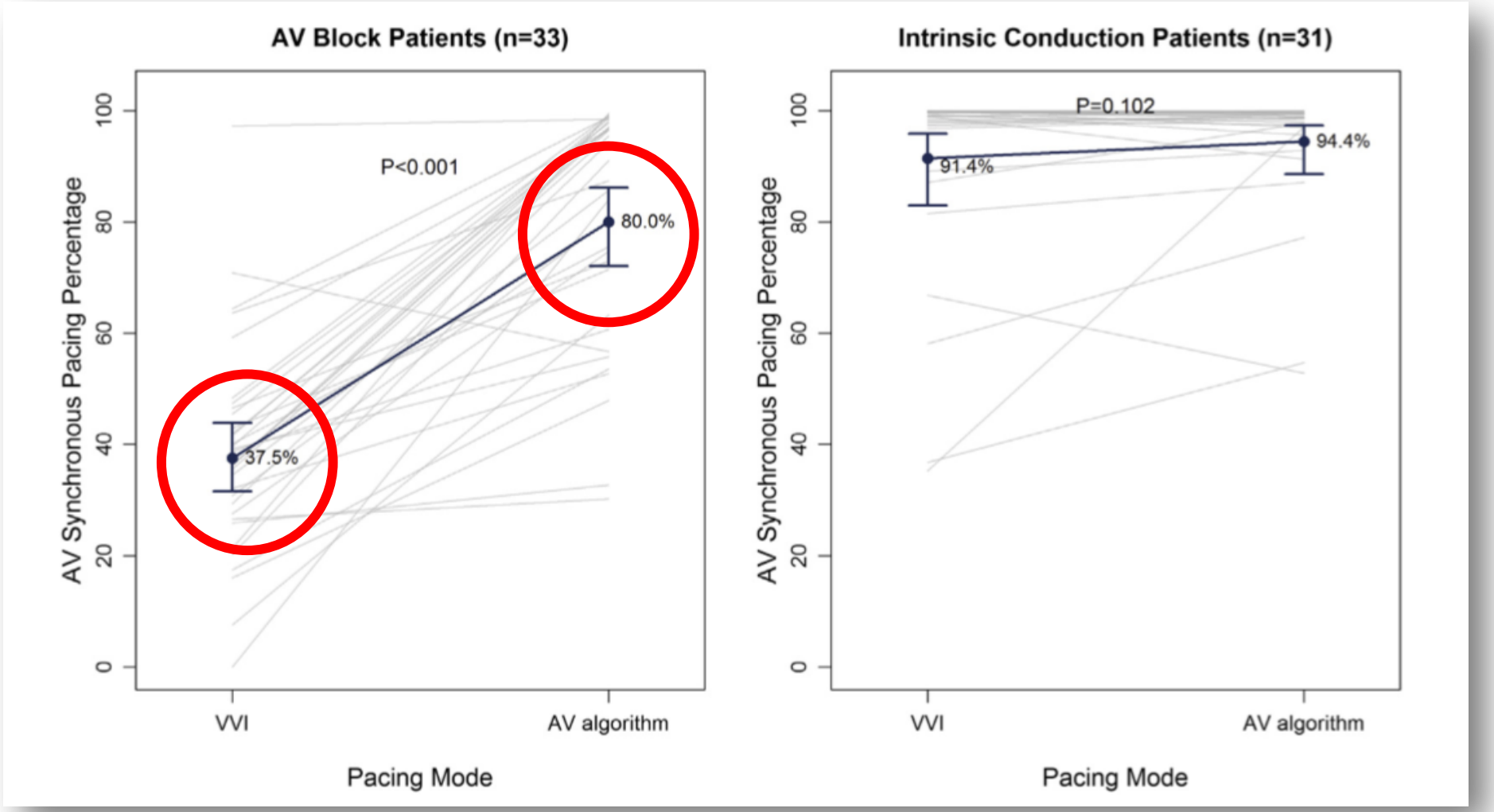

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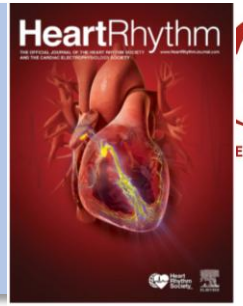
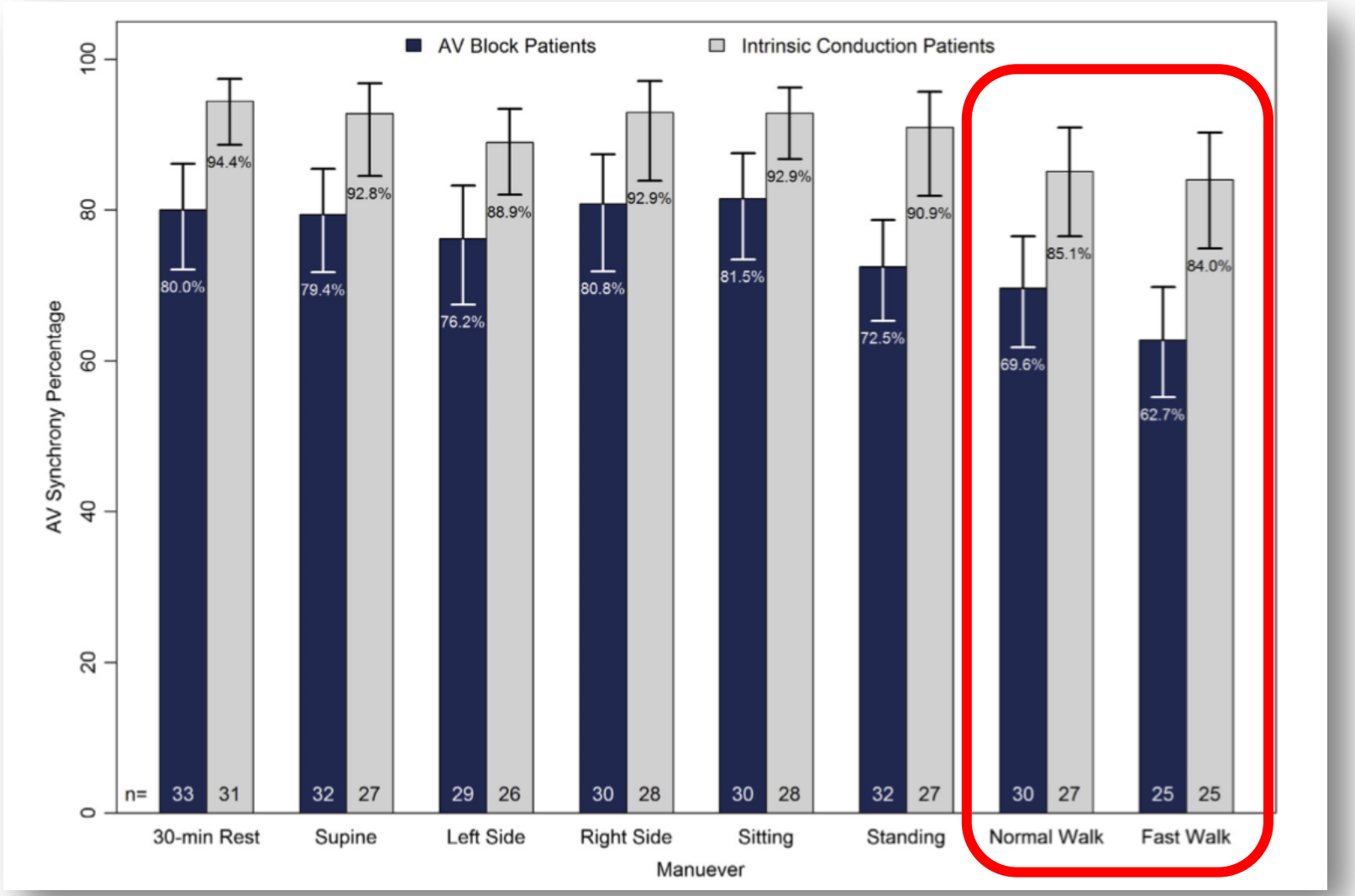
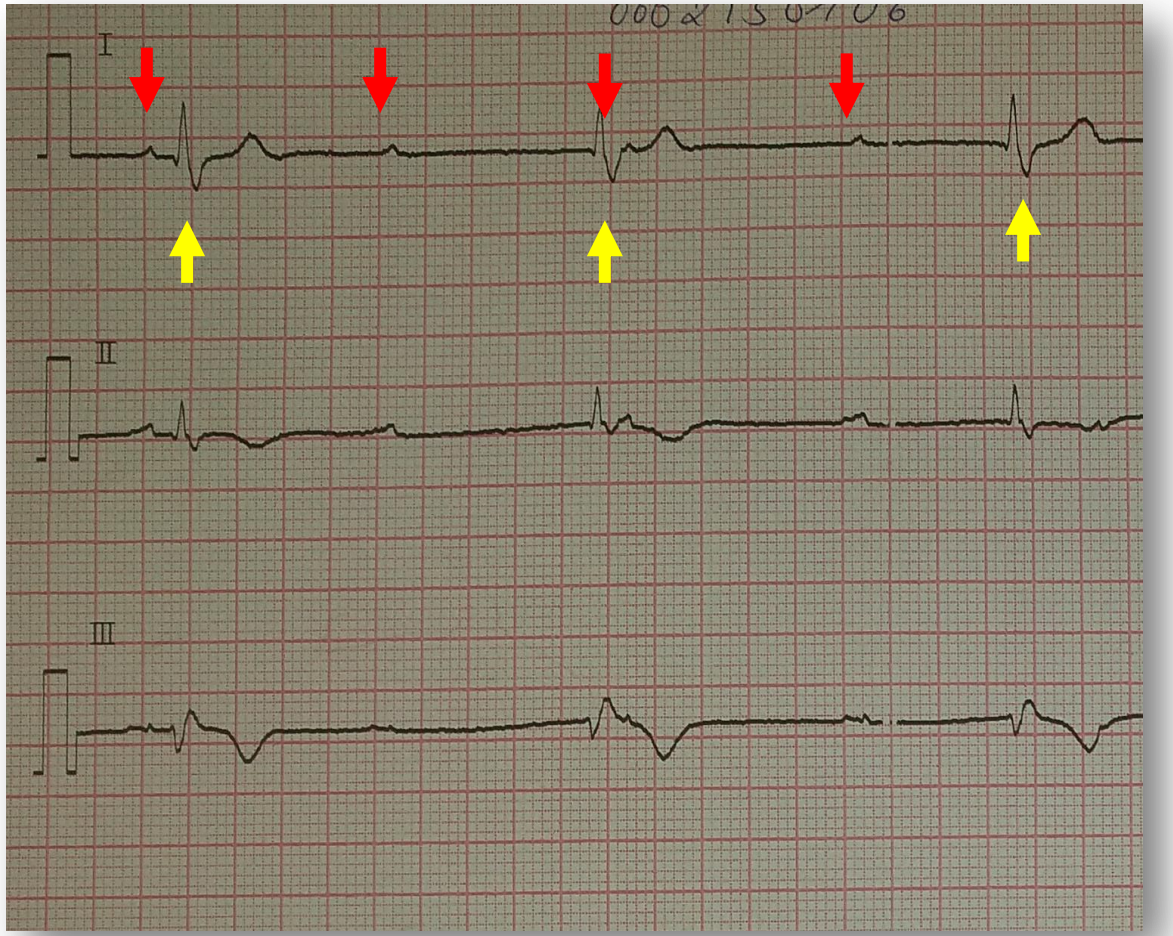
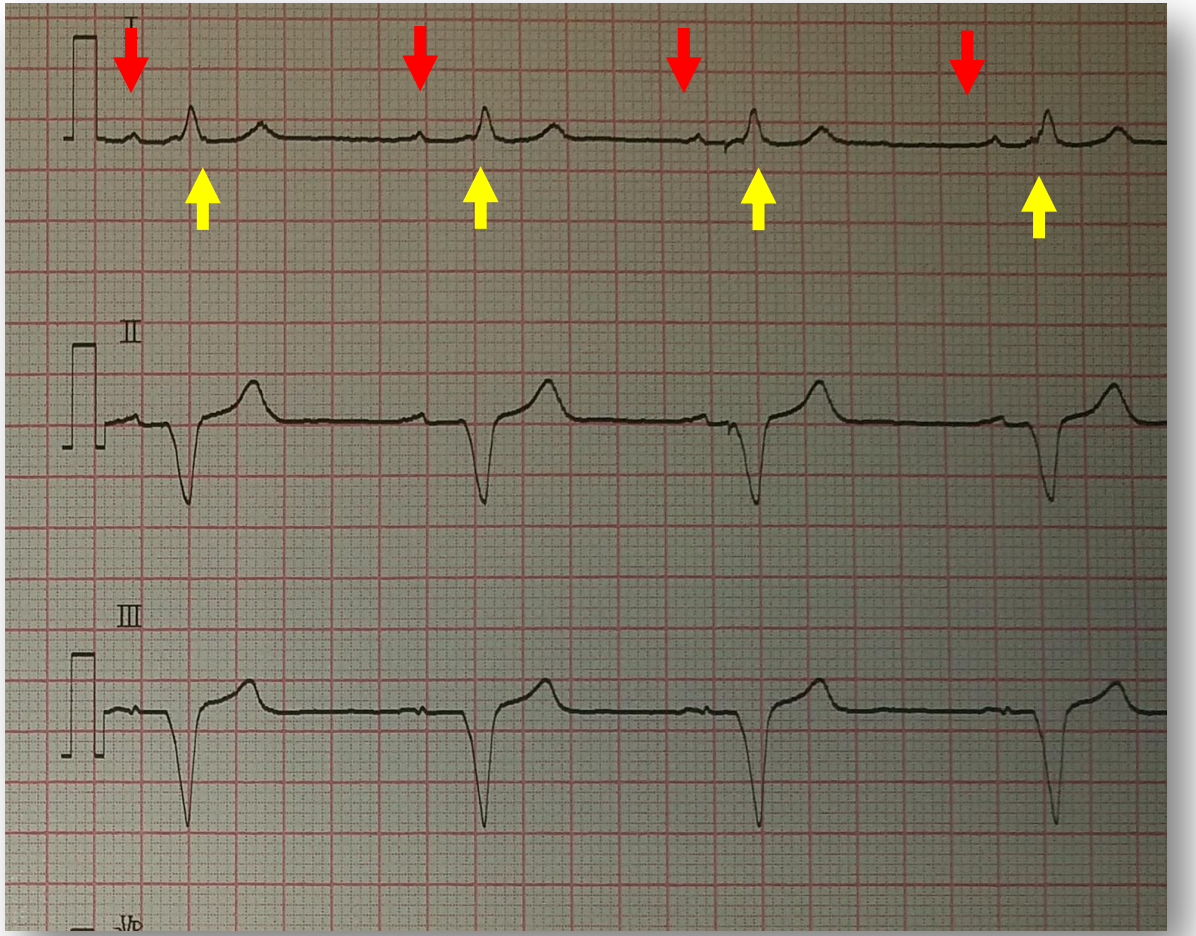




EKG

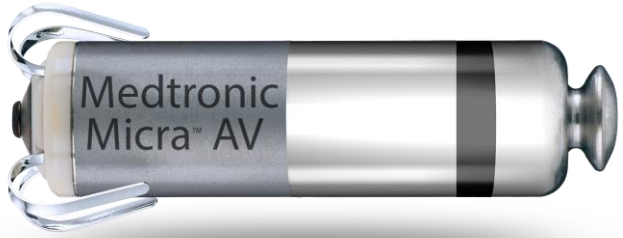




Závěry studie MARVEL

- Snímání síňové aktivity softwarovou úpravou akcelerometru leadless stimulátoru MICRA je možné a funkční
- Až 90% srdečních stahů bylo v AV synchronii
- Žádné nežádoucí účinky
- „Selhání“ softwaru: sinusové arytmie/pohybové artefakty
  nízká amplituda A4 (vlny P)
  komorová ektopie

MARVEL 2



- **nové:**
- automatický setup
- automatické nastavení senzovacích algoritmů **(auto A3 end, auto A3 a A4 threshold)**
- funkce AMS

- Multicentrická studie (10-20 center)
- Cíl: 100 pacientů
- Nabírání pacientů: 1/2019 - 7/2019 …. výsledky 10/2019

ECHO (LVOT VTI)

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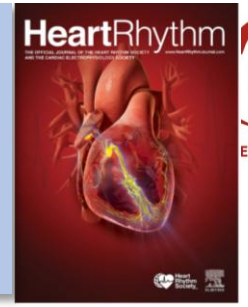
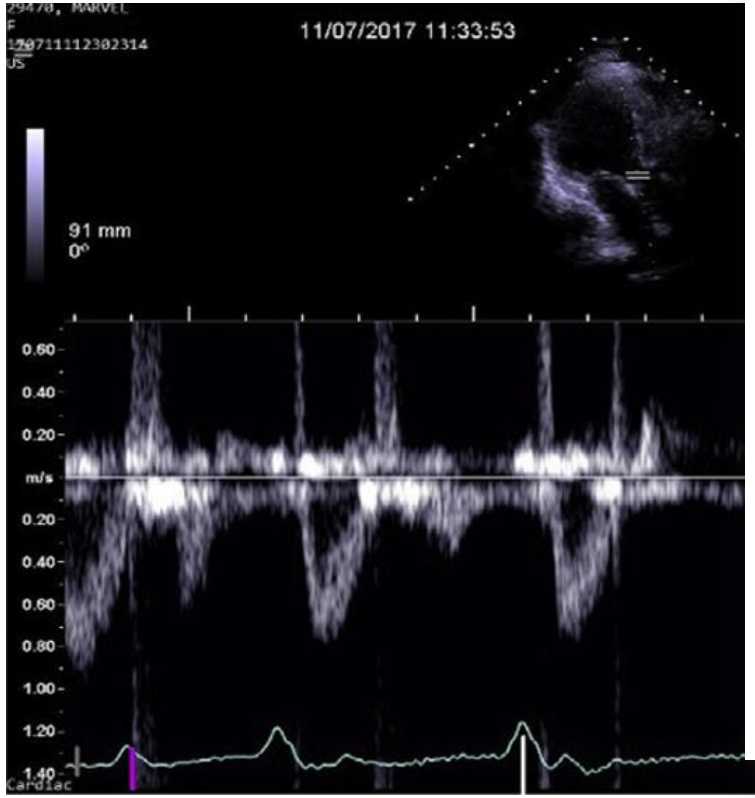
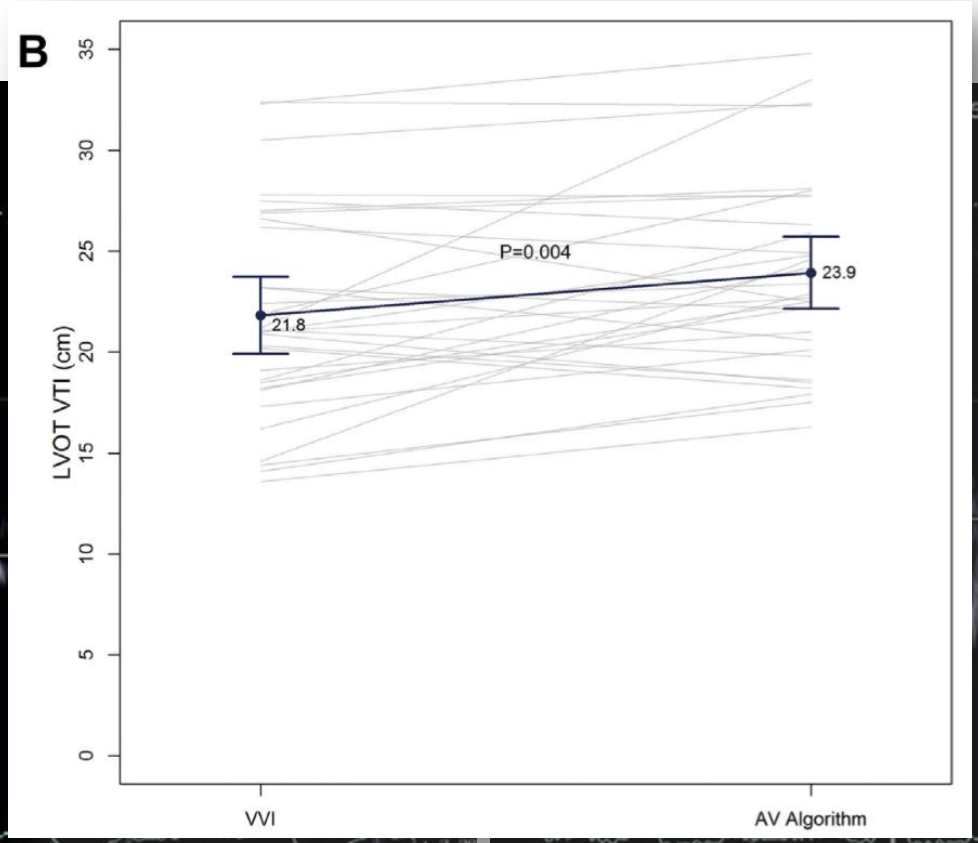
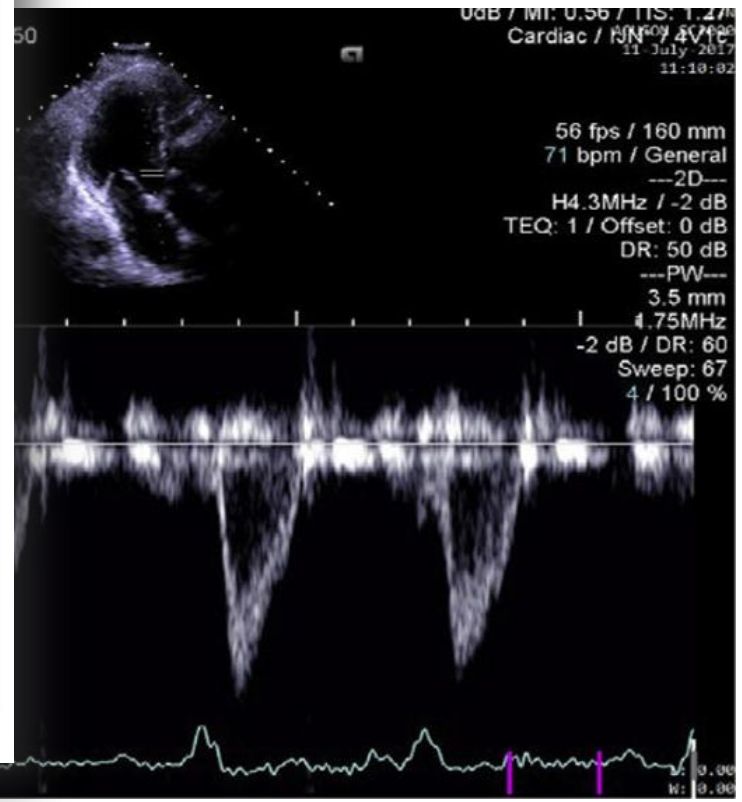


- 31/33 pacientů s AV blokem



VVI režim





VDD režim

MARVEL 2

- Vstupní kritéria:
  - Subject has been implanted with Micra TPS (Model MC1VR01) with remaining device longevity of 6 years or more, or is expected to be implanted with a Micra TPS
  - **Subject has history atrioventricular (AV) block**
  - Subject is ≥ 18 years old and as per required local law.
  - Subject is willing and able to comply with the protocol.

- Primární endpointy:
  - Efektivita: průkaz AV synchronie (VP/VS) u více než 70% ověřených vln P
  - Bezpečnost: absence pauz (> 2CCL) a epizod oversenzingem navozených tachykardií

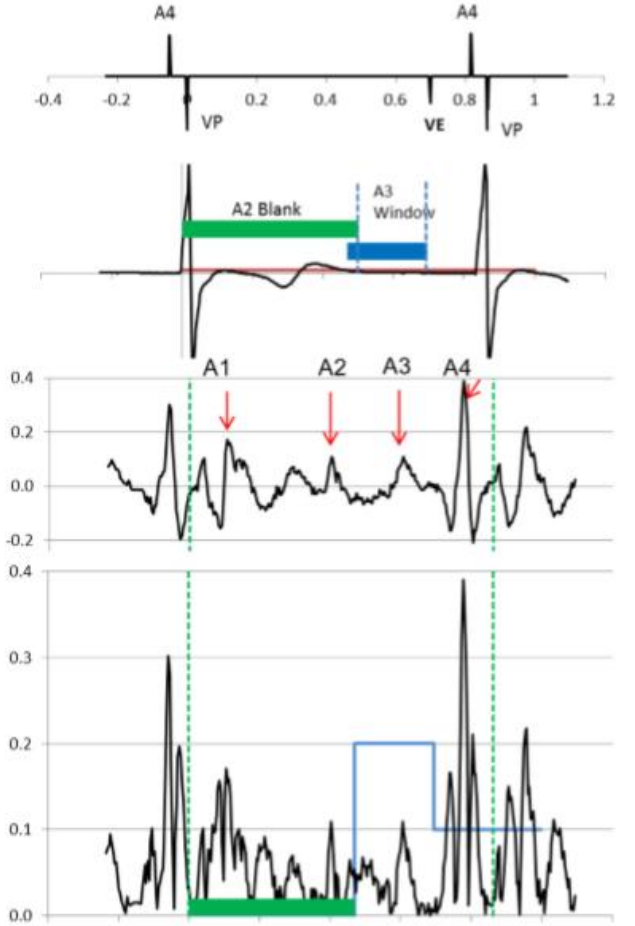


Figure 1 Overview of the atrioventricular synchronous algorithm developed from MASS/MASS2 accelerometer signals. **Top:** Device marker channel and programmable A2 and A3 blanking windows. VE = end of A3 window. **Middle:** Accelerometer signal in relation to the ventricular event (*dashed green vertical 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.

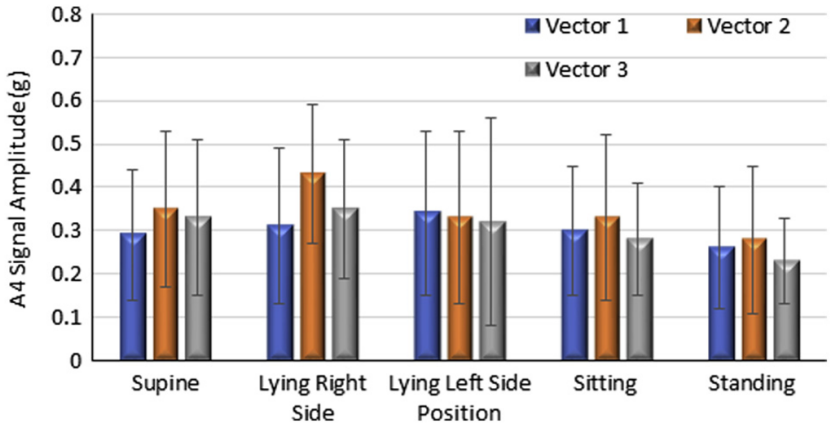


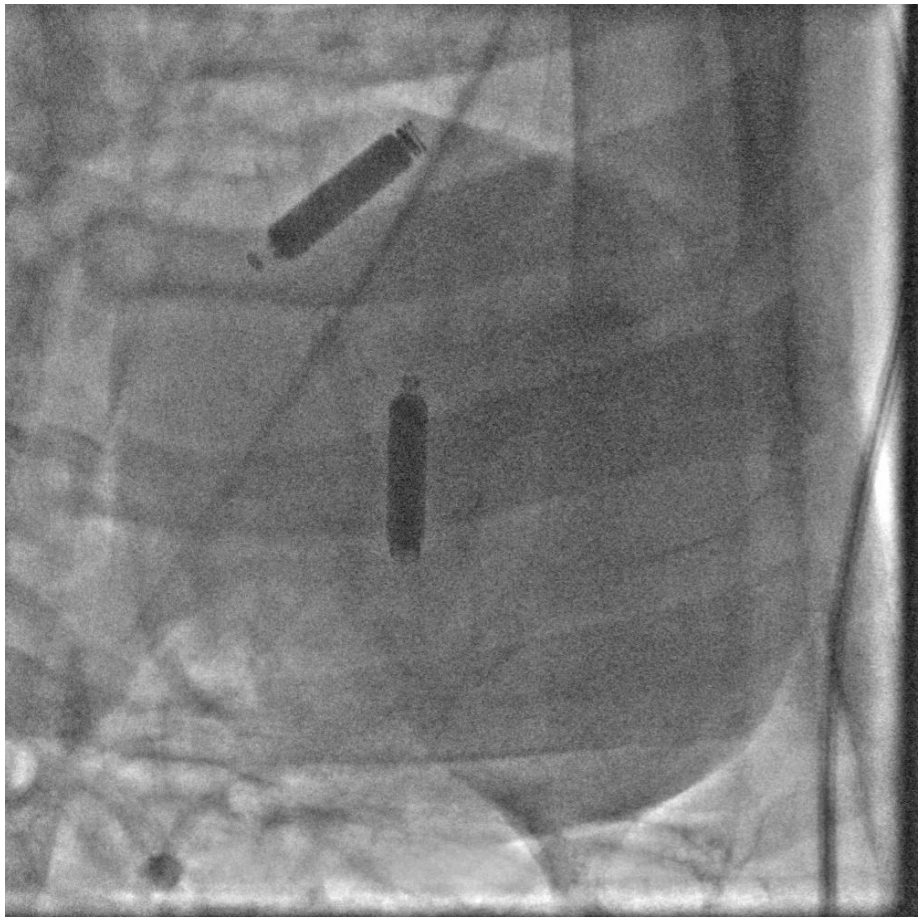
Figure 2 A4 signal amplitude from patients with normal sinus function and intrinsic conduction requiring infrequent pacing. Error bars represent standard deviation. Units (g) on the y-axis represent acceleration. N ranged from 22 in vector 3, left position, to 38 in vector 1, supine position.

Table 1 Baseline and medical history of patients in MARVEL

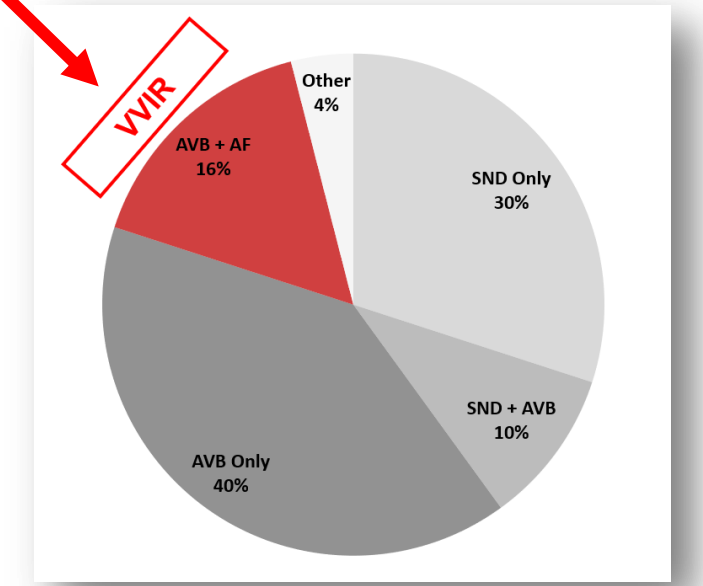
Characteristics	Enrolled (n = 70)	Usable Holter (n = 64)
Age (years)		
Mean ± SD	71.3 ± 15.1	72.0 ± 14.4
Range	24–92	30–92
Female	24 (34)	20 (31)
Months from Micra implant		
Mean ± SD	11.6 ± 12.3	11.5 ± 12.4
Range	0–41.4	0–41.4
Comorbidities		
Hypertension	41 (59)	38 (59)
Paroxysmal atrial fibrillation	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)

VVI(R) režim je vhodný jen pro 16% pac. indikovaných ke stimulaci

- DDD stimulace



Nanostim LCP, Abbott



Based on PANORAMA, SavePace, MOST, OPTI-MIND, ESC Country & US Registries

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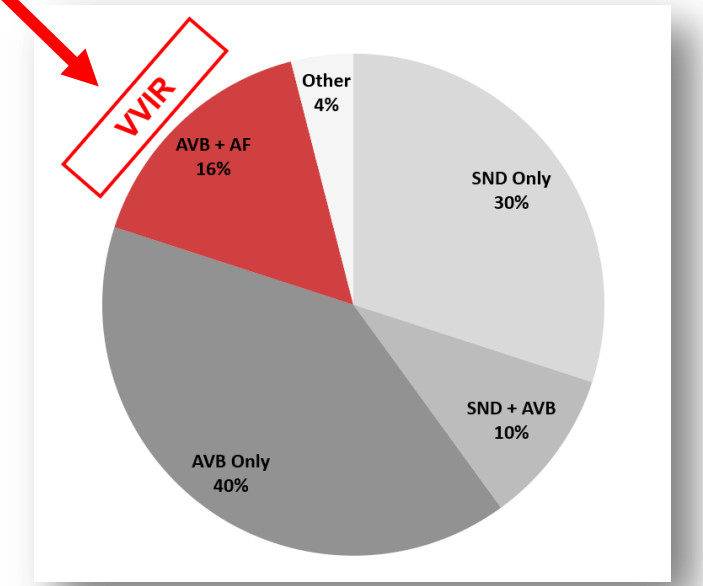

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Schéma aktivace softwaru a monitorace

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  - Snímací vektor, A2 blanking period, A3 end time, A3 threshold, A4 threshold (vsedě, vleže)

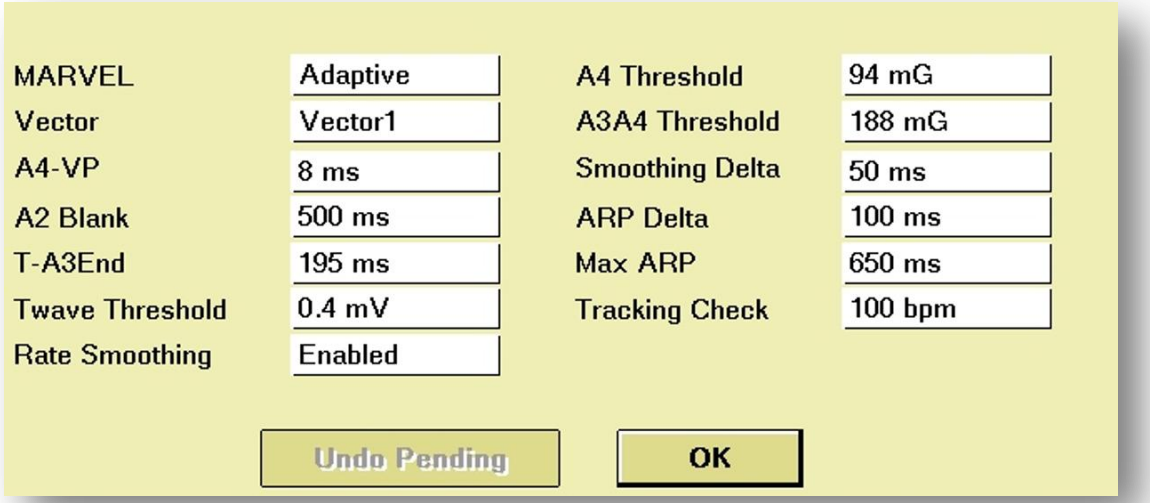
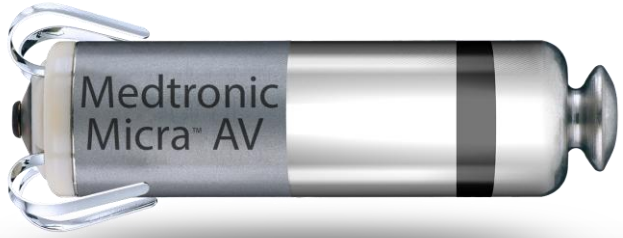


Schéma studie



Day 1: Meets I/E-Subject Enrolled

→ Download MARVEL 2 software & place Holter Monitor (10 min)

→ Perform auto setup procedures (VDI data collection) (20 min)

→ Verify Auto Setup

Confirm auto setup works as expected

→ Perform MARVEL 2 performance procedures (Resting period, postures, hall walk) (20 min) (5 min) (5 min)

Confirm algorithm works as expected with higher HRs and diff postures

→ Echocardiogram w/M2 & monitor mode (30 min)

Assess screening criteria, stroke volume

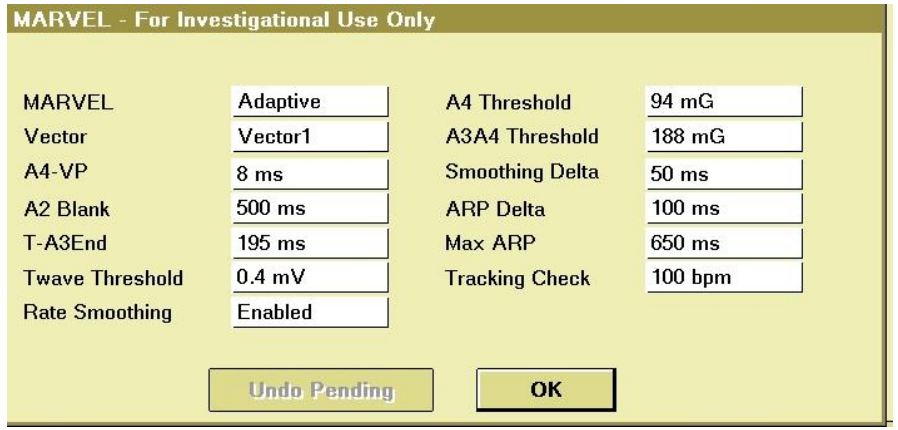
→ Remove Holter & MARVEL 2 software

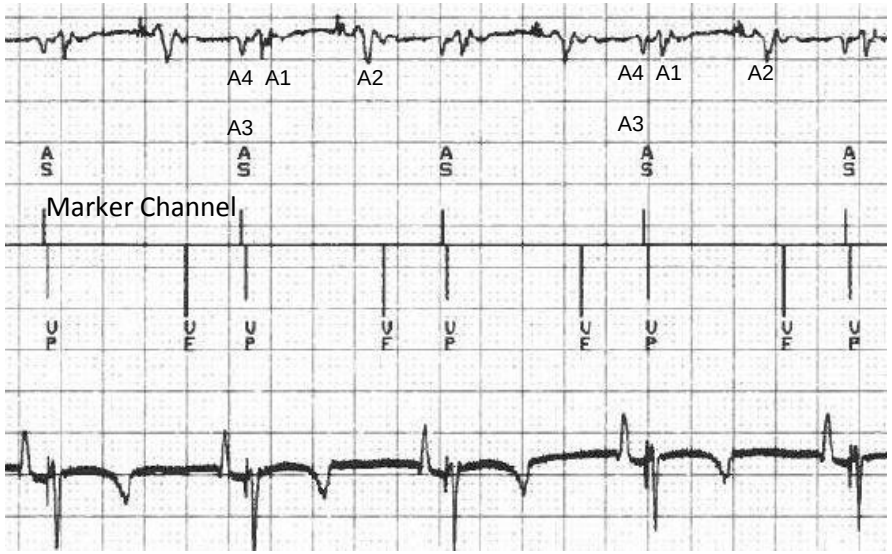
→ Return Micra to previous settings & final interrogate

→ Subject study exit

- BACKGROUND: Micra TPS© is a leadless VVI mode pacemaker that is implanted in the right ventricle and provides rate response via a 3-axis accelerometer (ACC). New software was developed to detect atrial contraction using the ACC enabling AV synchronous pacing to get VDD pacing mode.
  OBJECTIVE: To sense atrial contractions from the Micra ACC signal and provide AV synchronous pacing.
  METHODS: The MASS/MASS2 early feasibility studies showed intracardiac accelerations related to atrial contraction can be measured via ACC in the Micra leadless pacemaker. MARVEL was a prospective multicenter study designed to characterize the closed-loop performance of an AV synchronous algorithm downloaded into previously implanted Micra devices.
  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 while 31 had predominantly intrinsic conduction during the study. Average AVS during AV algorithm pacing was 87.0% (CI: 81.8%-90.9%); 80.0% in high-degree block patients and 94.4% in patients with intrinsic conduction. AVS was significantly greater ($P<0.001$) during AV algorithm pacing compared to VVI in high degree block patients while AVS was maintained in patients with intrinsic conduction. In our center 6 patients (4 M/2W) were enrolled with high degree AV block in 4 and lower degree AV block in 2. In our cohort VDD response was similar compared to all study patients.
  CONCLUSION: Accelerometer-based atrial sensing is feasible and significantly improves AV synchrony in patients with AV block and a single-chamber leadless pacemaker implanted in the right ventricle.

Optimization phase
ADJUSTING PARAMETERS DETAILS



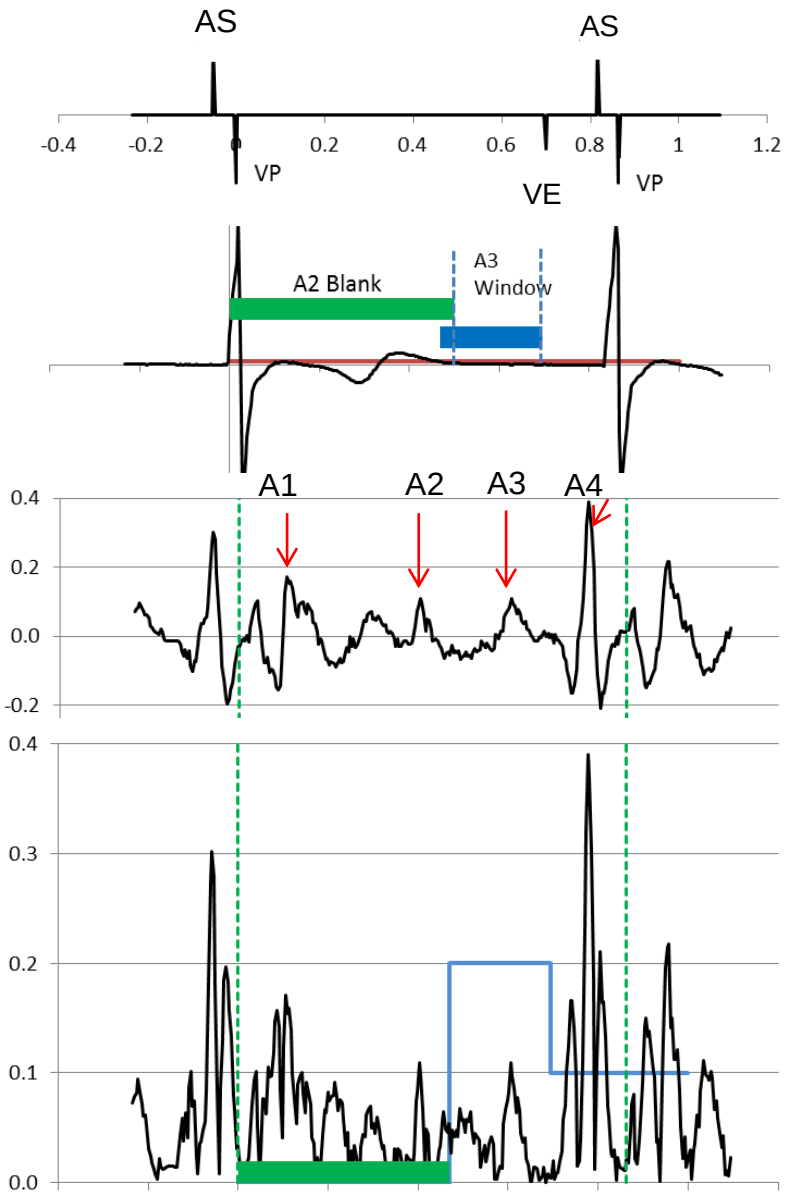


AV blocked pig with AV synchrony restored with MARVEL

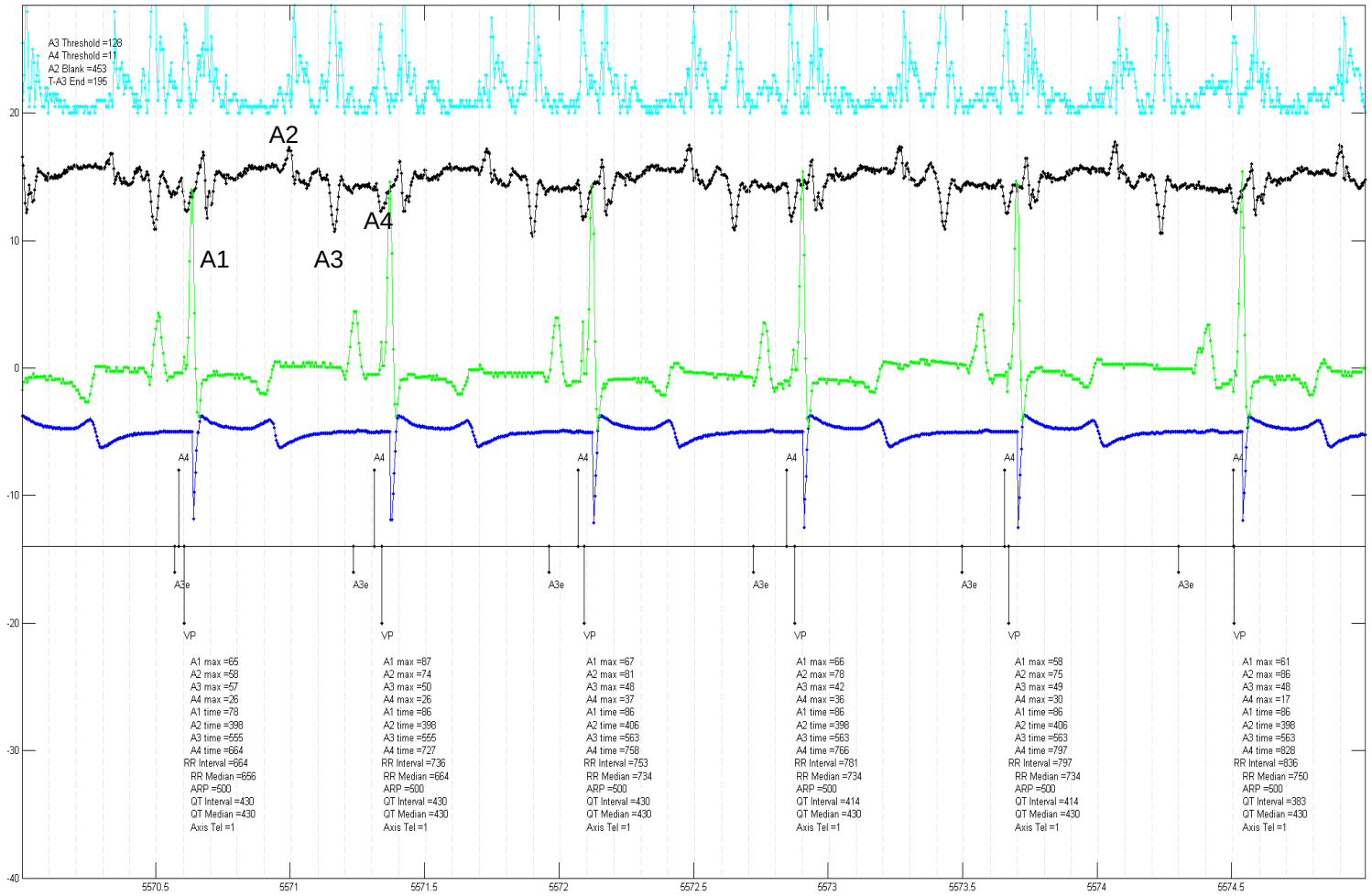
- MARVEL includes two new markers:
  - AS for when A4 detected.
  - VE for when algorithm expects no more ventricular related accelerometer signals.
  - Accelerometer waveform signal is provided
- Adjust VE marker
  - T-wave end + T-A3 end
  - Should be adjusted beyond A3 signal.
- Detect A4 (AS)
  - Adjust A4 threshold to detect A4 without detecting end of A3

Algorithm Description

- High pass filter accelerometer (5-10Hz)
- Rectify filtered accelerometer
- Blanking after ventricular sense
- Blanking or increased threshold after T-wave to blank A3
  - Measurements in hardware, blanking set by firmware
- Detect A4 as first crossing of threshold of rectified, filtered accelerometer
  - Typically 0.10-0.15g



MARVEL PROVIDING AV SYNCHRONY IN AV BLOCKED PORCINE



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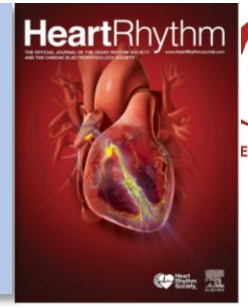
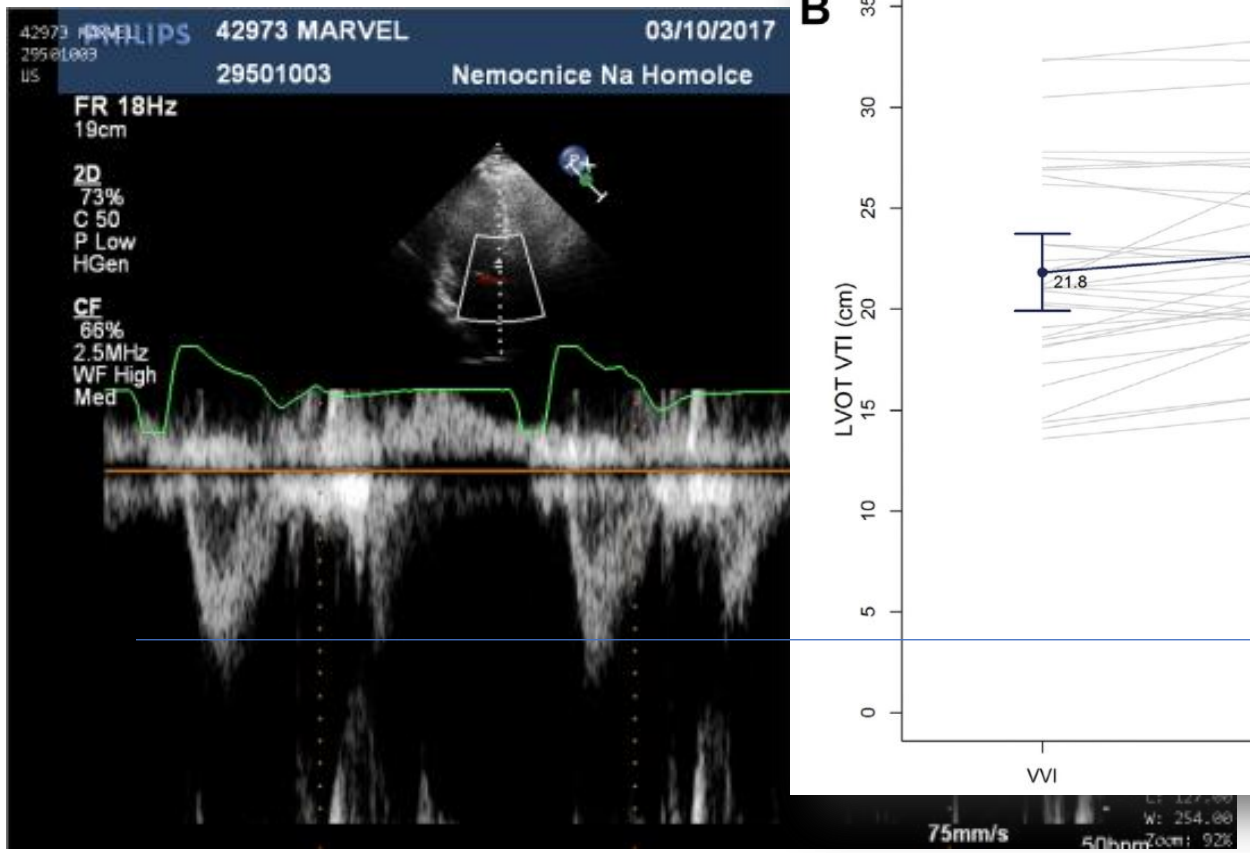
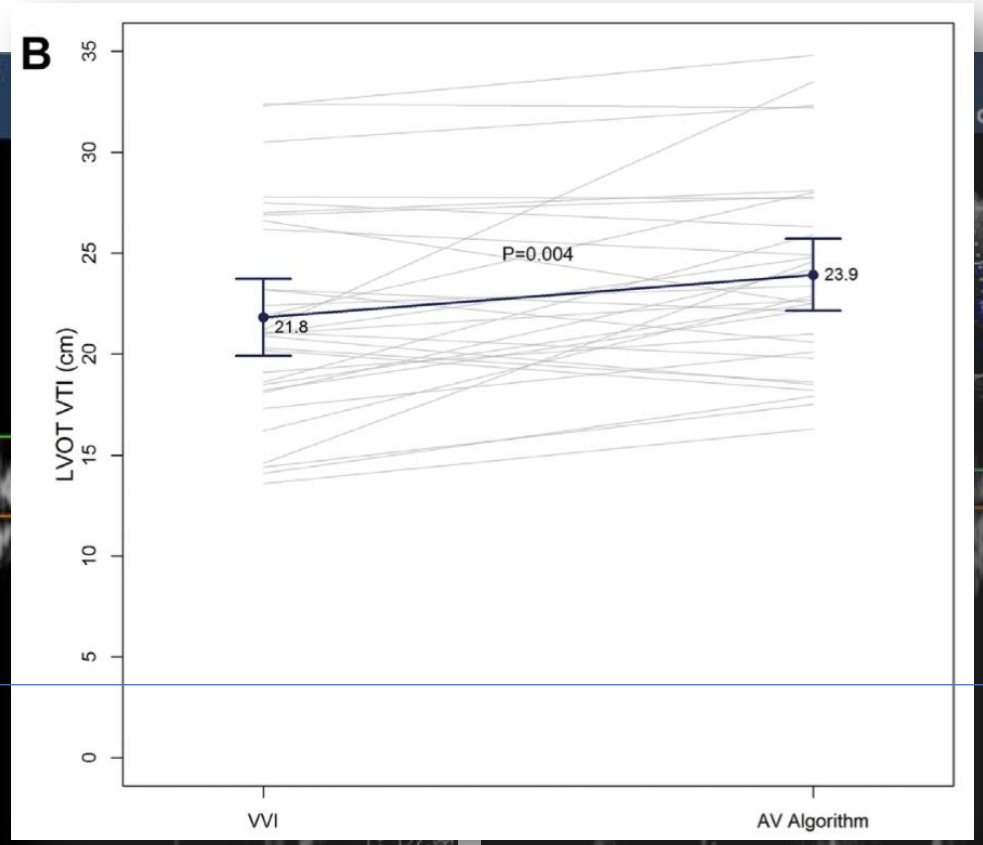
Heart Rhythm. 2018 Sep;15(9):1363-1371.

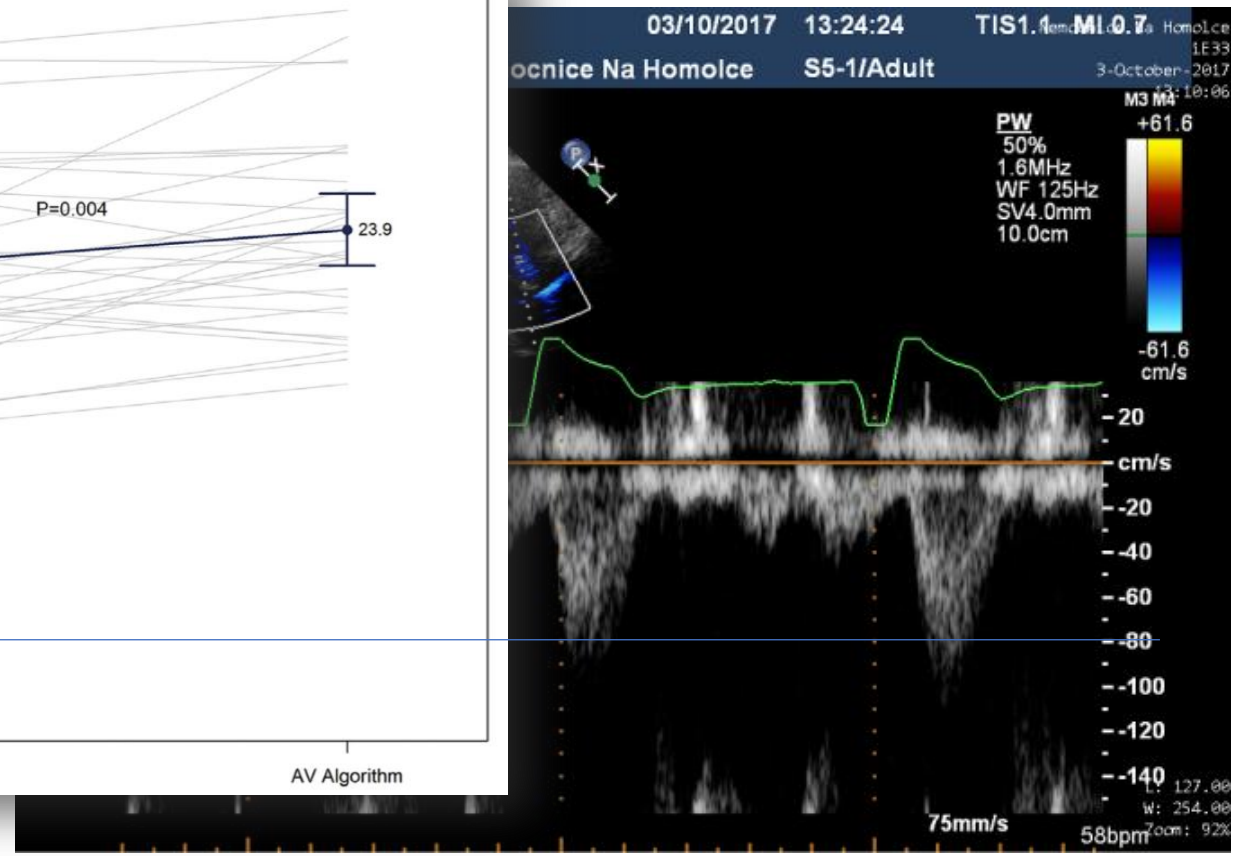


- 31/33 pacientů s AV blokem



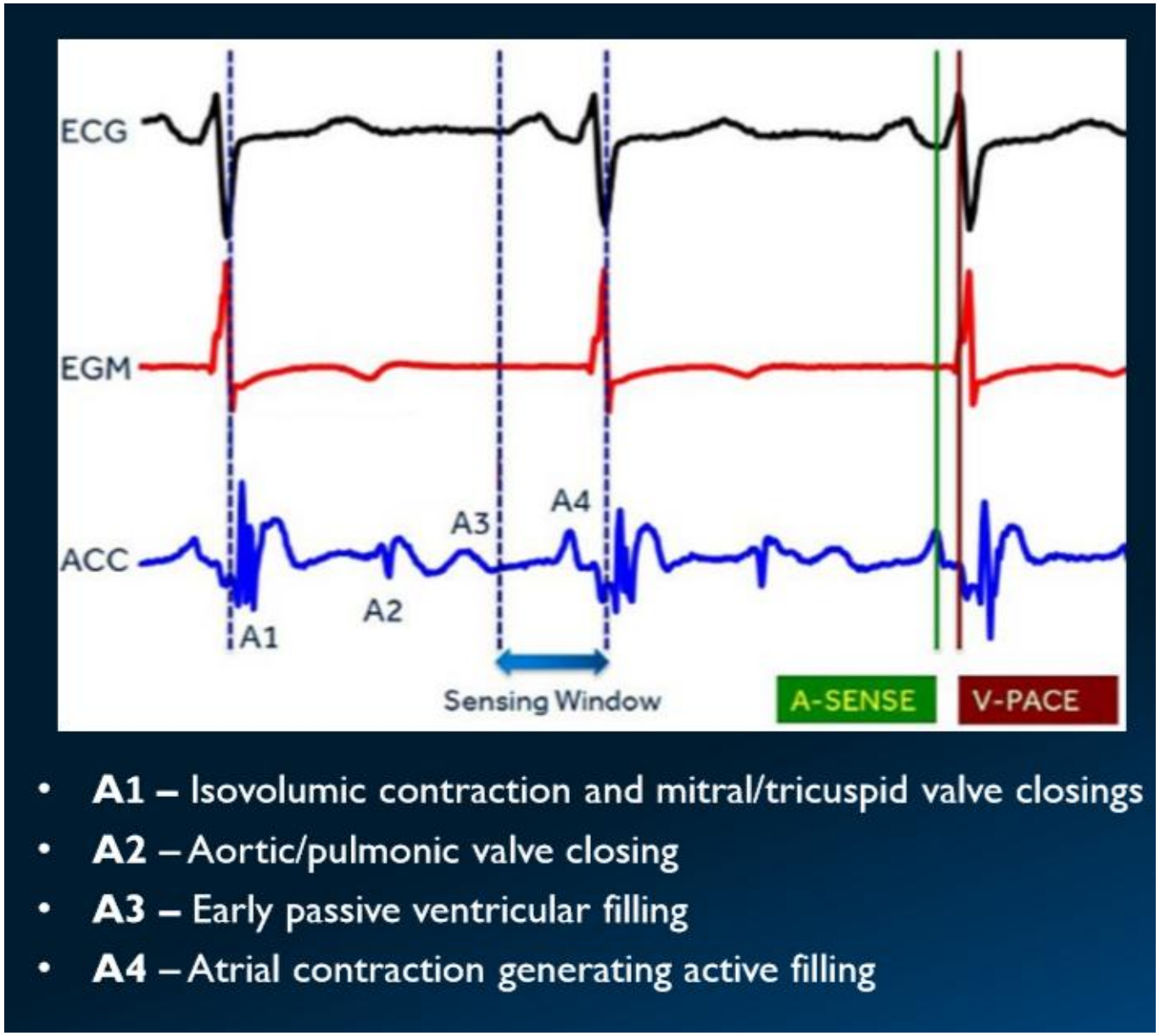
VVI režim





VDD režim

VDD režim ....



Larry A. Chinitz, MD, FHRS, Heart Rhythm Scientific Sessions, May 2018, Boston