Increased cardiac output and left ventricular contractility in pigs paced with vs. without restored respiratory sinus arrhythmia - proof of principle of a newly developed pacing device

M. Riesenhuber¹, A. Spannbauer¹, E. Hasimbegovic¹, K. Muller-Zlabinger¹, D. Lukovic¹, K. Hamzaraj¹, E. Han¹, R. Hemetsberger¹, S. Aasmul², M. Leonhardt³, C. Kushwah³, A. Nogaret³, C. Hengstenberg¹, M. Gyongyosi¹

¹Medical University of Vienna, Department of Internal Medicine II, Division of Cardiology, Vienna, Austria
²Bakken Research Centre, Medtronic, Maastricht, Netherlands (The)
³University of Bath, Department of Physics, Bath, United Kingdom of Great Britain & Northern Ireland

Funding Acknowledgements: Type of funding sources: Public grant(s) – EU funding. Main funding source(s): European Union’s Horizon 2020 Future Emerging Technologies Programme

Background: Heart rate variability (HRV) correlates with the severity and mortality of heart failure. Respiratory sinus arrhythmia (RSA) is defined by the dynamic increase and decrease in heart rate between breaths. Restoration of RSA might be beneficial in patients with heart failure and/or patients in need of permanent pacing.

Purpose: The aim of this translational, proof-of-principle study was to investigate the effect of pacing with or without RSA using a newly designed pacing device on the left ventricular contractility and cardiac output.

Methods: The project was initiated with the aim of designing a new pacing device capable of restoring RSA in paced hearts with the help of lung inflation sensors. Neuronal networks were designed to reconstruct the human brain using ultra-low energy-consuming technology. The lung inflation sensor fed the detected inspiration data back to the pacing device, which paced the heart via pacing leads (DDD) in the right atrium and ventricle. In total, 5 intubated but spontaneously breathing landrace pigs were paced without RSA (fixed-rate pacing) and with restored RSA.

Stroke volume and cardiac output were measured by echocardiography (diameter of left ventricular outflow tract and velocity time integral measured by pulsed wave doppler averaged over three heart beats). Preload-independent cardiac contractility was measured via a pressure-volume loop catheter in the left ventricle during occlusion of the inferior vena cava. Fig. 1 indicates the setup of the trial. The trials were conducted according to the relevant rules (NIH Publication no. 85-23 revised 1985) and in accordance with national law.

Results: Echocardiography (n=5) showed a mean left ventricular outflow tract diameter of 21 ± 0.1 mm. The mean intrinsic heart rate was 87 ± 14 bpm, and the mean paced heart rate was 104 ± 5 bpm in the pigs (65 ± 3 kg). The main outcomes are displayed in Fig. 2: The left ventricular stroke volume increased by 11ml (+21%, p=0.036) with 100% RSA compared to pacing without RSA, while cardiac output increased by 1.14 l/min (+21%, p=0.037). The pressure volume area is proportional to the total myocardial oxygen consumption and decreased by 6234 mmHg*ml (-39%, p=0.004). EF represents the relative amount of blood being pumped consuming one unit energy and increased by 0.163 (+72%, p=0.033). End-systolic pressure volume relationship demonstrated a non-significant increase by 0.183 mmHg/ml (+45%, p=0.25).

Parameters of diastolic function (Tau) did not differ between the groups.

Conclusion: Restoration of RSA by our newly developed pacing device significantly improved the cardiac contractility/output in our proof-of-principle large animal translational model. Chronic trials will be required to definitively confirm the positive effects of RSA on cardiac remodeling.
Fig. 1: Set-up of the animal trials.
Fig. 2: Main results (mean/std error)