evaluated the transmural conduction time at multiple transmural pathway in canine early repolarization model.

Methods: The Study followed the “Principles of laboratory animal care”. Transmural pseudo-ECG and endocardial/epicardial action potentials were recorded from coronary-perfused canine left ventricular wedge preparations (n = 14). The Ito agonist NS5806 (7-10 M) and Ca2⁺-channel blocker verapamil (3 μM) were used to pharmacologically mimic ER syndrome genotypes. Transmural conduction times were measured before and after the provocative agents infusion at the 5 fixed epicardial unipolar electrodes. Transmural conduction time was defined as the time from endocardial pacing to onset of signal at the unipolar electrode.

Results: Polymorphic VTs (pVT) developed in 10 of 14 preparations. There was no delayed phase 0 upstroke in transmembrane action potential in any preparation even with induced pVT. In all preparation, transmural conduction time increased significantly (1.7 ± 0.4, p < 0.05) after NS5806 (10 M) perfusion. However, dispersion of transmural conduction time did not show heterogeneity (7.1 ± 3.5 vs. 7.7 ± 4.55, p = 0.240).

Conclusion: In early repolarization model, polymorphic ventricular tachycardia can be induced without regional conduction velocity heterogeneity. It may support the early repolarization theory.

113 Ectopic activity from optogenetically-sloped oxidative stress pattern contradicts conventional sink-source mismatch theory

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Background: Ectopic arrhythmia is a common type of arrhythmia and often predestinates occurrence of reentrant activity. Such ectopic beats are often caused by triggered activity. Hypothetically, this triggered activity can arise from areas of local tissue damage. In previous studies we used optogenetic induction of oxidative stress (OS) to produce such triggered activity. These local OS caused occurrence of zones of ultra-long action potentials (AP) (1.5-20s long) and associated ectopic beats.

Purpose: To investigate the relationship between the shape of OS induced ultra-long AP zone and initiation points of ectopic beats both experimentally and computationally.

Methods: We performed optical mapping on monolayers of neonatal rat ventricular myocytes. The optogenetic tool miniSOG (mini singlet oxygen generator) was expressed by means of lentiviral delivery. Local OS production and subsequent appearance of ultra-long AP zone was achieved by 470 nm 0.3 mW/mm² light projection using a patterned illuminator for 3-6 minutes. We performed numerical simulation using low-dimensional model of cardiac cells.

Results: In line with previous results, ectopic beats were initiated from ultra-long AP/healthy tissue interface. Surprisingly, we found that emission points of ectopic beats coincide with areas of highest curvature on ultra-long AP pattern. Since ultra-long APs could be interpreted as quasi-stable depolarized state of the cell, this result contradicts to the conventional sink-source mismatch theory. However, we reproduced these effects numerically using generic models. In addition, from simulations we found that such eccentric beats coincide purely due to electrotonic coupling between ultra-long AP zone and healthy tissue without automatically on single cell level, like early or delayed afterdepolarizations.

Conclusion: We found a condition of sink-source mismatch violation for ectopic beats induced by optogenetic production of localized OS in cardiac tissue. We showed the effect both in vitro and in silico. Due to the generic nature of the numerical model, we expect this effect to be found also in other pathological conditions of cardiac tissue.

114 An in-silico analysis of the effect of changing activation wavefronts on voltage amplitudes in patients with heart failure

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Background: Voltage amplitudes are commonly used for the detection of non-excitable tissue, but may be influenced by the propagation of the activation wavefront with respect to the recording electrode.

Objective: The aim of this study was to investigate the influence of changing activation wavefronts on unipolar voltage amplitudes (UnipV) in-silico using tailored models of patients with heart failure.

Methods: Five patient-tailored bidomain models were created. Propagating wavefronts and electrograms were computed with state-of-the-art techniques. Simulations were performed with the Propap-5 software on 2304 cores of the Bullx cluster “Curie” (TGCC, CEA, France). The baseline simulation was fitted on geometrical and electro-anatomic mapping data during intrinsic rhythm from heart failure patients. Fibrosis was not incorporated in the simulations allowing only one source of variation on UnipV. UnipV from simulations of single point right ventricular (RV) pacing and left ventricular (LV) pacing were compared at the LV endocardium and epicardium with the baseline simulation (intrinsic rhythm) using paired analyses.

Results: A total of 26,872 paired endocardial (5,374±1,165 per patient) and 51,756 epicardial electrograms (10,351±2,068 per patient) were analysed. At baseline, three patients had a left bundle branch block (LBBB) and two patients a non-specific intra-ventricular conduction defect. A significant correlation of UnipV (LV) with UnipV (RV) was not observed. The distribution of UnipV was poorly for both endocardial (RV pacing: R = 0.38, LV pacing: R = 0.30) as well as epicardial UnipV (RV pacing: R = 0.30, LV pacing: R = 0.13). The mean absolute change in UnipV between baseline and RV and LV pacing was respectively 3.9±1.2 mV and 3.8±1.2 mV (both 31% of baseline) for the endocardium, and 5.8±3.8 mV and 6.4±5.4% (36% and 41% of baseline) for the epicardium. RV pacing resulted on average in lower endocardial UnipV in 1 patient, and higher UnipV in 4 patients, while lower epicardial UnipV were observed in 4 patients, and higher UnipV in 1 patient (all p < 0.05). LV pacing resulted in lower endocardial UnipV in 5 patients and higher UnipV in 3 patients, while lower epicardial UnipV was observed in 4 patients and higher UnipV in 1 patient (all p < 0.001). There was no linear correlation between activation time and UnipV, neither for the endocardial nor the epicardial measurements (all R = 0.05, p > 0.05). Conclusion: UnipV was strongly influenced by changing activation wavefronts, influencing the characterization of low-voltage areas and possibly the localization of non-excitatory tissue. There is no linear correlation between the activation time and UnipV.