evaluated the transmural conduction time at multiple transmural pathways in canine early repolarization models.

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 tetrodotoxin (TTX)-sensitive (70-10 μM) Ca2+ channel blocker verapamil (3 μM) was 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 (p < 0.001) for both 5 (70-1 μM) (p = 0.001) and 3 μM (p < 0.001). However, dispersion of transmural conduction time did not show heterogeneity (7.1 ± 4.3 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-spatied oxidative stress pattern contradicts conventional sink-source mismatch theory
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Background: Ectopy arrhythmia is a common type of arrhythmia and often predestines 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. There 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 anisotropic behavior results purely due to electronic 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 originating from areas of oxidative stress. The aggressive pattern of oxidative stress (OS) is the right driver to explain the emergence of such activity.

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 Propag-5 software on 2304 cores of the Bulk cluster “Curie” (TGCC, CEA, France). The baseline simulation was fitted on geometrical and electro-anatomical 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 (intrinsinc rhythm) using paired t-tests.

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 block (IVB). Conduction defect on UnipV (LV) was not found in any patient. Wavefront were passing 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 ± 3.5 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). In 10 patients, the UnipV distribution changes substantially with different activation wavefronts.

Conclusion: UnipV’s are strongly influenced by changing activation wavefronts, influencing the characterization of low-voltage areas and possibly the localization of non-excitable tissue. There is no linear correlation between the activation time and UnipV.