conductivity in the BZ was decreased to investigate the effect of uncoupling on DAD-mediated conduction block.

**Results:** Subthreshold DADs occurring within the infarct BZ inactivated the fast sodium current which led to block of S2 beats. This occurred most readily in narrow isthmus regions where electrotonic load was attenuated by the inexcitable scar. DADs rendered the entire isthmus area refractory establishing a substrate for unidirectional block and reentry (Fig). Reduced tissue coupling further enhanced this mechanism increasing the vulnerable window for reentry initiation (700ms < S2 CI < 900ms).

**Conclusion:** Subthreshold DADs provide a substrate for arrhythmogenesis in the infarct BZ. Tissue uncoupling enhanced the arrhythmogenic risk by increasing the time window of unidirectional block.

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CHRONIC VAGAL NERVE STIMULATION REDUCES VENTRICULAR ARRHYTHMIAS FOLLOWING MYOCARDIAL INFARCTION

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**Background:** Myocardial infarction (MI) and its associated sympathoexcitation promote ventricular electrophysiologic heterogeneity and ventricular arrhythmias.

**Objective:** To evaluate whether chronic vagal nerve stimulation (VNS) reduces the inducibility of ventricular arrhythmias following MI.

**Methods:** Yucatan minipigs were divided into chronic MI (n = 10) and chronic MI + chronic VNS (n=8) groups. Chronic VNS therapy was applied to the right cervical vagus nerve using implantable pulse generators and titrated to optimal intensity based on heart rate dynamics using telemetry (5Hz, 250 μs, 2.1 ± 0.3 mA, 17.5% duty cycle) in the conscious state. MI was induced by percutaneous microsphere embolization of the left anterior descending coronary artery and VNS therapy was initiated 2 days following MI. Electrophysiologic mapping was performed using a 128-electrode array across the left ventricular scar, border zone, and normal myocardium. Unipolar electrograms were analyzed for activation time, which was defined by the minimum dV/dt in the activation wavefront. Ventricular arrhythmia inducibility was evaluated using extrastimulus pacing with up to 3 extrastimuli.

**Results:** At terminal study, mean activation time across the anterior left ventricle was greater in porcine with MI (42.8 ± 1.8ms) compared to MI + chronic VNS (34.7 ± 2.1ms, p = 0.01). Similarly, dispersion of activation was over 1.5-fold greater in MI vs MI + chronic VNS groups (Figure 1A-B, p < 0.01). Chronic VNS therapy led to a significant reduction in the inducibility of early collagen deposition were observed. Active caspase-3 was observed in LV myocardium 1,2,4,8,12, and 16 weeks after irradiation. The strongest active caspase-3 signal was observed in the lesion 8 weeks post-irradiation. There was no signal for active caspase-3 in the tissue outside the target zone.

**Conclusion:** Proton beam ablation creates transmural LV lesions which are visible in LGE-MRI and histology. Apoptosis of the ventricular myocardium after proton beam radiation sharply reached its peak 8 weeks after irradiation and continued with a gradual decrease until 16 weeks and disappeared after 20 weeks. The apoptosis effect was confirmed in histology.