

OPTICAL MANIPULATION OF THE CARDIAC CONDUCTION PATHWAY

C. Crocini^{1,2}, C. Ferrantini³, R. Coppini⁴, P. Yan⁵, L. Loew⁵, E. Cerbai⁴, C. Poggesi³, and F.S. Pavone^{1,2}, L. Sacconi^{1,2}

¹National Institute of Optics–National Research Council (INO-CNR), Florence, Italy; ²European Laboratory for Non-Linear Spectroscopy (LENS), Florence, Italy; ³Division of Physiology, Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy; ⁴Division of Pharmacology, Department, University of Florence, Florence, Italy; ⁵Richard D. Berlin Centre for Cell Analysis and Modelling (CCAM), University of Connecticut Health Centre, CT, USA.
Email: sacconi@lens.unifi.it

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Current rescue therapies for life-threatening arrhythmias disregard the pathological electro-anatomical substrate and base their efficacy on a generalized electrical discharge. Here, we developed an all-optical platform to examine less invasive defibrillation strategies. An ultrafast wide-field macroscope operating at 2 KHz (100 x 100 pixel) was developed to optically map action potential propagation with a red-shifted voltage sensitive dye (di-4-ANBDQPO) in whole mouse hearts. Control of the electrical activity was achieved by employing transgenic mouse hearts expressing Channel Rhodopsin-2 (ChR2). In order to draw arbitrarily-chosen ChR2 stimulation patterns with sub-millisecond temporal resolution, the macroscope was implemented with a random-access scanning head based on acousto-optic deflectors (AODs). AODs rapidly scan the laser beam across the whole field of view exciting different volume with a commutation time of few μ s. At the end of one cycle the AODs return to the initial position and repeat the stimulation cycle. Alternatively, a simpler optical solution based on digital micromirror device (DMD) in combination with a high power LED was used to manipulate light positioning in a real simultaneous manner. We employed the macroscope to study the mechanistic features of ventricular tachycardia and we designed mechanistically-based cardioversion/defibrillation patterns exploiting the transient refractoriness of myocardium produced by the ChR2 stimulation. Multiple regions of conduction block revealed to efficiently defibrillate arrhythmic hearts but with lower energy requirements as compared to whole ventricle interventions. To confirm that the cardioversion efficiency is rigorously dependent on the mechanistic-based design, we positioned multiple regions of conduction block regardless of the re-entry arrhythmic wavefront obtaining a dramatically reduced cardioversion rate. In conclusion, this work demonstrates that defibrillation energies can be substantially reduced by applying discrete stimulation patterns and promotes the investigation of new anti-arrhythmic strategies.