Effects of Optogenetic Defibrillation on Cardiac Electrophysiology

S Ohnemus, L Tillert, J Vierock, P Kohl, F Schneider-Warme, V Timmermann

Institute for Experimental Cardiovascular Medicine, University Heart Center Freiburg-Bad Krozingen and Faculty of Medicine, University of Freiburg, Freiburg, Germany

**Introduction:** Optogenetic defibrillation offers a new approach for terminating cardiac arrhythmias based on timed activation of light-gated ion channels known as channelrhodopsins (ChR). So far, studies mainly used cation non-selective ChR, such as ChR2, or anion non-selective ChR, such as GtACR1. However, both terminate arrhythmias by membrane depolarisation, and thus, their activation may contribute to intracellular Ca\(^{2+}\) and Na\(^{+}\) overload. In contrast, K\(^{+}\)-selective ChR (KChR) may be better alternatives, as their activation will keep cardiomyocytes (CM) close to their natural resting potential. Experiments indicate that WiChR, a predominantly K\(^{+}\)-selective ChR, presents a promising target for optical defibrillation.

**Methods:** Employing the O’Hara model of a human ventricular CM, we incorporated ChR2, GtACR1 or a KChR. For ChR2 and GtACR1, we used existing models and simulated illumination with 470 nm or 515 nm light at intensities of 5 mW/mm\(^2\). For KChR we used a simple model including only a K\(^{+}\)-conductance (1.4 mS/cm\(^2\)) during light-activation. To assess CM behaviour without optogenetic manipulation, we paused the electrical pacing during the illumination period as a control scenario. Moreover, we are currently parameterising a computational model of WiChR to achieve a more realistic representation of KChR functionality.

**Results:** The simulations predict an increase in intracellular Ca\(^{2+}\) and Na\(^{+}\) during activation of ChR2 and GtACR1. In the case of KChR, the results do not indicate significant differences in these ion concentrations compared to control (see Fig. 1).

**Outlook:** We will test our hypothesis that ChR ion selectivity determines the efficacy and safety of optogenetic defibrillation in 2D and 3D simulations.