Cardiac Safety Pharmacology: Increased predictivity with laser-induced action potential like cardiac action potential recordings on MEA systems

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Live-threatening drug-induced cardiac arrhythmia is often preceded by a prolonged cardiac action potential (AP), commonly accompanied by small proarrhythmic potential fluctuations. The shape and time course of the repolarizing fraction of the AP can be pivotal for the presence or absence of arrhythmia.

Microelectrode arrays (MEA) allow easy access to cardiotoxic compound effects via extracellular field action potentials (fAP). Although a powerful and well-established tool in research and cardiac safety, the fAP waveform does not allow to infer the original AP shape due to the intrinsic AC filtering of the recording principle.

The newly developed device LUCE by Foresee Biosystems can repetitively open the membrane of cardiomyocytes growing on top of the MEA electrodes at multiple cultivation time points, using a highly focused nanosecond laser beam. The laser poration enables transcellular voltage recordings, resulting in transforming the electrophysiological signal from fAP to intracellular-like APs. This intracellular access allows precise quantification of the AP shape and better classification of proarrhythmic potentials, including early and late afterdepolarizations and ectopic beats (in comparison to regular MEA recordings).

This system is a revolutionary extension to existing electrophysiological methods, permitting accurate evaluation of cardiotoxic effect with all advantages of MEA-based recordings (easy acute and chronic experiments, signal propagation, etc.).

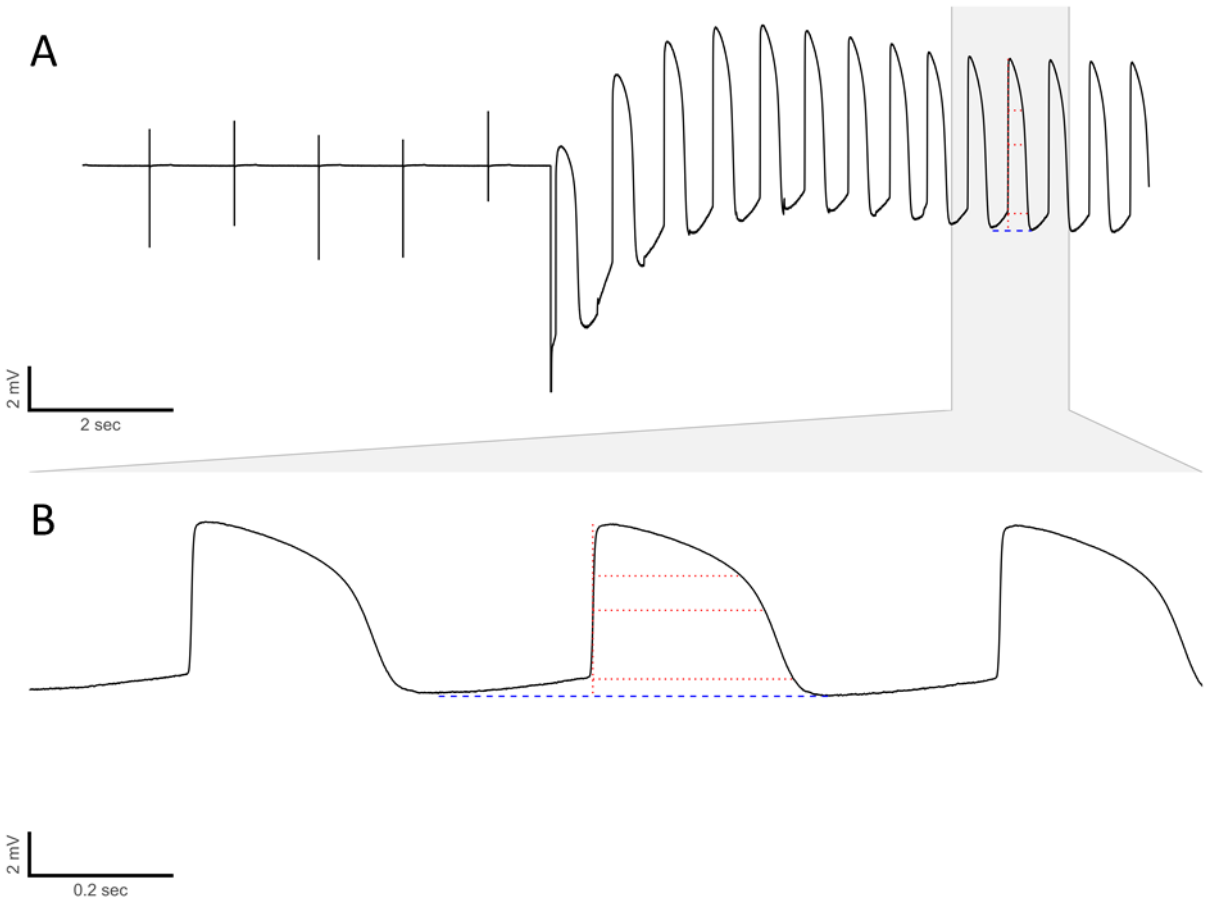

Figure 1: Laser poration transforms fAP signals into intracellular like APs

A Trace of a MEA recording showing the transformation of fAP signals to intracellular like APs of cardiomyocytes after being porated by the highly focused laser beam. *B* Close-up of the intracellular like action potential shape which allows quantifying different action potential parameters such as the action potential duration (APD, indicated with red horizontal lines), action potential amplitude (APA, indicated with red vertical line) and the interspike interval (ISI, indicated with blue line).