In silico Electrophysiological Evaluation of Scaffold Geometries for Cardiac Tissue Engineering

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Human-induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs) cultured on bio-printed scaffolds have shown promising results for cardiac function restoration in regenerative medicine. Nevertheless, arrhythmogenesis due to reduced electrical wavefront propagation of the hiPSC-CMs-scaffold complex has been poorly characterized. The aim of this study is to characterize the effect of different scaffold geometries on activation time (AT) of cultured hiPSC-CMs as part of an arrhythmic risk evaluation.

In silico hiPSC-CM electrophysiological models were used in combination with the finite element method to simulate electrical propagation in hiPSC-CM-scaffold complexes. Model parameters representing fiber alignment and intercellular coupling were fitted to match simulated AT maps to AT maps computed by optically imaging cultured hiPSC-CMs in different scaffolds. Three-dimensional square, auxetic and elongated hexagonal (honeycomb) scaffold pore shapes were assessed to determine the most biomimetic structure in terms of tissue anisotropy and action potential propagation velocity.

The results showed that hexagonal pore design facilitates the alignment of cardiac fibers at the longitudinal direction, mimicking cardiac anisotropy. Furthermore, from evaluated hexagonal structures, elongated hexagons with 120º degrees angle produced a maximum AT of 25 ms whereas for the 60º degrees elongated hexagons it was 13 ms.

In conclusion, elongated hexagonal pore shape scaffolds with 60º degrees angle lead to optimal activation of hiPSC-CM cultures. This structure is suggested in scaffold design to reduce the probability of developing in vivo pro-arrhythmic events.

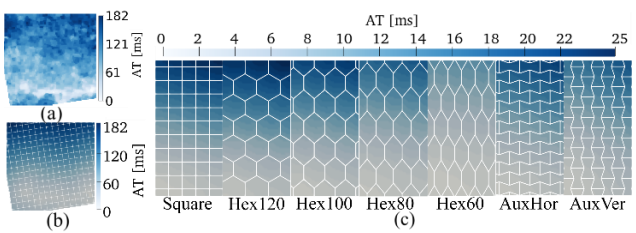

Figure: (a) Activation Time (AT) map obtained from optical mapping. (b) Simulated AT map. (c) Evaluated scaffold geometries with distinct pore geometries.