A higher throughput heart tissue model for predictive drug screening

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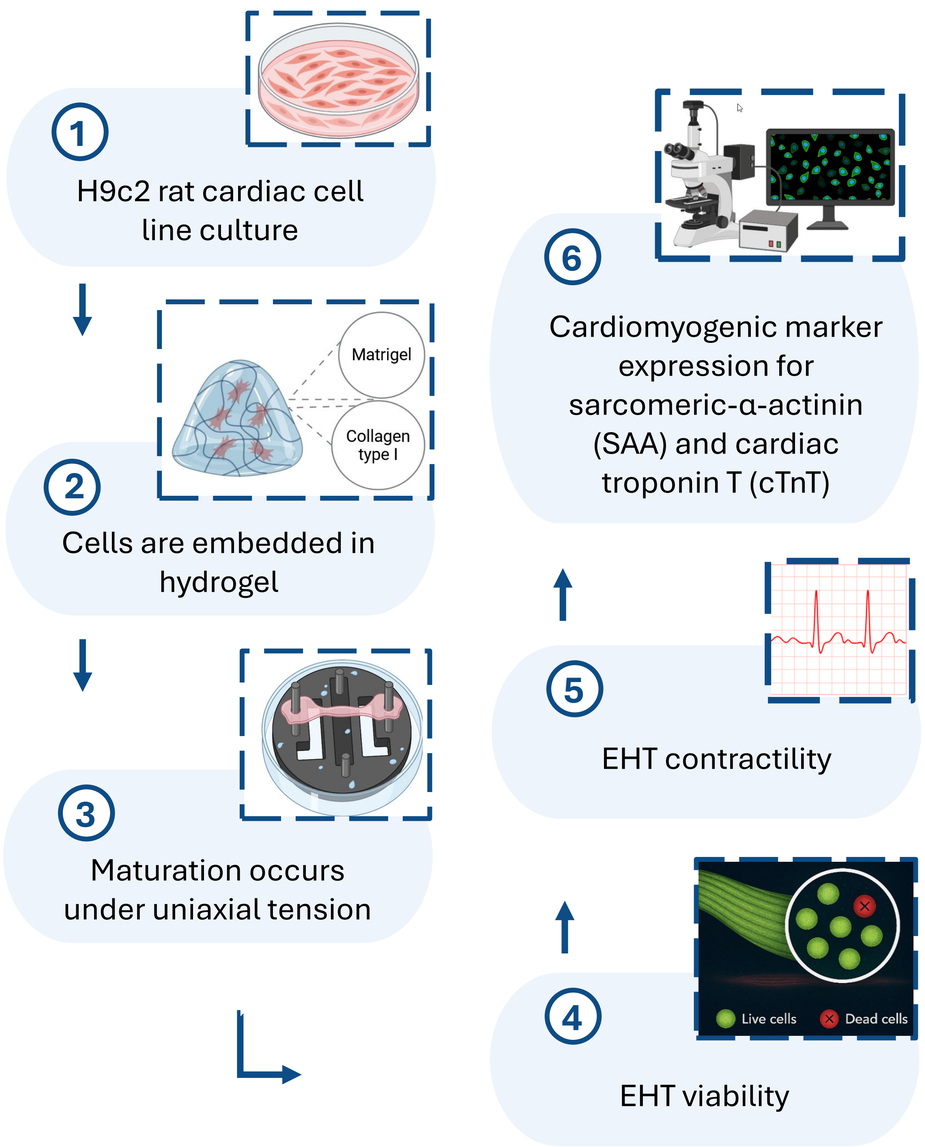
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BACKGROUND

Cardiovascular diseases (CVDs) are one of the main causes of death worldwide, killing nearly 18 million people/year. The development of new drugs targeting CVDs is very low (2%), especially when compared to cancer drugs (45%). The attrition rate for new cardiovascular drugs is 80%, meaning that only 2 out of 10 drugs reach the clinical trial stage. The absence of a robust *in vitro* model of human heart allied with the wide use of animal models contributes to the low number of new drugs reaching the clinical trial stage. The present study aims to develop and characterise a higher-throughput platform to generate engineered heart tissue (EHT).

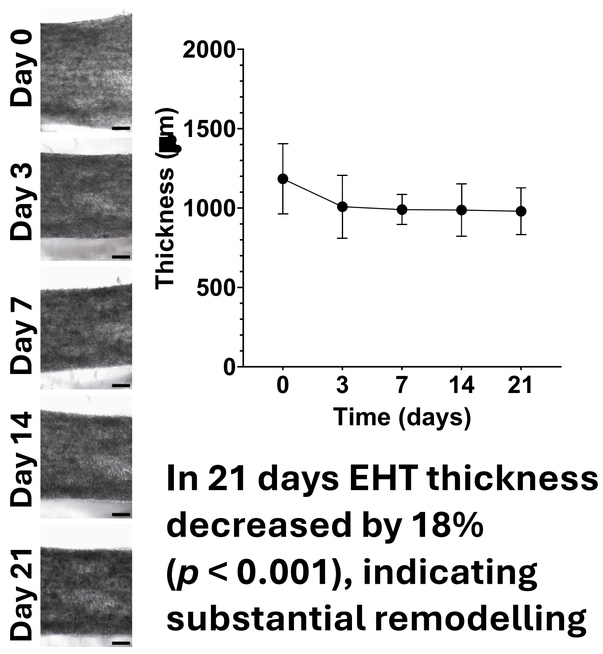
METHODOLOGY

Steps in H9c2-derived EHT generation and downstream analysis:



RESULTS

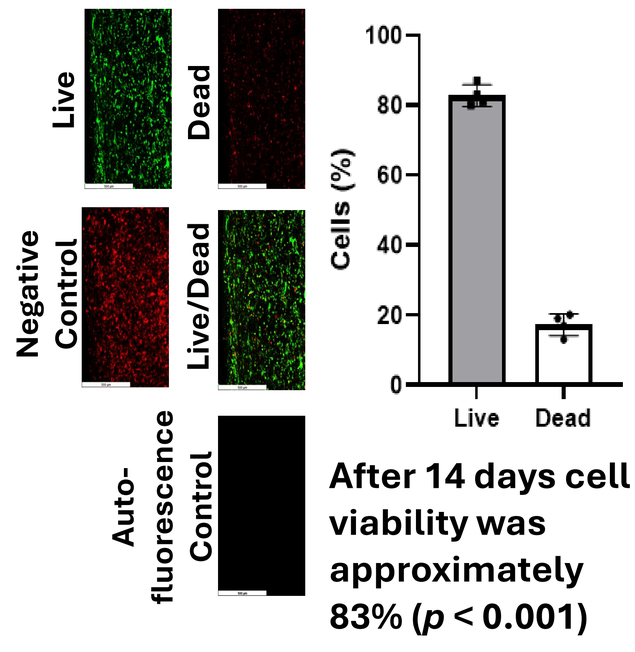
TISSUE REMODELLING



In 21 days EHT thickness decreased by 18% ($p < 0.001$), indicating substantial remodelling

Scale: 250 µm

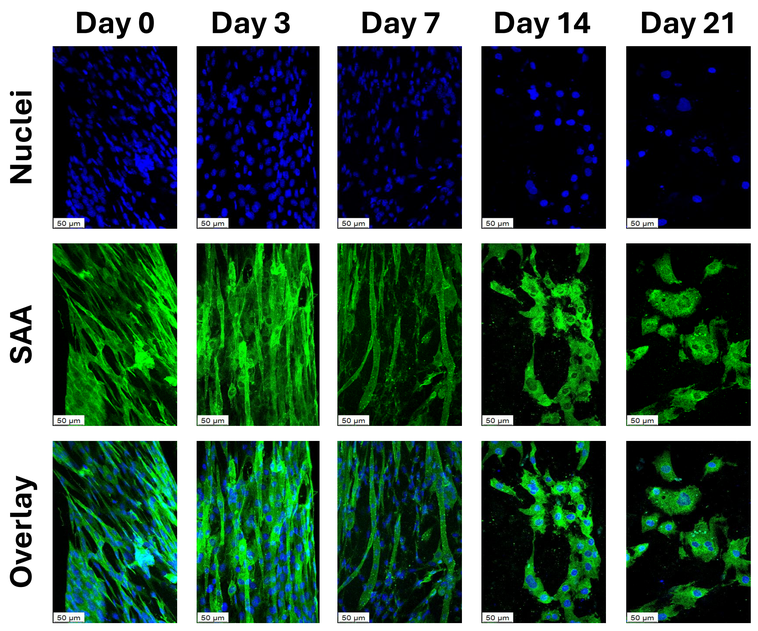
EHT VIABILITY



After 14 days cell viability was approximately 83% ($p < 0.001$)

Scale: 500 µm

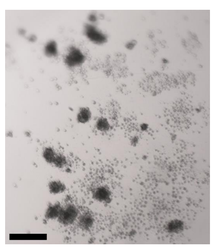
CARDIOMYOGENIC MARKERS



Scale: 500 µm

Cardiomyogenic markers declined across the first week, and no contractile activity was observed

Contractility was absent in spheroids derived from the same cell line



14-day differentiated H9c2-derived spheroids

Scale: 250 µm

CONCLUSIONS

- Development and characterisation of a high-throughput platform to generate EHT at scale.
- Although expression of cardiomyogenic markers declined over 21 days and contractility was absent in H9c2-derived EHTs and spheroids, this EHT remains compatible with acute and short-term experiments.
- Preliminary hiPSC-CM-derived EHT trials demonstrate compatibility with the platform enabling scalable EHT generation.

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