3D PRINTED MICROFIBRE ARCHITECTURES WITH NONLINEAR ELASTIC BEHAVIOUR FOR TUNABLE MYOCARDIAL CONSTRUCTS

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Introduction

The heart is an extremely complex organ at a structural level, and the orientation of cardiac muscle fibres determines cycles of healthy contraction-torsion and cardiomyocytes activation. In the event of ischemic heart disease, cardiac muscle alignment is disrupted, resulting in decreased pumping function. Current approaches for reproducing the biomechanical properties of cardiac muscle, in particular using fibre-based scaffolds, still fail to mimic the specific 3D geometry of cardiac muscle, and importantly, lack its complex elastic behaviour. Previous work shows that hexagonal structures can reversibly store more elastic strain energy and further promote cardiomyocyte (CM) maturation, compared to rectangular structures [1]. Thus, we hypothesised that the geometry of hexagonal lattice units in melt-electrowritten (MEW) scaffolds can be modified to tailor their anisotropic mechanics, thus allowing to produce tunable bioengineered myocardial constructs (BMC) that promote cardiac cell alignment and subsequent contraction in vitro.

Methods

MEW scaffolds (0.5-mm thick) with hexagonal pores and internal half-angles of 30°, 45°, and 60° were designed using TrioBASIC-based software and printed from medical-grade poly(ε-caprolactone) using an in-house built device (Fig. 1A). Print fidelity and fibre diameter were quantified using brightfield (BF) and scanning electron microscopy (SEM) (Fig. 1B). The linear and nonlinear components of the elastic behaviour in each geometry were analysed by uniaxial monotonic and cyclical testing. An ad hoc MATLAB script was developed to isolate the linear elastic behaviour from the toe region (the nonlinear strain-stiffening elastic regime at low strains) using mathematical modelling [2]. The elastic modulus, the transition point from the toe to linear elastic region, and the strain energy density in both regimes were quantified for each geometry.

Results

Modified hexagonal MEW meshes showed an individual fibre diameter of ~9 µm for all geometries evaluated (Fig. 1C). 30° scaffolds showed a 32% decrease in print fidelity with respect to 45° and 60° scaffolds due to the small separation between adjacent rows and higher electrostatic interactions during printing. 30° scaffolds showed a 5-fold increase in tensile modulus compared to 60° scaffolds, whereas the strain range of the toe region in 60° meshes was up to 8 times greater than in 30° meshes (Fig. 1D). 60° scaffolds showed the widest nonlinear elastic (toe) region from 0 to 20% strain, which is ascribed to greater potential for fibre alignment under loading.

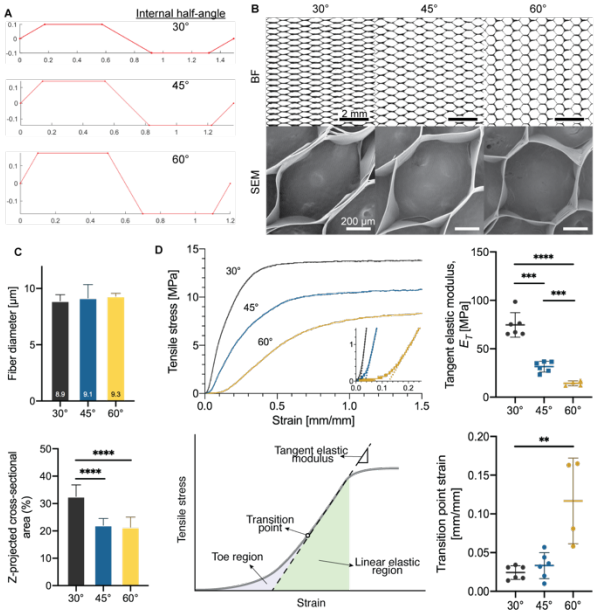

Figure 1: A) Design of MEW hexagonal architectures with different internal half-angles and constant side length (0.4 mm). B) Fibre morphology and organization in MEW printed scaffolds. C) Fibre diameter and projected area as indicator of print quality. D) Representative tensile curves, definitions and quantification of mechanical parameters.

Discussion

The findings of this study shed light on the close connections among scaffold architecture and mechanics. This, together with the tunability that MEW provides as a microfabrication technique, can then be leveraged to probe cardiac cell function in response to scaffold geometry and mechanical microenvironment. Our approach allows for complex optimisation of anisotropic microarchitecture in order to tune BMC mechanical performance, which can guide CM alignment.

References

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