waveforms, peripheral artery waveforms and coronary artery waveforms. Coronary and peripheral waveforms were generated based on both generic shape profiles and patient-specific profiles.

***Results:** We demonstrate that vascular cells such as human coronary artery endothelial cells (hCAECs), smooth muscle cells (SMCs) and human fibroblasts (hFBs) show distinct changes in morphology, gene and cell surface marker expression under physiological conditions (120/80 mmHg, 60 ml/min, 20 dyne/cm^2) compared to either static or conventional (peristaltic) pumping conditions.

***Conclusion/Significance:** Culturing vascular cells under physiologically relevant haemodynamic conditions led to significant changes compared with static culture controls, highlighting a key role for exposure to these forces in addition to relevant 3D scaffolds and biomaterial properties. The bioreactor is a new platform for studying cell behaviour and their interactions with biomaterials under physiological and pathological conditions.

430 - 3D In Vitro Modelling Of Human Cardiac Fibrotic Tissue Through Bio-hybrid Stretchable Scaffolds

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***Purpose/Objectives:** Human cardiac fibrotic tissue is a pathological condition that arises after myocardial infarction. It is characterized by outnumber fibroblasts activated into myofibroblasts, increased stiffness and passive mechanical stress during heart functionality. New advanced regenerative approaches are currently under investigation to reduce or revert cardiac fibrosis and in vitro;models of human cardiac fibrotic tissue may improve their preclinical investigation. Herein, an in vitro model of human pathological cardiac tissue based on stretchable scaffolds, able to mimic the biophysical and biochemical properties of post-infarct fibrosis was developed.

***Methodology:** Scaffolds of polycaprolactone (PCL) with parallel-wavy fibers pattern were designed and fabricated by melt-extrusion additive manufacturing (MEAM). Gelatin methacrylate (GelMA) hydrogels with different concentrations (5, 7, 10% w/v) were prepared using lithium phenyl-2,4,6 trimethylbenzoylphosphinate (LAP) as photoinitiator. Photo-rheology allowed to define the optimal hydrogel curing protocol. Both PCL scaffolds and GelMA hydrogels were analysed by SEM imaging.PCL scaffold pores were filled with GelMA hydrogels, to mimic extracellular matrix (ECM)-like microenvironment. To improve interfacial adhesion between GelMA hydrogel and scaffold structure, PCL were surface functionalized with poly(4-Dihydroxy-DL-phenylalanine) (polyDOPA). Static and cyclic tensile tests were performed on PCL/GelMA scaffolds. Human Cardiac Fibroblasts (HCFs) were seeded in PCL/GelMA scaffolds (cell density: $5{\cdot}10^6$ cells/mL) and cultured for up to 2 weeks. HCFs viability was tested through Resazurin assay, while their morphology and distribution were analyzed through F-actin staining in order to identify optimal GelMA concentration for HCFs culture. Then, cellularized PCL/GelMA scaffolds were subjected to cyclic mechanical stimulation for 7 days. Fibroblast activation into myofibroblasts was analyzed through immunofluorescence of α-Smooth Muscle Actin (α-SMA).

***Results:** Stretchable PCL scaffolds with high shape fidelity were obtained by optimizing MEAM processing parameters. Analytic and finite element analysis analyses allowed the validation of the experimental results. Mechanical properties of PCL/GelMA scaffolds were tailored by PCL scaffold thickness, mesh geometry, and GelMA hydrogel concentration in order to mimic the stiffness (1-9 MPa) and maximum elastic strain (15-22%) of human cardiac fibrotic tissue. GelMA hydrogel pore sizes increased by reducing GelMA concentration. PCL/GelMA scaffolds preserved stretchability and integrity after both static and cyclic tensile tests. HCFs viability after 7 and 14 days was significantly higher for cells cultured in PCL/GelMA 5% w/v and PCL/GelMA 7% w/v, compared to PCL/GelMA 10% w/v. F-actin staining showed homogeneous cell distribution inside GelMA hydrogels, while an elongated morphology was noted only on HCFs in PCL/GelMA 5%. Finally, HCFs demonstrated α-SMA expression only on samples treated with cyclic mechanical stimulation. Secretion of fibrotic ECM proteins such as Collagen I, Collagen III, and Fibronectin are under investigation.

***Conclusion/Significance:** In this work, an in vitro model of human fibrotic cardiac tissue based on stretchable PCL/GelMA scaffolds was developed. The model demonstrated fibrotic hallmarks in a dynamic cyclic culture environment. In the future, this model will be validated for use in preclinical testing of new cardiac regenerative strategies, with the advantage to allow long-term dynamic testing.

Acknowledgment: BIORECAR project has received funding from the European Research Council (ERC) under the H2020 research and innovation program (772168).

431 - DEVELOPMENT OF PHOTOCROSSLINKABLE BIOINKS WITH IMPROVED ELECTROMECHANICAL PROPERTIES FOR 3D BIOPRINTING OF CARDIAC BIORINGS

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***Purpose/Objectives:** 3D bioprinting is an advanced fabrication technique to build biomimetic constructs for different biomedical applications. Here, we developed composite bioinks based on photocrosslinkable natural polymers, gelatin methacryloyl (GelMA) and alginate methacrylate (AlgMA), and electroconductive reduced graphene oxide (rGO) nanomaterials. The ring-shaped cardiac constructs were further 3D bioprinted with different cardiac cells for the fabrication of an automated high throughput heart-on-a-chip model.

***Methodology:** The bioinks based on GelMA, AlgMA, and rGO were synthesized and characterized, and the bioinks were formulated with different concentrations. The physicochemical, structural, rheological, electromechanical, printability and printing fidelity, swelling and degradation properties, and cytotoxicity of these bioinks were investigated. The bioinks were further 3D bioprinted in a ring-shaped construct (hereafter BioRing), and cell viability, proliferation, migration, spreading, and functionality were demonstrated. Finally, heart-on-a-chip platforms containing micropillars were designed and fabricated to support these Cardiac BioRings for a proof-of-concept automated high throughput heart-on-a-chip application.

***Results:** In this study, a 3D bioprinted ring-shaped cardiac tissue model was successfully developed based on photocrosslinkable natural biopolymers (AlgMA and GelMA) and conductive nanomaterials (rGO). All of these three components of the bioinks were synthesized and validated by different characterization techniques. The structural, electromechanical, rheological, printability, and biodegradation properties of 3D biohybrid constructs were highly tunable using varied concentrations of AlgMA and rGO. The optimization process was performed to achieve an ideal bioink composition that mimics the properties of the native extracellular matrix of cardiac tissue. This optimal bioink was composed of 5 % GelMA, 1 % AlgMA, and 0.2 mg/ml rGO. Cellular evaluations (with encapsulated cardiac fibroblasts (CFs)) confirmed its ability to support high levels of cell adhesion, viability, proliferation, and migration. Cardiac BioRings were further created using different cardiac cell types (primary CFs and cardiomyocytes (CMs) as well as HL-1 CMs), and functional characterizations showed a high level of cell growth, alignment, spreading, elongation, alignment, and interconnection between the cardiac cells with phenotypic morphology (spindle-like CFs and rod-shaped CMs) and detectable troponin complex and sarcomeric structures in CMs. The functionality of cardiac BioRings was further confirmed by calcium transients and cellular contractions. As proof of concept, these cardiac BioRings were bioprinted on PDMS chips containing pillars, and the automated high-throughput bioprinting on-chip was confirmed using 24-well plates.

***Conclusion/Significance:** These bioprinted cardiac models could create new outlooks in cardiac tissue engineering and heart-on-a-chip platforms towards contractile biological pumps, heart regeneration, high throughput drug discovery and screening, and cardiovascular disease modeling.

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