Behavior of CMPCs in unidirectional constrained and stress-free 3D hydrogels

structure not only directly promoted cells adhesion and differentiation, but also could deliver growth factors to enhance its biofunctionalization. Moreover, after strontium ions incorporation, MAO-Sr coating showed obvious angiogenic and osteogenic effects on canine BMSCs via MAPK/Erk and PI3K/Akt signaling pathways. In details, the MAO-Sr coating facilitated their osteogenic differentiation and promoted angiogenic growth factors secretion to recruit endothelial cells and form blood vessels. On the large animal implantation models, the MAO-Sr coating significantly enhanced fast bone formation within initial six weeks. The *in vivo* performance of the MAO-Sr coated dental implants on rapid osseointegration was comparable to that of commercially available ITI implants. These results therefore suggest a novel implant coating to achieve rapid osseointegration by enhancing both of angiogenesis and osteogenesis.

Behavior of CMPCs in Unidirectional Constrained and Stress-free 3D Hydrogels

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Cardiomyocyte progenitor cells (CMPCs) are a candidate cell source for cardiac regeneration therapy. Although, like other stem cells, after cell transplantation into the heart, cell retention and differentiation capacity of CMPCs is low, probably due to the mechanical loads imposed by the heart. A possible solution to overcome this problem is to combine cells and biomaterials, since encapsulation of CMPCs may stabilize survival and proliferation. By combining CMPCs and hydrogels more insight into the behavior of CMPCs upon encapsulation in a biomaterial and/or after injection into the beating host tissue can be gained. Therefore, we cultured CMPCs in unidirectional constrained and stress-free 3D collagen/Matrigel hydrogels. Our data suggest that CMPCs in a 3D environment are viable and keep their cardiac progenitor profile for at least 9 days. Moreover, the 3D environment induced the cardiomyocyte differentiation potential of CMCPs and increased their expression of matrix producing and remodeling genes. Constrainment of 3D hydrogels causes CMPCs to become readily mechanosensitive. They respond to the constrainment by orienting in the direction of the constraint. Furthermore, constrainment appears crucial for cardiac marker expression. In summary, our data demonstrate that culturing CMPCs in a 3D environment since encapsulation of CMPCs enhance the differentiation and remodeling capacity of the cells, which may improve efficiency of cardiac stem cell therapy.

Acknowledgments: This research forms part of project P1.04 SMARTCARE of the research program of the BioMedical Materials institute, co-funded by Dutch Ministry of Economic Affairs, Agriculture and Innovation. The financial contribution of Nederlandse Hartstichting is gratefully acknowledged.

Jet-sprayed Hybrid Nanofibrillar Matrices with Controlled Deposition and Delivery of Nanoparticles

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Objectives: Combination of biodegradable nanoparticles (NP) with nanofibrillar (NF) matrices to localize and deliver active biomolecules is a sensible approach to modulate cell environments along tissue formation. Since jet-spraying creates nanofibers by airflow diffraction of polymer solutions, we hypothesized that NP could be permanently deposited onto NF surfaces during their formation by co-projection. Alternatively, we postulated that electrostatic interactions would allow NP post-adsorption and controlled release from highly porous NF matrices.

Methodology: Poly(lactic-acid) (PLA) fluorescent NP were synthesized by nano-precipitation and co-projected (paintbrush) during jet-spraying of poly(lactic-co-glycolic-acid) (PLGA) NF. Alternatively, NP aqueous solutions were incubated with jet-sprayed PLA matrices, either blank or poly-lysine (PLL) pre-coated. NP and NF structure, distribution, efficiency of NF/NP association and NP release were determined (DLS, SEM and fluorescence quantitation).

Results: NP co-projection during jet-spraying efficiently deposited fluorescent NP (254 nm, zeta potential – 67 mV) on fiber surfaces as droplets-like structures. The adjustable amount of NP fully covered NF (305 μg/mg of NF), while matrices remained highly porous and interconnected.

Incubation of negatively charged NP with jet-sprayed PLA NF matrices either blank (negative surface) or pre-coated with PLL (positive surface) resulted in complete and homogeneous fiber covering, although in lower amount than co-projection (38 and 83 μg/mg for blank and PLL-coated NF). However, NP release could be modulated (up to 4 days), unlike co-projection, where NP remained bound to the NF.

Significance: Controlled NP association and release from NF matrices allows providing defined functionality to inert structures. Ongoing experiments with protein-loaded NP will further confirm their safety and resulting bioactivity.

Multi-functional Materials and Materials Processing for Nerve Guidance Scaffolds

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Approximately 1.2 million Americans are disabled by spinal cord injuries (SCI). Approximately 500,000 surgeries are performed each year to repair peripheral nerve injuries (PNI). While physical rehabilitation can improve functional recovery, in some cases, the lack of spontaneous recovery requires interventional technology. The purpose of this work is to develop an acellular therapy to bridge the nerve gap. The approach consists of multifunctional nerve growth scaffolds (NGS) providing physical cues to guide axons toward distal targets while simultaneously eluting growth factors to stimulate growth. Progressing toward clinical relevance, the focus now turns to material selection, engineering, and NGS design. In this work, the integration of FDA approved materials into NGS is discussed, e.g. synthetic polymers and hydrogels. Details describing mechanical properties, degradation rates, cell attachment, and integration into various NGS designs will be presented. Specific attention to porosity control and the effect on stiffness and strength is a focus. Optimizing these properties enable thin-wall NGS designs to maximize open channel volume. Drug delivery of brain derived neurotrophic factor (BDNF) from pH-triggered polyelectrolyte functionalized hydrogel NGS will also be discussed. The goal is to achieve a 50 ng BDNF/ml per day dose response for two weeks to stimulate axon growth. Though not the emphasis of this paper, SCI and PNI *in vivo* efficacy test data will also be presented.

3-D Printing Fabrication for Periodontal Complex Regeneration; Bone-PDL-Cementum Regeneration Platform Developments

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Introduction: The physiological periodontal functionalities to support tooth-structures are provided from spatiotemporal organization of fibrous connective tissues, periodontal ligament (PDL)[1]. Recently, we have investigated the freeze-casting fabrication method to manage pore angulations in gelatin scaffolds with structural similarity to healthy PDL[2]. However, due to poor physical/mechanical