Transactions on Additive Manufacturing Meets Medicine
Trans. AMMM, 2023, Vol. 5, No 1, Suppl. 1, Article ID 812, 1 Page

Infinite Science Publishing

Abstract

Fabrication of biodegradable tailor-made bone cartilage implants by TPA

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In tissue engineering, a major challenge lies in identifying effective therapies for repairing bone cartilage defects, commonly caused by arthrosis or sporting accidents. In the U.S., clinical osteoarthritis affected 27 million adults in 2005, with joint operation surgeries to repair these defects costing approximately $42.3 billion in 2009. With an aging population, these numbers are projected to rise in the coming decades, necessitating more efficient and cost-effective therapy options. Current approaches, such as Pride drilling, chondrocyte transplantation, and acellular scaffold implantation, aim to stimulate cell regeneration by drilling holes in the damaged bone or by transplanting autologous or donor cells or by implanting an acellular scaffold into the affected area. However, a significant limitation is the resultant fibrous cartilage instead of hyaline cartilage, which lacks the ability to withstand compression, particularly in joint areas. Scaffold implantation is based on artificial extracellular matrices (ECM) that mimic natural tissue and serve as physical and bioactive support for the generation of autologous bone and cartilage cells capable of replacing or repairing damaged tissue material. State-of-the-art scaffold materials often have the drawback that the creation of hyaline cartilage and subchondral bone ingrowth is not guaranteed. A promising approach in scaffold production is 3D printing via Two-Photon Absorption (TPA) with the advantage of design freedom and a monolithic fabrication process. The aim of the funded Poly-IMPLANT-Druck project is to fabricate monolithic biphasic scaffolds from biodegradable polymer-based materials as bone cartilage implants for patients with osteochondral defects (e. g. arthrosis) to realize an ECM with a defined morphology from the micro- to the macroscale for cell adhesion, migration, proliferation, and differentiation. Different specific filling types for the cartilage and bone region will enable the growth of hyaline cartilage and bone tissue. The fabrication of individually designed scaffolds adapted to patients' bone cartilage defects open new therapy options for personalized medicine in the future. Within this contribution, the novel TPA fabrication machine designed for the fabrication of scaffolds is introduced and presented. Unlike conventional TPA machines which are typically limited to fabrication sizes of a few millimeters and don't provide the needed throughput for cm sized structures, the prototype enables stitchless and rapid in-situ fabrication of cm-sized structures at micrometer resolution. This is achieved by switching the conventional microscope objective with a f-Theta lens and then printing within an inverted bath setup thus providing the generation of scaffolds with a height of 10 mm and a diameter of 7 mm in under 1.5 hours with even further room for improvement. Based on a biomimetic design, the scaffold is divided by a separation layer into a 3 mm tall cartilage phase and a 7 mm tall bone phase. Due to total freedom in design, the mechanical properties such as porosity and Young's modulus of the respective phases can be adjusted to closely resemble real structures of bone and cartilage. To ensure biocompatibility and biodegradability of the scaffolds the materials poly-((D, L)-lactide-co-ε-caprolactone)-dimethacrylate (LCM) and poly(amide-co-ε-caprolactone)-dimethacrylate (ACM) were used. The cytocompatibility was carefully tested and very promising as demonstrated in a first publication. In addition, tests of the scaffolds filled with implantation-proved biological matrix to improve cell migration and differentiation are promising and are currently followed up by an animal study which will be completed summer 2023.

DOI: 10.18416/AMMM.2023.2309812