3D TEXTILE IMPLANTS FOR BONE REGENERATION FROM SILK GENERATED BY ADDITIVE MANUFACTURING

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ABSTRACT

In order to overcome the limited source of autologous bone graft substitutes for filling bone defects, various experimental approaches have been investigated. The combination of silk and ceramic materials in the the form of membranes or sponges has proven to be promising. For this reason, continuous filaments were spun from native silk solution and manufactured into three-dimensional textile implants using an additive manufacturing process. Cell culture analyses showed good biocompatibility of the implants and an induction of bone differentiation, thus demonstrating the high potential for ceramic functionalized textile silk implants.

Key Words:, Silk, additive manufacturing, textile implants, bone regeneration

1. INTRODUCTION

Bone regeneration is a complex, well-organized physiological process of bone formation observed during normal fracture healing and involved in continuous remodeling throughout adult life. However, there are complex clinical conditions that require large amounts of bone regeneration, such as skeletal reconstruction of large bone defects caused by trauma, infection, tumor resection and skeletal abnormalities [1].

Currently, many orthopedic devices function mechanically satisfactorily, but are not sufficient for osseointegration and vascularization with surrounding bone formation. This leads to undesired implant migration, loosening and ultimately mechanical destabilization.

An ideal medical device for bone regeneration must have similar properties to natural bone and provide a better quality of life for humans. An essential feature is the presence of interconnected pores within the device to allow penetration into blood vessels and cells, enabling material biodegradation and bone ingrowth. Other mandatory demands are an excellent resorption rate, 3D structure similar to natural bone, biocompatibility, customizable to multiple patient-specific geometries combined with adequate mechanical strength.

Currently, bone graft/scaffold engineering using silk biomaterials has received increasing interest. However, toward, this goal several biological parameters need to be met including biocompatibility, biodegradability, surface roughness, porosity, and osteoconductivity (2).

Silk fibroin from *Bombyx mori* was chosen for the current study due to its desirable properties including biocompatibility with low inflammatory and immunogenic responses (2). However, most studies using silk for bone regeneration focused on hydrogels, porous sponges or nanofibrous scaffolds, so far. Thus, a new concept is presented applying a textile-based approach generating an interconected pourous structur functionalized with an osteoconductive ceramic material.

2. MATERIAL AND METHODS

Endless silk fibers were spun from native silk solution isolated from silkworm larvae [3] and functionalized with osteoconductive ceramic materials like hydroxyl apatite (HA) during the wet spinning process. After generation of short fibers from silk and ceramic modified silk, 3D textile implants were assembled using an additive manufacturing approach [4,5]. Scaffold structure was investigated using electron microscopy. Textile implants were characterized in terms of porosity, compressive strength, and cyclic load. For evaluation of cytocompatibility according to ISO 10993-5, viability of cells was monitored and cell distribution on the textile structures were compared by confocal laser scanning microscopy. In addition, osteogenic differentiation of mesenchymal stem cells was evaluated.

3. RESULTS AND DISCUSSION

The different short fibers (1 mm) from pure native silk and native silk functionalized with HA were successfully converted into porous three-dimensional textile structures applying an additive manufacturing process. Electron microcopy analysis of textile structures revealed no differences in porosity and interconnectivity between structures from native silk or HA-functionalized silk (figure 1). Comparing fiber structures, HA functionalization is covering the silk fibers (figure 1 right) and thus a complete ceramic surface is presented to the cells.

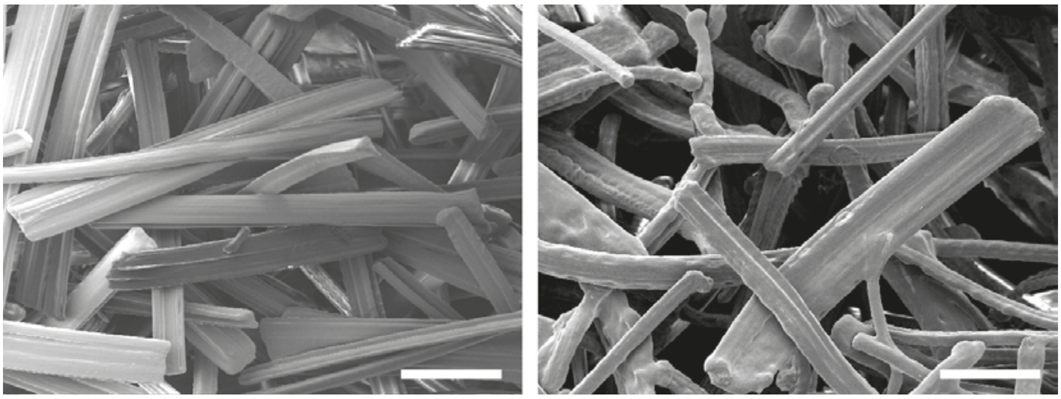

Figure 1: Electron microscopy pictures of 3D textile structures manufactured from short fibers of native silk (left) and HA-functionalized silk: The short fibers have been assembled into interconnected porous structures using an automated additive manufacturing process. The scale bar corresponds to 200 µm.

Silk fiber based 3D textile implants demonstrated good cytocompatibility as shown in the confocal microscopy images in figure 2. On both textile structures (native silk (A) and HA-functionalized-silk (B)) human mesenchymal stem cells attach on the fiber surfaces and grow well. In addition, the cells begin to divide and bridge the pore spaces. both form the basis for an even settlement of the textile implant. However, the successful integration of such an implant requires the ingrowth of vessels. Due to its open porous structure, the textile structure allows the implant to be integrated into the body to a particularly high degree and thus contributes to the progress of healing.

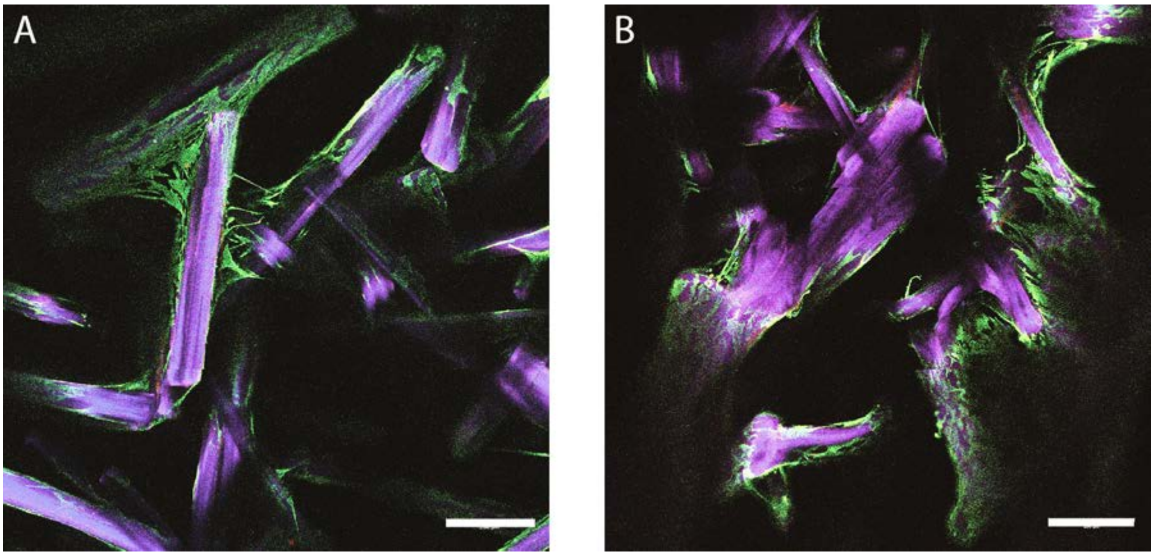

Figure 2: Confocal laser scanning microscopy pictures of textile structures: Short fibers from native silk (A) and HA-functionalized silk (B) were seeded with human mesenchymal stem cells. Silk fibers are shown in violet (autofluorescence) and cells are stained for vimentin using a fluorescence labeled antibody (green). The scale bar corresponds to 200 µm.

Molecular biological analysis demonstrated that the mesenchymal stem cell cultured on ceramic material functionalized silk implants were differentiating into bone cells without any addition of osteogenic differentiation inducing agents. Thus, the combination of silk and HA-functionalization together with an open porous interconnected textile structure acts osteogenic on human mesenchymal stem cells and consequently, might offer a new route for faster ingrowth of new bone into the structure after implantation.

4. CONCLUSION

Additive manufacturing of short fibers into 3D structures provides an excellent technique to produce standardized textile implants. Hydroxyl apatite functionalized silk is a good biomaterial for induction of bone growth. Thus, 3D interconnected porous textile scaffolds were proved as promising biomaterials for bone regeneration.

5. REFERENCES

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