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A single integrated osteochondral in situ composite scaffold with a multi-layered functional structure

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ABSTRACT

This work focuses on the optimization design of a functional biomimetic scaffold for the repair of osteochondral defects and includes the study of single integrated osteochondral tissue engineering scaffolds with a multi-layered functional structure. Rabbit model experiments were used to evaluate the repair of osteochondral defects. The results revealed that good integration was achieved both at the interfaces between the scaffold material and the host tissue and between the newly formed subchondral bone and cartilage. The highest total histological score of 24.2 (based on the modified O'Driscoll scoring system at 12 weeks post-operation) was achieved for osteochondral repair. The completely repaired cylindrical full-thickness defects for the rabbit animal model reached 5 mm in diameter. The thickness of the regenerated cartilage was almost in line with that of the surrounding normal cartilage, the number and arrangement of cells in the superficial area of cartilage were very close to those of normal hyaline cartilage, and there were clear cartilage lacunas in the regenerated cartilage. The hybrid-use of growth factors and LIPUS stimulation exhibited good potential in enhancing vascularization and the formation of new bone and cartilage, providing better conditions for the overall osteochondral repair.

1. Introduction

In recent years, as bone and cartilage tissue engineering and their interface develops, the study of osteochondral tissue engineering scaffolds is becoming more and more mature and is thus receiving more attention [1–3]. It will become the focus of tissue engineering studies for the skeletal system in the future, and the related research will make full-thickness joint damage repair possible. To date, the design of tissue-engineered osteochondral scaffolds is primarily divided into the following categories: 1) Scaffolds are used for the repair of the bone layer but not the cartilage layer. Chondrocytes and chondroblasts are seeded on the top surface of the scaffolds, and scaffolds with these cells are implanted into the osteochondral defects directly or after culture in vitro. 2) Two types of scaffold materials are adopted for bone and cartilage construction. After they are cultured in vitro into tissue engineering bone and cartilage, they are sequentially implanted into osteochondral defects or co-implanted into osteochondral defects after being assembled together through adhesion or surgical suture. 3) The monolayer integrated scaffolds are used for both bone and cartilage layers. 4) The integrated scaffolds composed of two different scaffold materials to match bone and cartilage layers are applied to repair osteochondral defects [4,5]. Because the bi-layered integrated scaffolds are designed according to the need for the growth of both bone and cartilage, they will have better features. Therefore, the bi-layered integrated scaffolds will be the main direction in future research into osteochondral tissue engineering scaffold materials.

Currently, the main problems for tissue engineering of osteochondral scaffold materials are low interfacial bonding between the regenerated bone and cartilage and poor integration of scaffold materials with host tissues [6–8]. These problems directly restrict their application in the clinic and have become a significant challenge in osteochondral tissue engineering research. The natural structure of joint tissue contains multiple areas including a cartilage zone, calcified cartilage zone and ossification area. Its organization and structure are gradually transitional, without an obvious interface between adjacent zones, and thus, the mechanical structure is stable. In contrast, there is no transition zone between the bone and cartilage layer for previously reported osteochondral tissue engineering scaffolds, and the Young's modulus of the adjacent

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materials cannot match each other; thus, the mechanical structure is unstable at the interface, and it is difficult to integrate the implant materials with both the surrounding host bone and cartilage [9]. This clearly shows that the calcified cartilage layer is an indispensable factor in the design of osteochondral tissue engineering scaffolds. Therefore, it is necessary to introduce a transition layer between the bone and the cartilage, which is called the calcified cartilage layer. The introduction of calcified cartilage is beneficial not only for matching the Young's modulus of cartilage and bone at the interface but also for the integration of the implants and host osteochondral tissues at the interface due to their similar structural and mechanical properties [10]. In addition, the transition layer between calcified cartilage and bone, which can not only act as a physical barrier to inhibit vascular invasion into the cartilage to

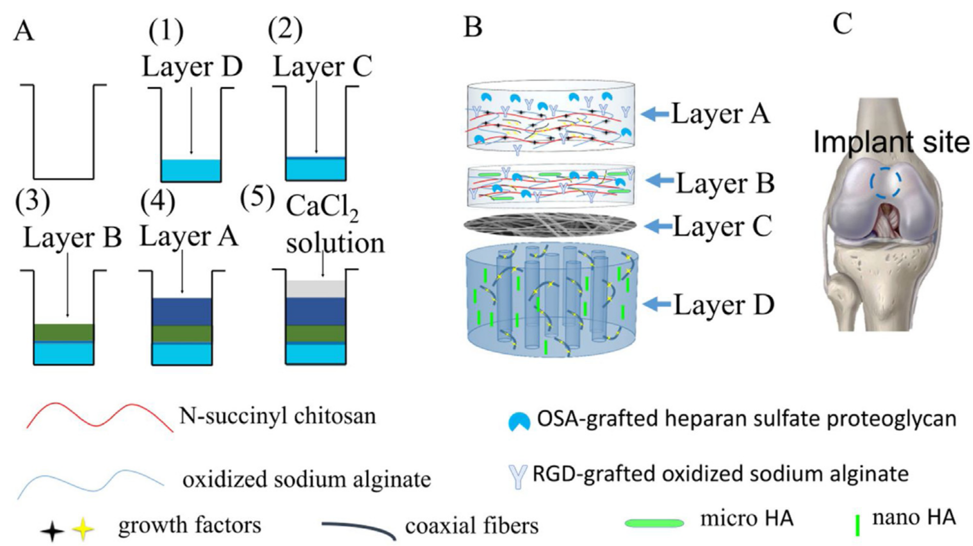

Fig. 1. Schematic diagrams for (A) synthesis of osteochondral scaffolds, (B) with four functional layers and (C) their implant site *in vivo*.

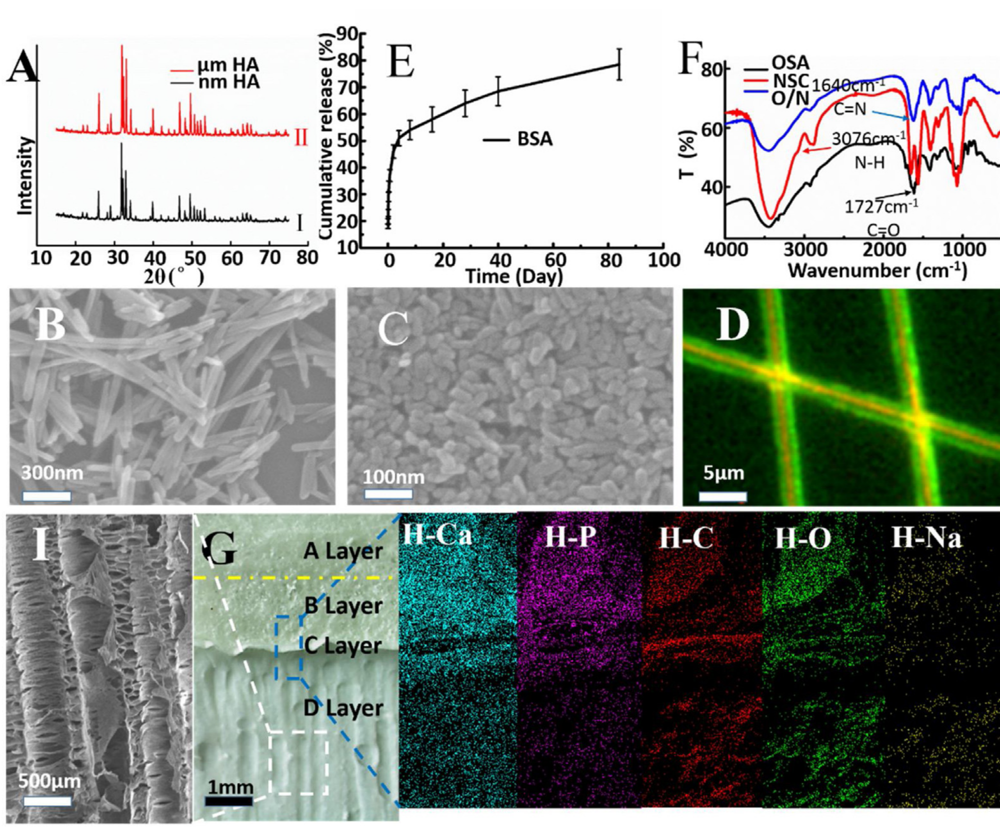

Fig. 2. Characterization of materials. (A) XRD spectra of synthesized (I) nano and (II) micron hydroxyapatite powders. (B and C) SEM images of synthesized (B) micron and (C) nano hydroxyapatite powders. (D) Fluorescent staining image of obtained coaxial fibres; green and red represent the shell and core layers of coaxial fibres, respectively. Cumulative release curve of BSA loaded in the core layer. (F) FT-IR spectra of (III) OSA, (IV) NSC and (V) the composite hydrogel. (G) Macroscopic image and (H) EDX images of inset marked with a blue dotted line in the single integrated scaffold. (I) SEM image of D layer. Abbreviations: H-Ca, H-P, H-C, H-O and H-Na represent EDX images of Ca, P, C, O and Na elements, respectively; O/N, composite hydrogel. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)