3D PRINTED HYBRID MULTILAYER SCAFFOLDS WITH CELL-ENCAPSULATING HYDROGELS FOR CARTILAGE TISSUE ENGINEERING

[1]YI-WEN CHEN, [2]MING-YOU SHIE, [3]WEI-CHE HONG, [4]YU-FANG SHEN

[1,2]3D Printing Medical Research Center, China Medical University Hospital, Taichung City, Taiwan
[1]Graduate Institute of Biomedical Sciences, China Medical University, Taichung City, Taiwan
[2]School of Dentistry, China Medical University, Taichung City, Taiwan
[3,4]Department of Bioinformatics and Medical Engineering, Asia University, Taichung City, Taiwan
[4]3D Printing Medical Research Institute, Asia University, Taichung City, Taiwan
E-mail: evinchen@gmail.com, eviltacasi@gmail.com, a0925051075@gmail.com, cherryuf@gmail.com

Abstract - Articular cartilage disease severely affects the quality of life of millions of people around the world. According to statistics, one out of every five people suffer from arthritis. Therefore, the recovery and treatment of cartilage diseases is an extremely important issue. At present, the function and structure of cartilage cannot be completely restored by using drugs or surgery. With the development of tissue engineering, the possibility of cartilage tissue regeneration and complete repair has been improved. However, cartilage tissue currently prepared by tissue engineering still differs from natural cartilage in structural composition and mechanical properties. In this study, a biomimetic cartilage scaffold with complex internal porous structure and different layers of different structures was fabricated by three-dimensional printing technology in modern times to simulate the structural and mechanical properties of natural cartilage, and improved by hydrogel materials with encapsulated cells to increase the potential for cartilage differentiation and the maturation of cartilage tissue. Furthermore, this study combines a digital light processing and extrusion type printing system to develop a new process to prepare a customized hybrid multilayer scaffolds with cell-encapsulating hydrogels.

Index Terms - About Four Key Words or Phrases in Alphabetical Order, Separated by Commas.

I. INTRODUCTION

Previous studies have reported cartilage tissue scaffolds made by different 3D printing techniques [1]–[5]. Both synthetic materials and natural materials can be applied to 3D printing technology to manufacture cartilage tissue scaffolds. However, both biopolymer hydrogels and synthetic polymer scaffolds have their unique advantages and disadvantages [6]. Hybrid scaffolds with biopolymer hydrogels and synthetic polymer scaffolds can take advantage of each other's characteristics to produce a synergistic effect. Synthetic polymer scaffolds can serve as a framework for the structure to provide mechanical strength, while hydrogels can serve as a carrier for cell encapsulation. In addition, previous studies have shown that by the nature of hydrogels, cell viability and metabolism are significantly increased on hybrid scaffolds. Glycosaminoglycan (GAG) performance of a mixed-package PLGA scaffold with cell-encapsulated alginate compared to a pure polylactic-co-glycolic acid (PLGA) scaffold The amount is 2.6 times higher [7]. Furthermore, the study in hybrid PLGA scaffolds with cell-encapsulating gelatin showed that cells retained their natural morphology even after implantation [8].

The manufacturing techniques of hybrid scaffolds are also different in different studies. The addition of hydrogels by infiltration is a commonly used method in cartilage tissue engineering, i.e., immersion in a hydrogel with or without encapsulated cells in a solid scaffold. A recent study prepared a mixed poly(L-lactide-co-εcaprolactone) with cell-encapsulated fibrin/hyaluronic acid hydrogel by infiltration (poly(L-lactide-co-ε-caprolactone) , PLCL) scaffolds, the results of the study showed that the mixed scaffolds after eight weeks of implantation formed homogeneous cartilage tissue, and has similar compression characteristics as natural cartilage[9]. In addition, Shim's group manufactured multilayer hybrid scaffolds with an extrusion-type 3D printing system with multiple printing heads [10]. Since the printing resolution of the extrusion type printing system is low, and the shape of the gel directly added to the hydrogel by the infiltration method cannot be precisely controlled, there is still room for improvement.

The digital light process (DLP) 3D printing technology uses a high-resolution projector to cure each layer in a slide-like one-shot projection to build objects layer by layer. It can finely control the accuracy of layer-by-layer descent, has higher vertical resolution [11], and is faster to manufacture. However, most of the photocurable polymers used in this technology are not biocompatible [12]. In the previous research of our group, a biocompatible water-based polyurethane (PU) has been developed for the preparation of digital light-processing 3D printing technology, and 3D polyurethane/hyaluronic acid (HA) scaffolds have been prepared for cartilage tissue engineering applications [4]. This material is printable and can exhibit different physical properties by blending the material ratio.

Although the composition of cartilage tissue is simple, its structure varies slightly with the thickness of cartilage layer [6], and the deep layer can withstand

the vertical pressure. It is difficult to make brackets of different layers and different structures in the conventional process. This study designed the cartilage scaffold structure, and useed DLP 3D printing technology to print different layers of different structures of the scaffolds and combined with the extrusion printing system to make a hybrid multilayer scaffolds with encapsulated cells, which is expected to fabricate high accurate cartilage scaffolds to facilitate the development of cartilage tissue regeneration and repair.

II. MATERIALS & METHODS

A light cured composite materials based on water-borne polyurethane was prepared, a porous scaffold was printed by DLP 3D printing technology (Fig. 1), and a hybrid scaffold was prepared by adding hydrogels with encapsulated cells through bioprinting technology. Fig. 2shows the experimental flow of this study.The cell attachment, proliferation and cartilage differentiation ability of the mesenchymal stem cells cultured on the scaffolds were analyzed, and the repair results after implantation of injured rabbit cartilage tissue were evaluated.

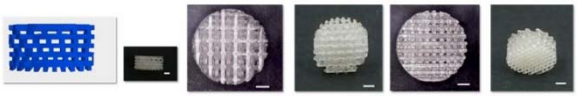


Fig.1. The images of the designed (blue) and printed scaffolds. Scale bar = 1 mm.

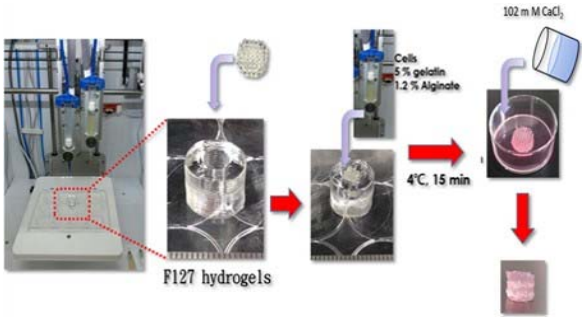


Fig. 2. Experimental flow of this study.

III. RESULTS

The results showed that the printed scaffolds had good biocompatibility. Photosensitive composites provided good printing resolution and have the potential to be customized for the scaffolds. In addition, mesenchymal stem cells cultured on a 3D printed porous scaffold had excellent cell attachment, proliferation, and cartilage differentiation capabilities, and hydrogels with encapsulated cells can be added to fabricated hybrid scaffolds. The hematoxylin and eosin (H&E) and Alcian blue (AB) staining analysis were used to compare the repair results of rabbit cartilage tissue. Hydrogels containing encapsulated cells were used to fabricate hybrid scaffolds with better repair ability than scaffolds only.

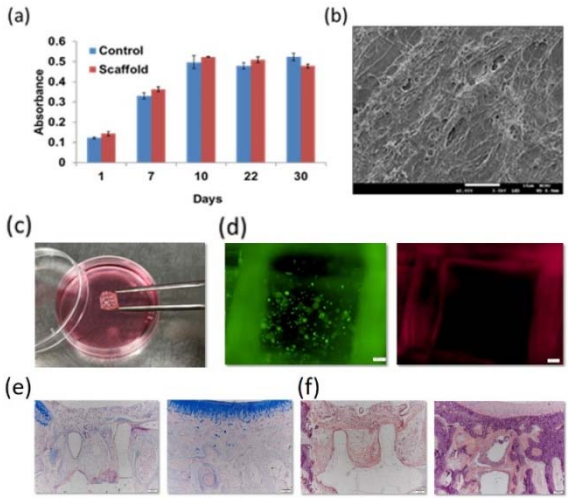


Fig. 3. (a) The cell proliferation of WJMSCs cultured on the scaffolds. (b) The SEM micrographs of hWJMSCs cultured on the scaffolds for 30 days. (c) The images of printed hybrid scaffolds. (d) The live/dead (green/red) cell staining of WJMSCscultured in hydrogels for 4days. (e)ABand (f) H &Estaining analysis of rabbit articular cartilage repair after implantation for 8 weeks.

CONCLUSION

This study combined a DLP 3D printing technology and bioprinting system to develop a new process to fabricate customized hybrid multilayer scaffolds with cell encapsulating hydrogels for cartilage tissue engineering.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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