

Enhancing Craniofacial Bone Reconstruction with Clinically Applicable 3D Bioprinted Constructs

Hyeongjin Lee, Carlos Kengla, Han Su Kim, Ickhee Kim, Jae-Gu Cho, Eric Renteria, Kyungsup Shin, Anthony Atala, James J. Yoo, and Sang Jin Lee*

Medical imaging and 3D bioprinting can be used to create patient-specific bone scaffolds with complex shapes and controlled inner architectures. This study investigated the effectiveness of a biomimetic approach to scaffold design by employing geometric control. The biomimetic scaffold with a dense external layer showed improved bone regeneration compared to the control scaffold. New bone filled the defected region in the biomimetic scaffolds, while the control scaffolds only presented new bone at the boundary. Histological examination also shows effective bone regeneration in the biomimetic scaffolds, while fibrotic tissue ingrowth is observed in the control scaffolds. These findings suggest that the biomimetic bone scaffold, designed to minimize competition for fibrotic tissue formation in the bony defect, can enhance bone regeneration. This study underscores the notion that patient-specific anatomy can be accurately translated into a 3D bioprinting strategy through medical imaging, leading to the fabrication of constructs with significant clinical relevance.

necessity of craniofacial bone reconstruction arises mainly due to congenital anomalies, oncologic bone resection, and bone loss after trauma or diseases. Globally, the most common congenital birth malformations in humans are cleft lip and/or palate, which occur in 1 in 500 to 1000 live births.^[2] In the U.S., head and neck cancers account for $\approx 3\%$ of all cancers, with 63 000 cases yearly and 13 000 cancer-related deaths.^[3] Among the global reconstructive surgeries, cases of post-trauma/injuries are 38% of surgical diseases, more common than oncologic resection and congenital anomalies, representing 19% and 9% of surgical disease processes, respectively.^[4]

Contemporary surgical interventions for craniofacial bone reconstruction include autogenous bone, allogeneic bone, and prosthetic devices.^[5] The gold standard for hard tissue grafting is autogenous bone,

which is taken from the patient's own body (e.g., iliac crest) and implanted into the defect site.^[6] However, the significant critical shortcomings of this autologous bone graft, in addition to limited availability, invasive intervention, and donor site morbidities, are consequential bone loss after the grafting surgery and unpredictable success rate: a considerable bone loss (50–60%) has been reported from long-term follow-up studies,^[7] and the success of the graft with regard to the new bone formation has

1. Introduction

Craniofacial bone reconstruction is a challenging medical intervention due to the complex anatomical structures and physiological functions of the head and face.^[1] Craniofacial defects can significantly affect the quality of life, as they can involve various essential functions, such as protection of the brain, breathing, optic tracts, mastication, speech, and hearing.^[1b] The


H. Leel^[+], C. Kengla, H. S. Kim, I. Kim, J.-G. Cho, E. Renteria, A. Atala, J. J. Yoo, S. J. Lee
Wake Forest Institute for Regenerative Medicine
Wake Forest University School of Medicine
Winston-Salem, NC 27157, USA
E-mail: sjlee@wakehealth.edu

C. Kengla, A. Atala, J. J. Yoo, S. J. Lee
School of Biomedical Engineering and Sciences
Wake Forest University-Virginia Tech
Winston-Salem, NC 27157, USA

H. S. Kim
Department of Otorhinolaryngology-Head and Neck Surgery
College of Medicine
Ewha Womans University
Seoul 07804, Republic of Korea

J.-G. Cho
Department of Otorhinolaryngology-Head and Neck Surgery
College of Medicine
Korea University
Seoul 02708, Republic of Korea

K. Shin
Department of Orthodontics
University of Iowa College of Dentistry
Iowa City, IA 52242, USA

 The ORCID identification number(s) for the author(s) of this article can be found under <https://doi.org/10.1002/adhm.202302508>

^[+]Present address: Department of Biotechnology and Bioinformatics, Korea University, Sejong 30019, Republic of Korea

© 2023 The Authors. Advanced Healthcare Materials published by Wiley-VCH GmbH. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

DOI: 10.1002/adhm.202302508