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Review

Three-dimensional macroporous materials for tissue engineering of craniofacial bone

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Abstract

Repair of critical-size defects caused by trauma, removal of a tumour, or congenital abnormalities is a challenge in the craniomaxillofacial region because of the limitations associated with treatment. We have reviewed research papers and updated information relevant to the various types of macroporous scaffolds. We have included papers on several biomaterials and their use in various craniofacial defects such as mandibular, calvarial, and others, as well as the latest technological developments such as 3-dimensional printed scaffolds. We selected all papers about scaffolds, stem cells, and growth factors for review. Initial selection was by review of titles and abstracts, and the full texts of potentially suitable articles were then assessed. Methods of tissue engineering for repair of critical-size defects in the craniofacial bones seem to be viable options for surgical treatment in the future. Macroporous scaffolds with interconnected pores are of great value in regeneration of bone in the craniofacial region. In recent years, various natural or synthetic materials, or both, have been developed, on which macroporous scaffolds can be based. In this review we present a review on the various types of three-dimensional macroporous scaffolds that have been developed in recent years, and evaluate their potential for regeneration of craniofacial bone.

Keywords: Craniofacial bone regeneration; Macroporous materials; Hydrogels; Cryogels; Composite; Bioactive foams

Introduction

The treatment of bone lost from the craniofacial region as a result of trauma, resection of tumours, or congenital deformities, is challenging. The cranium is a complex structure made up of bone, cartilage, soft tissues, nerves, and vasculature, so impairment may have an appreciable effect on both function and aesthetics. The goal of reconstruction is to restore form and function to facial aesthetics, and to enable the patient to achieve a reasonable quality of life with early oral functional rehabilitation. In this review we provide a brief description of current surgical techniques and give updates about 3-dimensional macroporous scaffolds for reconstruction of bone in the craniomaxillofacial region.

Metals

Common metals used in craniofacial applications are steel, chrome, and molybdenum, but titanium is the most widely used, as it is biocompatible and resistant to corrosion. Its modulus of elasticity is more like that of bone than any other metals. Currently it is being used in the reconstruction of mandibular bone, calvarial defects, and for osteosynthesis.[1–3] Miniplates and microplates made from titanium alloys have important advantages because of their biocompatibility and stability.[2] In recent years, porous metals (those with a pore size of >100 μm) have been developed with intrigu-

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ing characteristics that enable them to heal bone with good osseointegration.[4] The advantages of these materials are their biocompatibility, ability to osseointegrate, and mechanical stability. However, their limitations include inherent lack of biological recognition.

Resorbable systems

Resorbable systems have the advantage over metals that they overcome the problems associated with metal implants such as a second operation for their removal, and they are technically easy to use and cost effective. Materials such as polylactic acid (PLA) and polyglycolic acid (PGA) are the most commonly-used materials. Compared with metal implants, resorbable materials have less tensile strength, but it depends on the type of fracture, and in non-load-bearing areas the resorbable systems work well. A copolymer miniplate and microplate system made of poly-L-lactic polyglycolic polymer has been shown to have more initial stability than metal plates for facial fractures.[5] In another study, bioabsorbable mesh and screws were used to fix various reconstructions for craniofacial trauma, and healing was effective in patients with frontal fractures and zygomaticomaxillary complex fractures. However, the fact that the resorbed material may cause a foreign body response with accumulation of macrophages and granulocytes is a major disadvantage.[6]

Bone substitutes

Autografts

Of many surgical techniques used to reconstruct lost bone, autologous bone tissue remains the gold standard for critical-size bony defects,[7] though allografts and xenografts are options.[8] The use of an autograft has limitations, including donor site morbidity, limited availability of tissue, an additional operation, and prolonged healing time.

Allografts

Allografted bone is harvested from human donors, mainly cadavers. The disadvantages include infection and immune resistance.

Xenografts

Bovine bone is a commonly-used material for a xenograft. However, the immunogenicity and transmission of infectious diseases are serious concerns.

Tissue engineering scaffold

The advent of tissue engineering techniques offers a promising choice for the reconstruction of critical-size craniofacial defects.[9,10] In bone tissue engineering, scaffolds act as the delivery vehicles of cells and growth factors. Autologous cells (from the patient's own tissue) are expanded and seeded on to the scaffolds either in vitro or in situ, and delivered to the appropriate anatomical site (Fig. 1).[11] The 3-dimensional scaffold serves as a temporary extracellular matrix (ECM) to provide mechanical support within an environment conducive to the growth of cells and regeneration of tissue.[12] However, the design of scaffolds used in the craniofacial region is extremely complicated. The scaffold must fit into a complex 3-dimensional anatomical defect, and should be temporarily load-bearing until the tissue forms. Scaffolds must also be porous enough to deliver biofactors, and sustain the mechanical forces until the regenerated tissue can bear them. There are therefore many considerations, including porosity, biocompatibility, degradability, surface morphology,[13] and mechanical strength, to be taken into account when designing a scaffold for the craniofacial region.[14,15]

Bone possesses a porous structure ranging from 20 to 400 μm, which is necessary for bone cells to penetrate, adhere, grow, and proliferate to form new bone.[16] To regenerate bony tissue and correct defects efficiently, scaffolds should mimic the hierarchical structure of bone. Three-dimensional porous scaffolds consisting of an interconnected macroporous network with diameters of at least 100 μm are required to facilitate the growth of cells, vascularisation, production of an ECM, and the removal of waste material.[17,18] Scaffolds synthesised by conventional methods, or with solvent leaching or gas foaming, have a fixed pore size that can be modulated by adding some stimulatory responsive pyrogens to generate tenability.[19,20]

In recent years a wide range of macroporous scaffold materials such as cryogels, injectable hydrogels, bioactive foams, and biocomposite materials have been developed for bony regeneration (Table 1). Materials used for tissue fabrication of scaffolds range from polymers such as self-assembled peptides,[21] arginylglycyl aspartic acid (RGD) peptides, proteins, and elastomers;[22] ceramics such as calcium phosphates[23] and bioactive glasses;[24] to metallic materials such as titanium oxide (Fig. 2).[25] Some of the macroporous scaffolds have been tested in clinical trials for the reconstruction of craniomaxillofacial bones (Table 2). In this review we provide an update on various types of macroporous scaffolds that have been developed during the last few years, and describe their current use and potential applications in the regeneration of craniofacial bone.

Hydrogels

Hydrogels are a specific class of biomaterials that have been used in various ways for tissue engineering. The hydrophilic polymers of these gels form 3-dimensional networks through crosslinking, either by covalent bonds or through physical intramolecular and intermolecular attractions. Hydrogels swell rapidly in contact with water, form structurally similar macromolecular-based components in the body,[26–28] and have excellent biocompatibility with minimal inflammatory responses.[29] Their inherent hydrated architecture allows the transport of soluble factors, nutrients, and waste.[30] During the process of synthesis, the pores in hydrogels can be formed

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