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Biomaterials, bone grafting and tissue engineering

Edited by Joël Ferri and Ernst B. Hunziker

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Preprosthetic and maxillofacial surgery

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Introduction

Ever since osteointegration principles were established by Bränemark, the use of implants in oral and maxillo-facial surgery are being more widely developed throughout the world. Use of these techniques has never been abandoned. The innumerable publications on the theme of oral implantology show the interest of the medical community for these rehabilitations.

However, even though implantations are exceptionally successful a minimum of bone is mandatory to guarantee a primary stability and so assure the bone integration. Whenever this bone is not present the implant insertion is more complicated requiring complex or more uncertain techniques. For these cases pre-prosthetic implantation surgery has been developed in order to repair the missing or insufficient bone in order to admit a simple implant insertion.

Classically, the reconstruction is done using the autogenous cancellous bone. Progressively, after development by many surgeons, the use of membranous bone has been suggested in order to assure both a less painful harvesting and a lower resorption rate. However, in complex cases such as amputations or after irradiation, the use of vascularized bone flaps or distraction procedures are the only solutions possible. Today these techniques are used widely throughout the world and permit the reconstruction of just about any deficit in nearly any situation.

Despite all this, and even for very simple surgery, any bone harvesting has a certain morbidity forever present in the surgical procedure. To lessen this morbidity the surgeons have 'dreamed' of being able to repair bone by 'creating' it from structures which would not be harvested from the patient. In this optic the use of biomaterials has been developed. These techniques have vastly progressed using scaffold, stem cells (to induce bone and blood vessels) and proteins which stimulate the bone growth. However despite the quality of the re-construction techniques using these biomaterials none have replaced the autogenous bone graft, which remains the 'gold standard' of bone reconstruction.

Far beyond bone reconstruction today's biotechnologies are studying how to make absent or lost teeth grow again. This is a major challenge for which we can imagine the consequences in maxillary reconstruction. In the light of their progress this dream could soon become reality. . .

The objective of this work is to take stock of all these techniques permitting the reconstruction of the bone which supports the implants and also to consider the future and bring to light all the possibilities that biomaterials and tissue engineering can offer. To this aim this work has been divided in three parts.

The first part (bone reconstruction in implantology and reconstructive pre-prosthetic surgery) talks of the techniques, which although recent, have been validated by the international medical community. It enlightens the reader on today's possibilities of reconstruction with recognized procedures even though the choice of techniques is often a subject of discussion.

The second part (reconstruction in particular situations) studies the reconstruction in certain circumstances. It guides the reader on particular cases. The techniques used are often complex for situations which are often complex themselves. For instance implants rehabilitation in irradiated fields or in cleft lip and palate are studied in this section.

The third part covers tissue engineering. It carries out a study on the state of what is known today about bone, gums and dental organs creation. It is an open window on the techniques which could rapidly become revolutionary in dento-maxillo-facial reconstruction.

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1
Bone tissue engineering

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Abstract: In modern regenerative medicine and tissue engineering, the reconstruction and repair of bony defects is one of the most intensively investigated subjects. Standard surgical approaches that are currently implemented to facilitate the repair of osseous tissue include guided bone regeneration, distraction osteogenesis and the autotransplantation of bone. In the field of tissue engineering, extracorporeal strategies, such as flap prefabrication and the seeding of biocompatible scaffolds with either stem cells, committed osteoprogenitor cells or osteoblast-like cells, are favoured options. In this chapter, the limitations and potentials of the various techniques and strategies are addressed.

Key words: bone-tissue engineering, bone repair, autologous bone, guided bone regeneration, distraction osteogenesis.

1.1 Introduction

Bone repair is one of the most intensively investigated subjects in reconstructive surgery (for a review of this topic, see Schultz *et al*., 2000). Current approaches to skeletal reconstructive surgery make use of biomaterials, autografts or allografts, but each technique has its drawbacks. These include donor-site morbidity and shortage of material for autografts (Damien and Parsons, 1991), immunological problems and the risk of transmitting infectious diseases for allografts. Many artificial materials, such as metals, ceramics and polymers, have been used as substitutes for bone in maintaining skeletal function (Binderman and Fin, 1990), none of which is an ideal replacement for autologous osseous tissue in current clinical practice. The use of biomaterials is a common treatment option. One of the main advantages of tissue grafts over non-living biomaterials is that they contain living cells and tissue-inducing substances which confer biological plasticity. Research is currently in progress to develop cell-containing hybrid materials and to create replacement tissues that remain interactive after implantation, imparting physiological functions as well as structure to the tissue or organ damaged by disease or trauma (Alsberg *et al*., 2001).

In the field of tissue engineering generally, and not least in that relating to bone, living cells are exploited in various ways to restore, maintain or enhance tissue functions (Langer and Vacanti, 1993; Lysaght and Reyes, 2001). There exist three principal therapeutic strategies for treating diseased or lost tissue in patients: (i) *in-situ* tissue regeneration, (ii) implantation of freshly isolated or cultured cells, and (iii) implantation of a bone-like tissue construct that has been assembled *in vitro* from cells and scaffolds. In the case of *in-situ* regeneration, the formation of new tissue is induced by the implantation of a specific scaffold or by the application of extrinsic growth factors, which stimulate the body's own cells and promote local tissue repair. Cellular implantation involves the direct injection of suspensions or small aggregates of autologous or allogenic cells into the damaged or lost region in the absence or presence of a degradable scaffold. In the case of tissue implantation, a complete three-dimensional construct is grown *in vitro* from a cell-seeded scaffold, which is introduced into the defect once it has reached 'maturity' (Loty *et al*., 2000; Meyer *et al*., 2004a; Schliephake *et al*., 2001). In this chapter, each of these strategies will be described. Alternatives to extracorporeal approaches that are important in clinical decision making will also be discussed; so, too, will the possibility of combining clinical techniques with extracorporeal tissue-engineering methodologies.

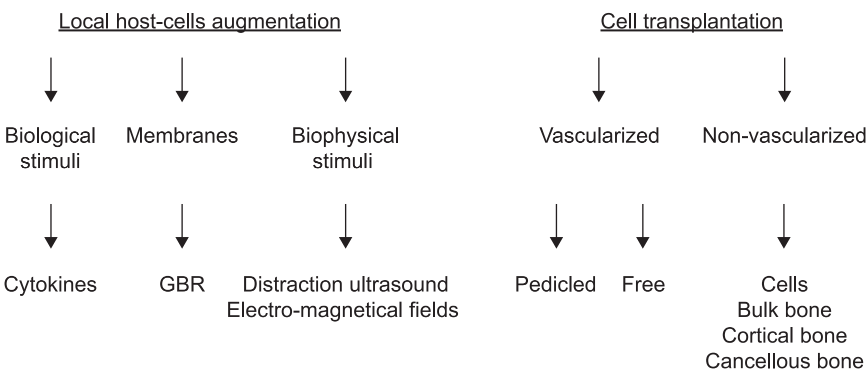
1.2 Bone-repair strategies

1.2.1 Autologous bone

The 'gold' standard for the reconstruction of osseous defects is autologous bone. There exist two classical ways of repairing bony defects using autologous cells: one involves augmenting local host-cell population, and the other the transplantation of grafted bone (Fig. 1.1).

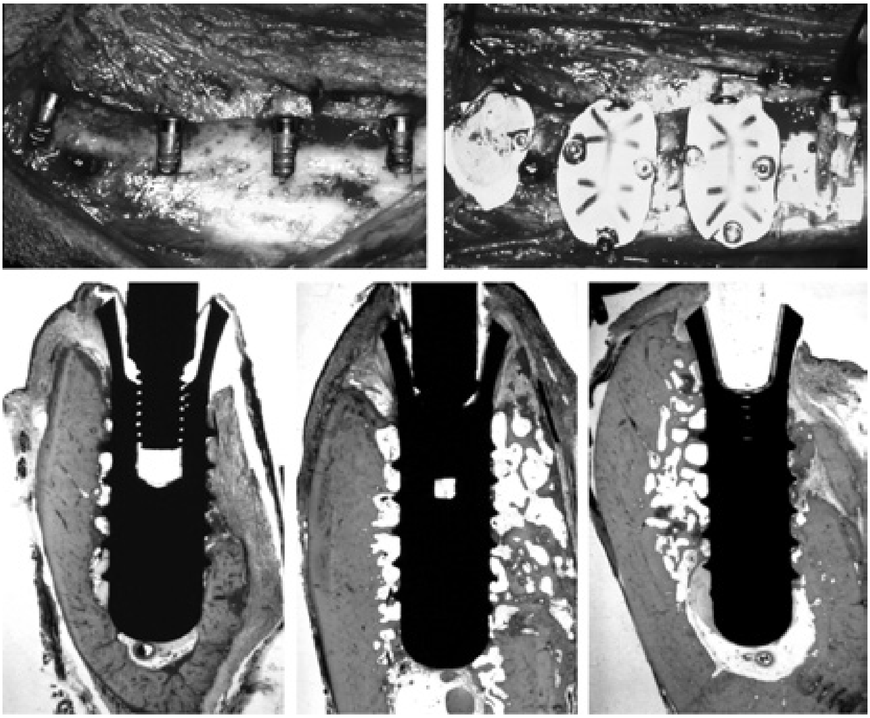
The healing of bony lesions can be promoted by augmenting the host-cell population only if the status of the repair site is conducive to this process. If the soft and hard tissues are still healthy, then the host cells can usually be induced to proliferate. But if the tissue is irritated or necrotic, or if the wound is infected, attempts in this direction will probably fail.

1.1 Bone repair by autologous cells



1.2.2 Guided bone regeneration

To improve defect healing by the ingrowth of local host cells, membrane techniques can be applied (Fig. 1.2). This approach, known as 'guided bone regeneration', is mainly used to repair bony defects in the maxilla and mandible. The principle of this method of bone regeneration is to effectively protect osseous tissue from the ingrowth of soft tissue by introducing a physical barrier (Lang *et al*., 1994). The success of this technique has been demonstrated in a number of controlled animal studies and clinical trials (Buser *et al*., 1996; Berglundh and Lindhe, 1997; Fiorellini *et al*., 1998). The pattern of healing has been shown to involve all steps of *de novo* bone formation, including blood-clot formation, invasion by osteoprogenitor cells and their terminal differentiation into osteoblasts. The extracellular matrix that is produced by the osteoblasts undergoes mineralization, and the woven bone that is thereby formed is later remodelled into lamellar bone (Hämmerle *et al*., 1998). The success of guided bone regeneration critically depends upon the size and the geometry of the defect. Osseous defects will be more effectively repaired if they are surrounded by more than two bony



1.2 Principle and histology of membrane-based guided bone regeneration.