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Medical applications of Bonelike® in Maxillofacial Surgery

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Abstract. Bonelike® is synthetic bone graft designed to mimic the inorganic composition of new bone using a patent process that consists of liquid sintering hydroxyapatite in the presence of a CaO-P₂O₅ based glass. This work reports the clinical application of this novel bone graft in maxillofacial surgery to reconstruct a bone defected area after cyst excision. Histological results clearly demonstrated an extensive new bone formation after 6 months implantation, with a significant degree of maturation. Scanning electron microscopy analysis revealed that the Bonelike® granules were almost completely surrounded by new bone, which proves its high osteoconductive capacity.

Introduction

In bone regeneration processes autologous bone is often successfully used in a very large number of surgical applications. Nevertheless, the use of autologous bone is restricted due to limited availability and additional strain for the patients caused by a second surgery. For homologous bone, the risks of immunological contamination, in particularly by AIDS and hepatitis should be considered. As alternative, synthetic bone grafts, such as hydroxyapatite (HA), Ca₁₀(PO₄)₆(OH)₂, differ from bone in structure and composition and are not replaced by new bone formation *in vivo*. Bonelike® is a synthetic HA that is sintered in the presence of CaO-P₂O₅-based glasses using a patented [1] process and its chemical composition mimics the mineral part of human bone tissues.

The physicochemical, mechanical and biological behaviour of Bonelike® has been extensively reported in literature [1-4]. Extensive *in vivo* animal studies have also shown its *in vivo* resorbability [4]. This work, reports medical applications of Bonelike® as a result of approved clinical trials that are currently being conducted in implantology and maxillofacial surgery.

Materials and Methods

To manufacture Bonelike® a P₂O₅-based glass with the composition of 65P₂O₅-15CaO-10CaF₂-10Na₂O, in %mol, was prepared from reagent grade chemicals using platinum crucible at 1400°C. The glass was ground and milled to powder form and mixed with medical grade HA in a proportion of 4wt%. Complete description of Bonelike® preparation has been reported previously [1-2]. Phase identification and quantification was performed using X-ray diffraction and Rietveld analysis.

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For the clinical trials granules size ranged from 150 μ m-1mm depending upon the bone defected area to reconstruct. This clinical trial reports the application of Bonelike[®] for bone augmentation of the maxillary sinus cavity after cyst removal. Pre-operative computer tomography scans (CT) and post-operative radiological examinations were performed whenever required according to standard follow-up protocols. Bonelike[®]/bone retrieved samples were also histologically analyzed using non-decalcified sections obtained perpendicular to bone length axis. Implant/new bone interface was also characterised by scanning electron microscopy.

Clinical Case

The patient was a 42 years-old male with a history of maxillary oedema and gingival enlargement with a clinically visible maxillary tumefaction on the first quadrant and therefore one CT-Scan was required. The CT-Scan evaluation revealed a maxillary lesion susceptible of being a cyst with a 5x3cm dimensions.

A buccal mucoperiosteal flap was reflected surgically. The exposed cortical bone revealed a fenestration that was enlarged with a drill burr, behind which was meaty tissue, not readily separable from the bone. Separation and curettage raised doubts as to the cystic nature of the process. Therefore, after the specimen had been removed, it was subjected to histopathologic examination and the result indicated a globulomaxillary cyst. Bonelike[®] granules were carefully mixed with physiological solution, which was afterwards remixed with patient's blood and placed in the bone defected area.

Results and Discussion

X-ray diffraction analysis revealed that due to the reaction between the HA matrix and the P₂O₅-based glass during the sintering process, the microstructure of Bonelike[®] was composed of crystalline HA and β and α -tricalcium phosphate phase, Ca₃(PO₄)₂. These last two phases are known to exhibit *in vivo* bioresorbability while HA is bioactive. Rietveld analysis revealed that the percentage of each phase in the microstructure of Bonelike[®] was HA= 67.7%, β -TCP=25.8% and α -TCP=6.5%.

Figure 1A) shows the pre-operative CT-scan frontal view of the globulomaxillary cyst. Classically, the globulomaxillary cyst is considered to be an inclusion or developmental cyst that arose from entrapped, nonodontogenic epithelium in the globulomaxillary suture [5], which occurs at the junction of the globular portion of the medial nasal process and the maxillary process [6].

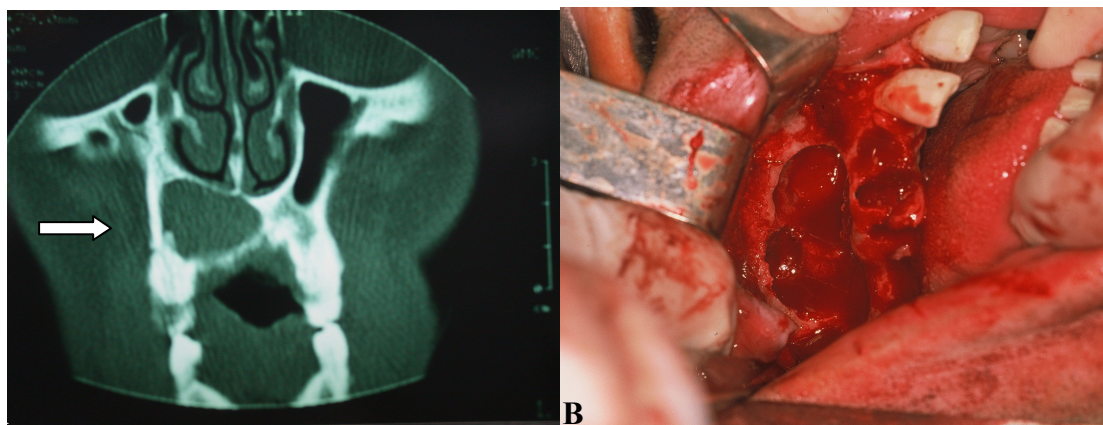


Fig. 1. Pre-operative CT-Scan in a frontal view (A), arrow indicates the globulomaxillary cyst. Formation of a window with a drill burr for the sinus cavity access (B)

The cyst is usually asymptomatic and appears on routine roentgenographic examination as an inverted pear-shaped radiolucency between the roots of the lateral incisor and canine. The globulomaxillary cyst sometimes occurs bilaterally [6].

In this clinic case the histological evaluation revealed that the cyst cavity was lined by ciliated columnar or stratified squamous epithelium, and the supporting fibrous connective tissue exhibited an inflammatory cell infiltrate. After formation of a window with a drill burr, Bonelike[®] granules were placed in the bone cavity, as it is depicted in Figs 1 and 2A.

Radiological examination of the bone defect was performed after 6 months of implantation and a large area of bone regeneration could be observed (see Fig. 2B).

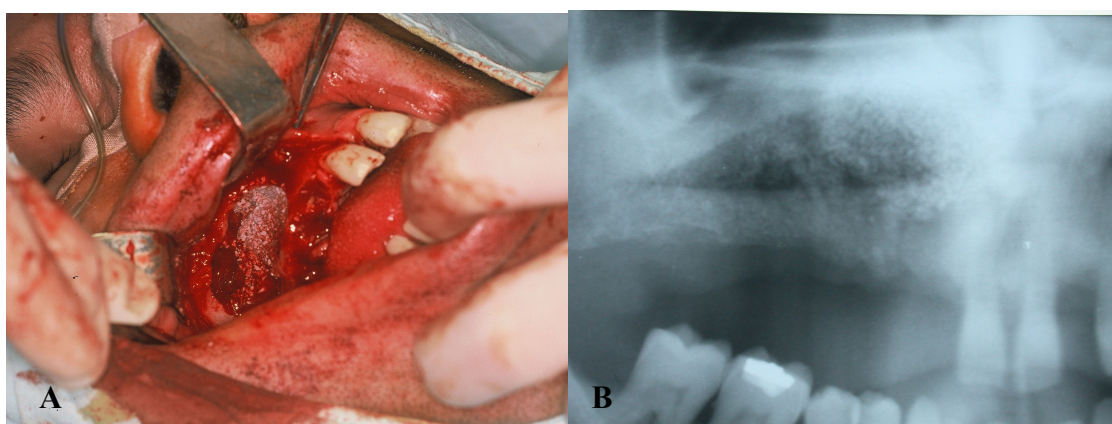


Fig. 2. Bonelike[®] placement into the bone defected area (A). Defected bone area almost completely regenerated (radiological examination) (B)

For prosthetic reasons the maxillary bone was remodulated and a specimen of the new bone was taken for histological analysis and SEM analysis was also performed to analyze the Bonelike[®]/new bone interface.

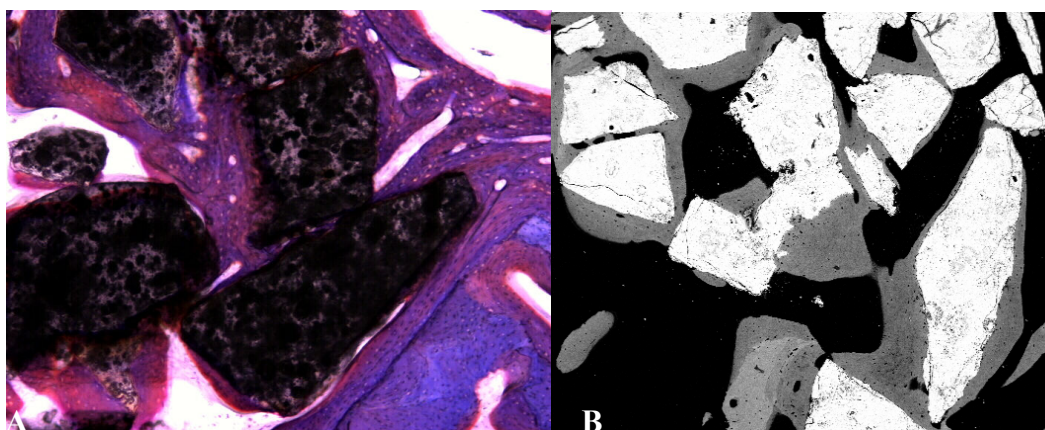


Fig. 3. Histological analysis of undecalcified sections stained with Solo-Chrome R (A) and SEM analysis (B) after 6 months of implantation (x100).

Histological sections demonstrated extensive new bone formation around implanted granules and continuous replacement by new bone. New bone apposition that almost completely surrounded the surface of the granules was observed using SEM analysis, indicating the highly osteoconductive

capacity of Bonelike[®]. Due to this extensive new bone formation in the defected area functional rehabilitation may be conducted. Resorption of Bonelike[®] granules was also observed, which should be attributed to the presence of controlled contents of bioresorbable β and α -Ca₃(PO₄)₂. Both histological and SEM analysis confirmed previous *in vivo* animal studies [4].

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