smartbook

DENTAL

swiss made

ibi

Industrie Biomediche Insubri SA
Via Cantonale 67
6805 Mezzovico-Vira
Switzerland

Second edition: January 2021
First edition: February 2019

CAUTION: The law restricts the sales of these devices made by, or on the order of, a dentist or surgeon.
Warning: Possible complications which may occur with any surgery include swelling at the surgical site, flap necrosis, bleeding, local inflammation, bone loss, infection or pain. Since SmartBone® contains collagen, cases of allergic reactions may occur in very rare circumstances.

This book is for healthcare professionals only, therefore the distribution to the general public is prohibited.

IBI-BOOK01 Rev. 1 01/21

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IBI SA: who we are

1.1 MISSION

IBI SA - Industrie Biomediche Insubri SA - is an innovative hi-tech Swiss biomedical company focused on research, development and production of proprietary technologies and medical devices for tissue engineering, founded on 26th February 2008.

IBI SA believes that regenerative medicine and tissue engineering represent the future for reconstructive surgery.

IBI has advanced competencies and core skills in processing materials for biomedical applications, which are used to develop proprietary technologies to build new and innovative medical devices.

IBI commits to safety and quality management: IBI Quality System is compliant to ISO 13485:2016. SmartBone® is CE marked according to 93/42/CE Directive classified as a class III Medical Device.

In July 2012 IBI introduced SmartBone® on the international market: SmartBone® is an innovative bone substitute specifically developed for bone regeneration, successfully used in oral and maxillofacial surgeries and traumatology. In the last years, following changes in references normative scenario, IBI consolidated two different certifications for SmartBone® according to the class of clinical indications of use: SmartBone® ORTHO for the orthopaedics applications and SmartBone® for the dental field.

During the 3 years IBI had been carrying on an observational study to collect clinical data obtained from patients who underwent reconstructive surgeries (from either trauma, or orthopaedic or oncology).

SmartBone® is osteoconductive, biocompatible, biodegradable and its microstructure has a porosity that promotes a fast and effective bone regeneration, thus successfully allowing its use in orthopaedic and spine surgery.

IBI keeps the biomedical, dental and orthopaedic community, as well as all end users, updated on its website (www.ibi-sa.com) and on its YouTube channel, with sections dedicated to company history, research, clinical cases, publications and much more.

Use a scan program to discover further information about IBI SA

bsi.

By Royal Charter

Certificate of Registration

QUALITY MANAGEMENT SYSTEM - ISO 13485:2016 & EN ISO 13485:2016

This is to certify that:

Industrie Biomediche Insubri SA
Via Cantonale 67
Mezzovico-Vira
Ticino
CH-6805
Switzerland

Holds Certificate Number: **MD 652245**

and operates a Quality Management System which complies with the requirements of ISO 13485:2016 & EN ISO 13485:2016 for the following scope:

Research and development, manufacture and sale of implantable medical devices for tissue engineering, also custom-made medical devices.

For and on behalf of BSI:

Stewart Brain, Head of Compliance & Risk - Medical Devices

Original Registration Date: 2016-04-11
Latest Revision Date: 2019-02-10

Effective Date: 2018-06-05
Expiry Date: 2021-06-04

Page: 1 of 1

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bsi.

By Royal Charter

EC Certificate - Full Quality Assurance System

Directive 93/42/EEC on Medical Devices, Annex II excluding Section 4

No. CE 644955

Issued To: Industrie Biomediche Insubri SA
Via Cantonale 67
Mezzovico-Vira
Ticino
CH-6805
Switzerland

In respect of:

The design and manufacture of resorbable bone graft with synthetic polymer and bovine and porcine tissues'.

on the basis of our examination of the quality assurance system under the requirements of Council Directive 93/42/EEC, Annex II excluding section 4. The quality assurance system meets the requirements of the directive. For the placing on the market of class III products an Annex II section 4 certificate is required.

For and on behalf of BSI, a Notified Body for the above Directive (Notified Body Number 2797):

Albert Roossien, Regulatory Lead

First Issued: 2019-02-21 Date: 2019-02-28 Expiry Date: 2024-02-20

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smartbone®

2. 1 INTRODUCTION

Since 1889, "modern" scientists started to focus their efforts on what can be defined as early bone tissue engineering [Senn, 1889; Gtelis, 2002]. Nowadays, hundred million surgical interventions are performed every year worldwide: current clinical gold standard for treatment of critical sized and nonunion bone defects is autograft bone.

Although autografts are advantageous for immunocompatibility, they carry a wide spectrum of risks (general anaesthesia, complex surgical maneuvers, secondary infections, fractures, pain, site morbidity, *etc*) that lead to a high percentage of failures (more than 10%) and are also followed by important cost increases [Younger, 1989; Hierholzer, 2006]. Furthermore, it is generally known that not all defects can be addressed, particularly the bigger ones, as far as few healthy sites can be harvested without a loss of function [Planell, 2009].

The need of adequate bone substitutes that promote an efficient remodeling of the native bone tissue is hence evident and it is supported by a wide spectrum of solutions proposed by academia, clinics and industry [Mistry, 2005]. In this framework, surgeons can choose among different types of substitutes that can be divided into three main categories:

- allografts, *i.e.* bone segments taken from either cadavers or living donors and duly acellularized and sterilized;
- xenografts, *i.e*. bone segments taken from animal bones (cows, horses, pigs, etc), duly acellularized and sterilized;
- synthetic scaffolds, such as *e.g.* bioceramics.

Allografts are an accepted alternative, but imply a higher risk, since disease transmission between humans is more likely than transmission between animal and human. Therefore, scientific research is progressively leading to the evaluation of other solutions [Haugen, 2019].

Xenografts and synthetic biomaterials represent an extremely valid alternative [Mistry, 2005; Winkler, 2018]. Nevertheless, to our best knowledge, only a few mixed composite substitutes are readily available on the market [Ramesh, 2017; De Grado, 2018; Ferraccini, 2018].

Finally, the hybrid approach (*e.g*. upgraded naturally derived materials) recently gains credit as of the most promising one [Rossi, 2015; Sarkar, 2015]: indeed, it enables the production of materials that can perfectly mimic healthy human bone, being rigid and elastic, compact but porous, and viable for cells and vessels [Ramesh, 2017; De Grado, 2018].

SUPPLEMENT ARTICLE

WILEY Journal of Clinical Periodontology

Bone grafts: which is the ideal biomaterial?

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Abstract

Bovine xenograft materials, followed by synthetic biomaterials, which unfortunately still lack documented predictability and clinical performance, dominate the market for the cranio-maxillofacial area. In Europe, new stringent regulations are expected to further limit the allograft market in the future.

Aim: Within this narrative review, we discuss possible future biomaterials for bone replacement.

Scientific Rationale for Study: Although the bone graft (BG) literature is overflooded, only a handful of new BG substitutes are clinically available. Laboratory studies tend to focus on advanced production methods and novel biomaterial features, which can be costly to produce.

Practical Implications: In this review, we ask why such a limited number of BGs are clinically available when compared to extensive laboratory studies. We also discuss what features are needed for an ideal BG.

Results: We have identified the key properties of current bone substitutes and have provided important information to guide clinical decision-making and generate new perspectives on bone substitutes. Our results indicated that different mechanical and biological properties are needed despite each having a broad spectrum of variations.

Conclusions: We foresee bone replacement composite materials with higher levels of bioactivity, providing an appropriate balance between bioabsorption and volume maintenance for achieving ideal bone remodelling.

KEYWORDS
bone graft, bone graft substitute, Bone replacement grafts, deal biomaterial

2.2 IBI'S APPROACH

In this sparkling context, IBI developed SmartBone®, following an engineering approach and a bottom-up multiscale strategy: that is upgrading natural existing biomaterials, introducing advanced characteristics on a unique structural composition and architecture.

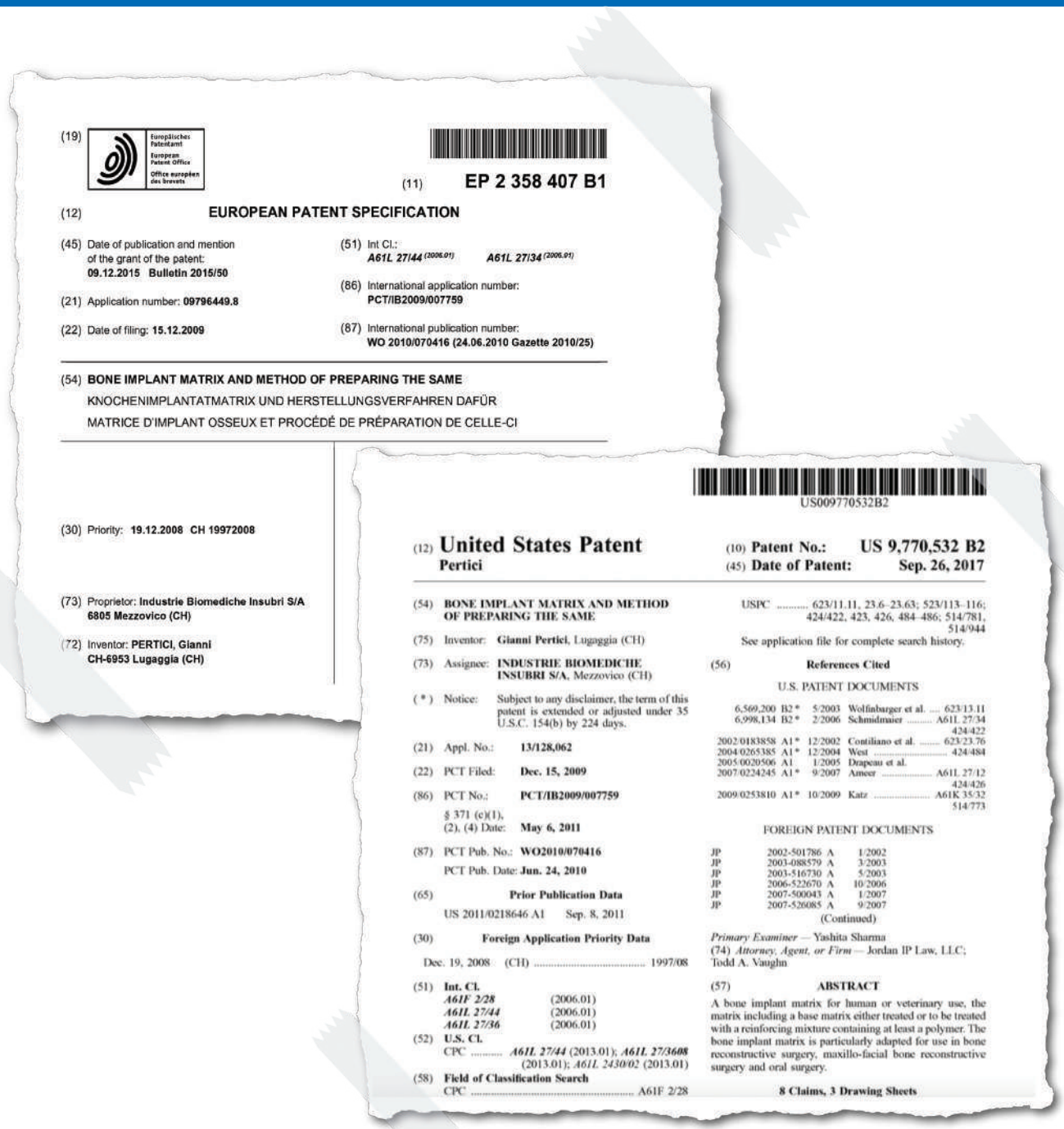
As a matter of fact, mimicking human bone's microstructure was the first point to address in order to ensure macro-scale properties: indeed, adequate-sized open porosity, combined rigid-elastic behavior and surface properties that ensure cell viability and colonization, are the key ingredients to finally obtain a remarkable and fast tissue integration and remodelling.

Giving biocompatibility as a granted request, the main features of IBI's innovative bone graft are thus the following (particularly intended with respect to other available bone grafts):

- **microstructure** comparable to the one of natural human bone (*i.e.* interconnected open porosity);
- **high mechanical performances**, close to those of a human healthy bone (*i.e.* rigid-elastic behavior, adequate elastic modulus, proper load bearing resistance, dust-free shaping, ability to be precisely modeled by all types of surgical tools, tenacity to fixation screws, hammering and heavy surgical maneuvering resistance, *etc*.);
- **high hydrophilicity** and thus high capability to absorb and retain blood (full of mesenchymal stem cells) once *in situ*;
- **high tissue integration** (*i.e*. high level of cell viability, proliferation, osteoconduction, osteoinduction).

Another key feature of SmartBone® is the high level of homogeneity among the various samples. Many bone grafts available on the market show very high sample variability, even in the same production lot: this is due to the natural origin of the raw material, which reflects into having pieces with a different microstructure, higher/lower porosity and thus different density, as well as highly variable physical and mechanical properties.

Even if one of the initial raw materials is natural, IBI's process aims at reducing this variability in order to offer regular and homogeneous bone grafts [Cingolani (1), 2018].



(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) **EP 2 358 407 B1**

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A61L 27/44 *(2006.01)* ***A61L 27/34*** *(2006.01)*

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PCT/IB2009/007759

(87) International publication number:
WO 2010/070416 (24.06.2010 Gazette 2010/25)

(54) **BONE IMPLANT MATRIX AND METHOD OF PREPARING THE SAME**
KNOCHENIMPLANTATMATRIX UND HERSTELLUNGSVERFAHREN DAFÜR
MATRICE D'IMPLANT OSSEUX ET PROCÉDÉ DE PRÉPARATION DE CELLE-CI

(30) Priority: **19.12.2008 CH 19972008**

(73) Proprietor: **Industrie Biomediche Insubri S/A**
6805 Mezzovico (CH)

(72) Inventor: **PERTICI, Gianni**
CH-6953 Lugaggia (CH)

US009770532B2

(12) **United States Patent**
Pertici

(10) **Patent No.: US 9,770,532 B2**
(45) **Date of Patent: Sep. 26, 2017**

(54) **BONE IMPLANT MATRIX AND METHOD OF PREPARING THE SAME**

(75) Inventor: **Gianni Pertici**, Lugaggia (CH)

(73) Assignee: **INDUSTRIE BIOMEDICHE INSUBRI S/A**, Mezzovico (CH)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 224 days.

(21) Appl. No.: **13/128,062**

(22) PCT Filed: **Dec. 15, 2009**

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US 2011/0218646 A1 Sep. 8, 2011

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A61F 2/28 (2006.01)
A61L 27/44 (2006.01)
A61L 27/36 (2006.01)

(52) **U.S. Cl.**
CPC ***A61L 27/44*** (2013.01); ***A61L 27/3608*** (2013.01); *A61L 2430/02* (2013.01)

(58) **Field of Classification Search**
CPC A61F 2/28
USPC 623/11.11, 23.6–23.63; 523/113–116; 424/422, 423, 426, 484–486; 514/781, 514/944
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

6,569,200	B2 *	5/2003	Wolfinbarger et al.	623/13.11
6,998,134	B2 *	2/2006	Schmidmaier	A61L 27/34 424/422
2002/0183858	A1 *	12/2002	Contiliano et al.	623/23.76
2004/0265385	A1 *	12/2004	West	424/484
2005/0020506	A1	1/2005	Drapeau et al.	
2007/0224245	A1 *	9/2007	Ameer	A61L 27/12 424/426
2009/0253810	A1 *	10/2009	Katz	A61K 35/32 514/773

FOREIGN PATENT DOCUMENTS

JP	2002-501786	A	1/2002
JP	2003-088579	A	3/2003
JP	2003-516730	A	5/2003
JP	2006-522670	A	10/2006
JP	2007-500043	A	1/2007
JP	2007-526085	A	9/2007

(Continued)

Primary Examiner — Yashita Sharma
(74) *Attorney, Agent, or Firm* — Jordan IP Law, LLC; Todd A. Vaughn

(57) **ABSTRACT**

A bone implant matrix for human or veterinary use, the matrix including a base matrix either treated or to be treated with a reinforcing mixture containing at least a polymer. The bone implant matrix is particularly adapted for use in bone reconstructive surgery, maxillo-facial bone reconstructive surgery and oral surgery.

8 Claims, 3 Drawing Sheets

2.3 RAW MATERIALS AND PRODUCTION PROCESS

The multi-functional structure that IBI wanted for its innovative bone graft was achieved by developing a new biohybrid material composed of:

1) a bovine bone derived matrix (as starting raw material);
2) biocompatible and biodegradable biopolymers (polyesters) to reinforce the structure and to obtain an excellent biomechanical performance;
3) collagen fragments.

1) The bovine derived mineral matrix:

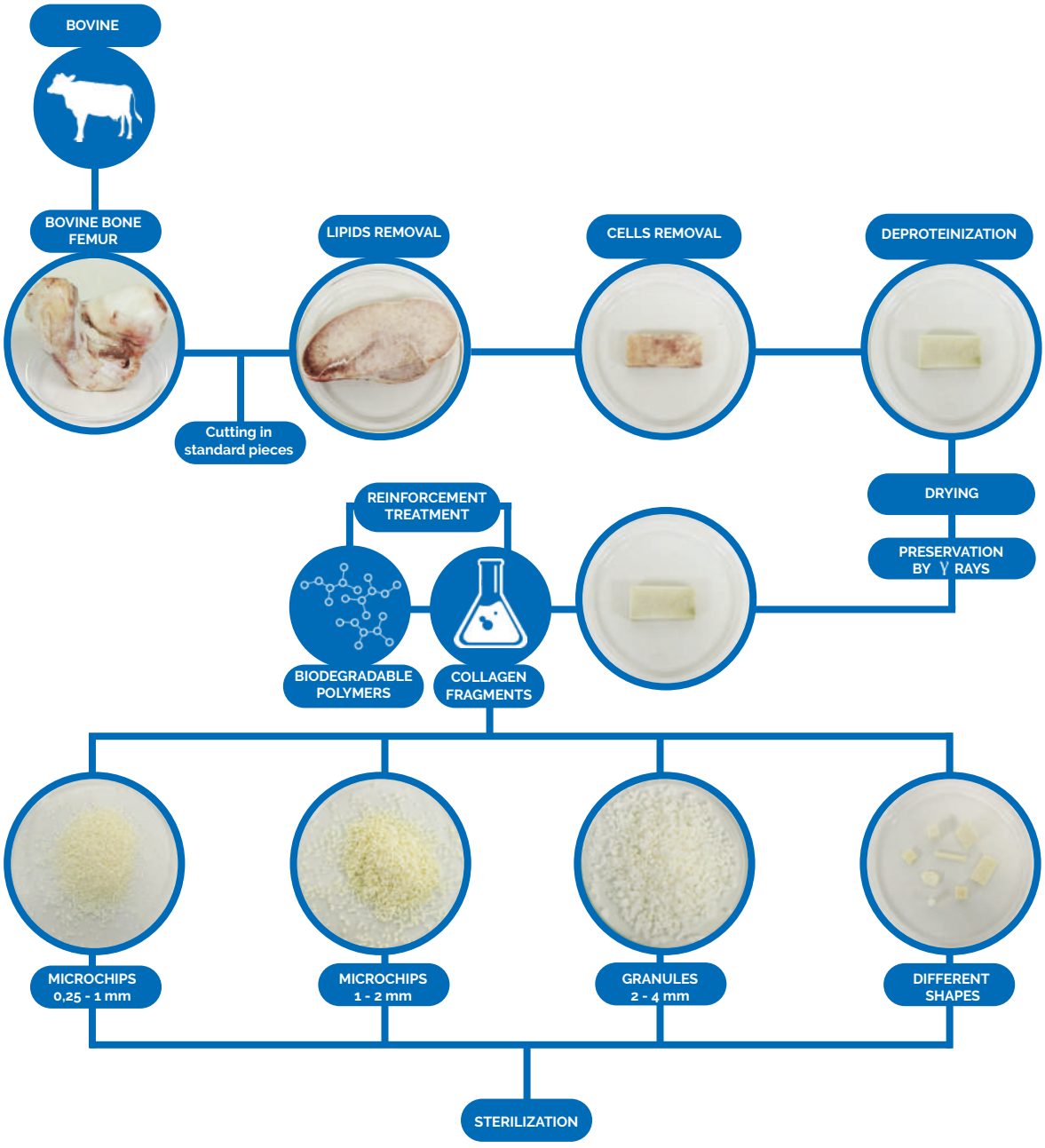
- has a chemical structure and a morphology that resemble the human bone;
- is rigid, but not elastic, and thus too fragile (since the mineral matrix loses its biomechanical properties without proteins);

2) The addition of a homogeneous polymeric coating helps to:

- reinforce the structure by adding a plastic component, thus improving resistance and reducing cracks propagation, making the graft elasto-plastic;
- protect the graft from reabsorption during first inflammation-healing period and ensures volumetric stability.

3) Finally, the presence of collagen fragments, even if in extremely low quantities:

- make the surface very viable for cells and thus enhances tissue remodeling and integration;
- promote cell adhesion;
- increase the graft wettability, making it highly hydrophilic.


BOVINE
BOVINE BONE FEMUR
Cutting in standard pieces
LIPIDS REMOVAL
CELLS REMOVAL
DEPROTEINIZATION
DRYING
PRESERVATION BY γ RAYS
REINFORCEMENT TREATMENT
BIODEGRADABLE POLYMERS
COLLAGEN FRAGMENTS
MICROCHIPS 0,25 - 1 mm
MICROCHIPS 1 - 2 mm
GRANULES 2 - 4 mm
DIFFERENT SHAPES
STERILIZATION

2.4 MICRO AND MACRO-STRUCTURE

SmartBone®'s major characteristic resides in its microstructure. In this sense, decellularized and deproteinized trabecular bovine bone already naturally presents a perfectly wide-opened, interconnected porosity, which is optimal for cell migration and colonization.

Nevertheless, in the frame of using it as base material for the development of implantable devices, a technique not only improving but also homogenizing the mechanical properties, making them independent on the raw, untreated material characteristics, is required. In this respect, IBI's proprietary process of adding resorbable polymeric components and collagen fragments improves material's mechanical and biological performances.

The combination of these two concepts is of utmost importance: on one hand, homogenous mechanical response is ensured; on the other one, cells proliferation is not only favoured by changes in the porous structure, but even further enhanced by the presence of collagen fragments. This way, full substitution by patient living healthy bone is recorded after complete remodeling.

The final geometrical characteristics of SmartBone® were further investigated using computer tomography and are reported in figure 1, where an exemplificative image of a 3D render of a SmartBone® 8x8x8 mm^3 cube is presented: it resulted that the tested sample had an equivalent volume of about 512 mm^3, a free volume of about 375 mm^3 and a free surface of about 2.300 mm^2.

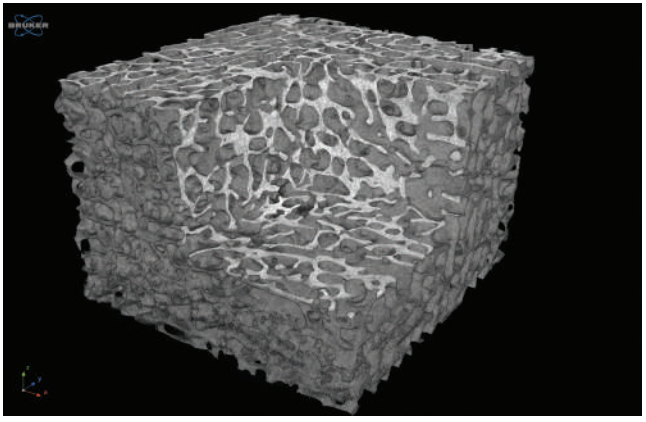


Figure 1: 3D render of an IBI's SmartBone® obtained via reconstruction from a microCT scan.

Annals of Oral & Maxillofacial Surgery 2014 Feb 14;2(1):4.

Emerging Technologies

Research study

Composite polymer-coated mineral grafts for bone regeneration: material characterisation and model study

G Pertici[1,2], F Rossi[3], T Casalini[3], G Perale[1,2,4*]

Abstract

Introduction

This study discusses composite polymer-coated mineral grafts for bone regeneration.

Materials and Methods

Bone xenografts are coated with degradable synthetic [poly(L-lactide-co-ε-caprolactone)] and natural(polysaccharides) polymers in order to increase their mechanical properties, on one side, and to improve cell adhesion, on the other, with the purpose of developing a novel composite material for bone tissue engineering. In vitro assayshelp examine the microstructure of the scaffold by Fourier transform infrared and environmental scan-ning electron microscopy analyses and the porosity of the material by micro-computed tomography. The good adhesion property of polymer coated on to the mineral scaffold is deeply analysed and proved. The in vitro polymerdegradation, in terms of time evolution of polymer-coating thickness, was rationalised with a mathematical model. The purpose of such modelling activity is to provide a simple but powerful-tool to understand the influence of design parameters on coating behaviour.

Results

The fabricated bone graft exhibited regular microstructure similar to healthy iliac bones with an average of 27% open porosity and an adequately rigid structure, which ensures a better osteointegration once implanted.

Conclusion

This approach avoids the use of trial -and-error methods and consents a better a priori material design.

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[4] Swiss Institute for Regenerative Medicine, Taverne, Switzerland

2.5 POLYMER DEGRADATION

When dealing with implantable medical device, product formulation and manufacturing need to follow specific procedures. In this respect, accurate selection of the base material has to be done. This has to take into consideration not only the characteristics of pristine, base polymers, but also the way they will be affected by all manufacturing and post-processing steps (including terminal sterilization).

Biodegradable polymers have the great advantage of naturally diseappear from patient body in a reasonable and controllable time after implantation, leaving minimal traces and small impact.

SmartBone® polymeric fraction is subject to a complete degradation which occurs in an average of 18 weeks. This represents an optimal result because it degrades and fades away approximately in four months, matching the new bone ingrowth and tissue integration.

As visible in Figure 2 in the first two months, the degradation occurs with the thinning of the polymer film. From the end of the third month, it drops dramatically, reaching a complete dissolution between the fourth and the sixth month, independently on the initial thickness, in the range of 2 - 10 µm.

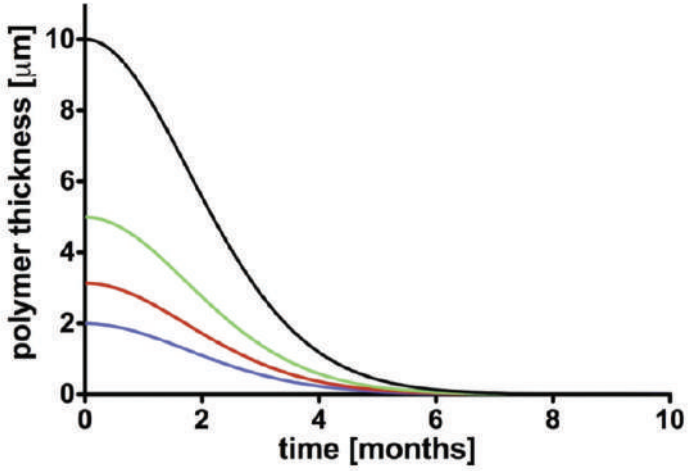

Figure 2: Polymeric film thinning during time as degradation proceeds almost independently from starting thicknesses (2, 3, 5, 10 (µm)).

polymers

MDPI

Article

A Methodologic Approach for the Selection of Bio-Resorbable Polymers in the Development of Medical Devices: The Case of Poly(L-lactide-*co*-"-caprolactone)

Alberto Cingolani [1,2], Tommaso Casalini [1,3], Stefano Caimi [1], Antoine Klaue [1], Mattia Sponchioni [4], Filippo Rossi [4,*] and Giuseppe Perale [2,3,*]

1 Institute for Chemical and Bioengineering, Department of Chemistry and Applied Bioscience ETH Zurich, Vladimir-Prelog-Weg 1-5/10, 8093 Zürich, Switzerland; alberto.cingolani@chem.ethz.ch (A.C.); tommaso.casalini@chem.ethz.ch (T.C.); stefano.caimi@chem.ethz.ch (S.C.); antoine.klaue@chem.ethz.ch (A.K.)

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Abstract: In the last decades bioresorbable and biodegradable polymers have gained a very good reputation both in research and in industry thanks to their unique characteristics. They are able to ensure high performance and biocompatibility, at the same time avoiding post-healing surgical interventions for device removal. In the medical device industry, it is widely known that product formulation and manufacturing need to follow specific procedures in order to ensure both the proper mechanical properties and desired degradation profile. Moreover, the sterilization method is crucial and its impact on physical properties is generally underestimated. In this work we focused our attention on the effect of different terminal sterilization methods on two commercially available poly(L-lactide-*co*-"-caprolactone) with equivalent chemical composition (70% PLA and 30% PCL) and relatively similar initial molecular weights, but different chain arrangements and crystallinity. Results obtained show that crystallinity plays a key role in helping preserve the narrow distribution of chains and, as a consequence, defined physical properties. These statements can be used as guidelines for a better choice of the most adequate biodegradable polymers in the production of resorbable medical devices.

Keywords: electron beam; ethylene oxide; medical devices; polymers; sterilization

Polymers 2018, 10, 851; doi:10.3390/polym10080851

2.6 MECHANICAL PROPERTIES

Mechanical handling and performances of bone grafts during surgical maneuvering is tremendously essential. Grafts are expected to undergo heavy stresses and loads, as far as they need to be shaped and cut before being placed. Furthermore, they need to withstand drilling and fixing of osteosynthesis screws and must remain firmly in place, offering a strong mechanical bond to the host tissue: the better the mechanical stability and the higher the surface contact with the host tissue, the higher and better the integration is achieved. A major point in this sense, is also represented by the necessity of having homogenous mechanical performance, even when the graft is shaped in complex geometries. IBI's treatement, not only reinforces the mechanical characteristics of pristine bone, but also ensures good homogeneity,

Full characterization from a torsional, flexural and compression point of view, have been run on SmartBone®, showing excellent mechanical response under each of these texts. Results are reported in the following Table 1.

Torsion	Max Torque [Nmm]	Max Stress [MPa]	Max Strain %	Torsional Elastic Modulus [MPa]	Kg/cm²
Medium Value	1'505.4	25.5	5.8	490.6	259.8
Standard Dev.	294.9	4.4	0.9	103.7	44.9
Bending	**Max Force [N]**	**Max Stress [MPa]**	**Max Strain %**	**Flexural Modulus [MPa]**	**Kg/cm²**
Medium Value	100.3	23.8	7.6	340.6	242.4
Standard Dev.	17.4	4.2	0.9	63.1	42.4
Compression	**Max Force [N]**	**Max Stress [MPa]**	**Max Strain %**	**Elasticity Modulus [MPa]**	**Kg/cm²**
Medium Value	1'914.2	25.8	2.2	1'245.7	262.9
Standard Dev.	590.6	7.8	0.4	225.9	80.1

Table 1: SmartBone® mechanical properties.

Current Pharmaceutical Biotechnology, 2018, 19, 1005-1013

RESEARCH ARTICLE

Improving Bovine Bone Mechanical Characteristics for the Development of Xenohybrid Bone Grafts

Alberto Cingolani[1,2], Carlo Francesco Grottoli[2], Raffaella Esposito[3], Tomaso Villa[3], Filippo Rossi[4] and Giuseppe Perale[2,5,6*]

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Abstract: ***Background***: The further functionalization of natural existing biomaterials is a very efficient method to introduce additional advanced characteristics on a unique structural composition and architecture.

Objective: As an example, different animal sources, if properly treated, can be used to develop bone xenograft active in hard tissues regeneration. In this sense, it is also important to consider that the selected process has to take into consideration the intrinsic variability of the base material itself and possibly being able to compensate for it.

Methods: In this work we characterize cancellous bovine bone treated by deposition of polymer and collagen and we show that the added components not only lead to a more resistant and more hydrophilic material, but also reduce the conventional correlation between apparent density and elastic modulus, which, in general, is a major source of uncertainty and risk in xenografts usage.

Results: Moreover, though intrinsically reinforcing the material, the deposition process leaves the specific open-porous structure, that allows cells proliferation and vessels ingrowth, basically unaltered.

Conclusion: The final material combines in a single piece and at the same time, mechanical resistance, homogeneous mechanical response and proper structural characteristics that allow further integration within the patient autochthonous tissues.

ARTICLE HISTORY

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DOI:
10.2174/1389201020666181129115839

Keywords: Hard tissues regeneration, xenografts, tissue engineering, biomaterials, bovine bone, biopolymers.

2.7 ISO BIOCOMPATIBILITY TESTS

Wide preclinical investigations have been carried out on SmartBone® during the development phase, both *in vitro* with different cell populations and *in vivo* on reference animal models.

Standard compulsory ISO 10993 investigations on biocompatibility were carried out under GLP conditions, specifically: Intracutaneous Reactivity Test, Systemic Toxicity Test and Delayed Hypersensitivity Test were performed, all resulting completely negative, thus confirming SmartBone® full biocompatibility.

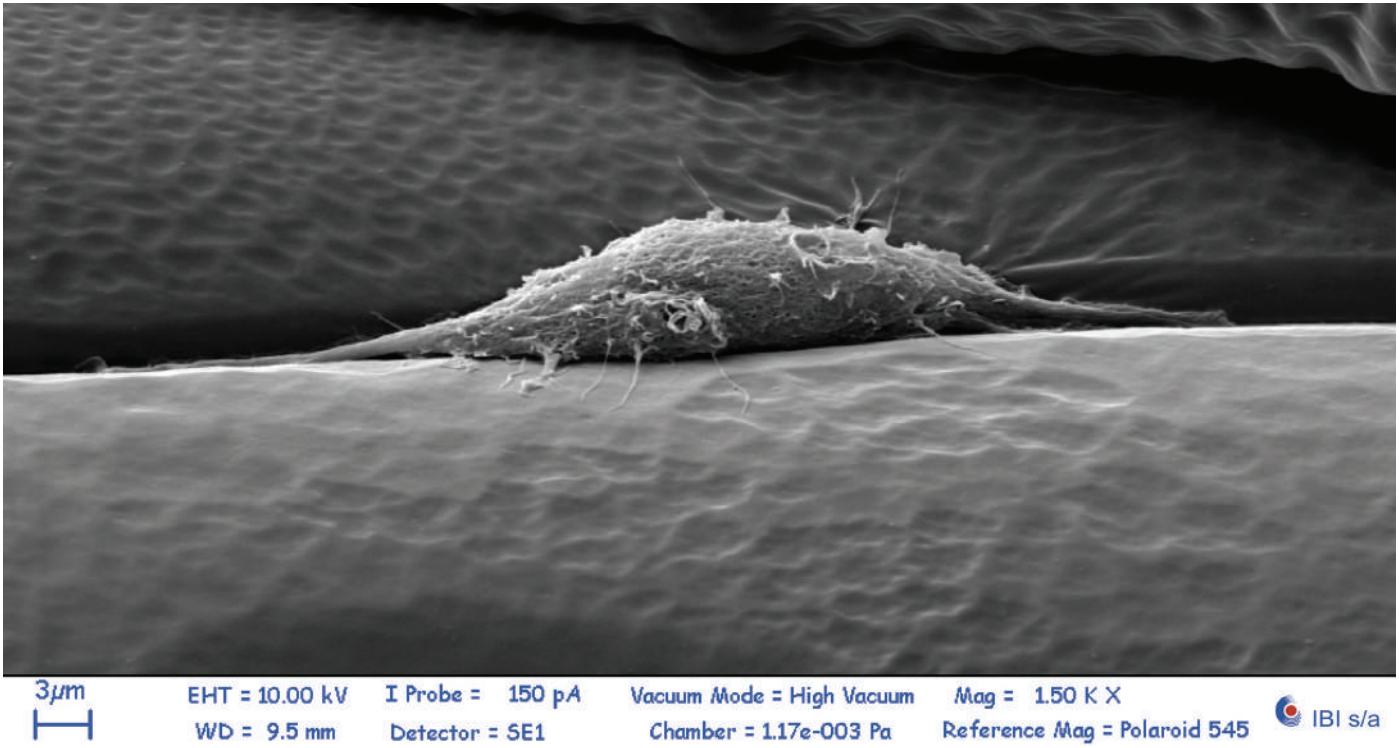

Figure 3: Exemplificative E/SEM zoomed-in image of a cell spreading onto a SmartBone® internal surface, well evidencing the high cell conductivity of SmartBone® surfaces.

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COMPOSITE POLYMER-COATED MINERAL SCAFFOLDS FOR BONE REGENERATION: FROM MATERIAL CHARACTERIZATION TO HUMAN STUDIES

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Bovine bone xenografts, made of hydroxyapatite (HA), were coated with poly(L-lactide-co-ε-caprolactone) (PLCL) and RGD-containing collagen fragments in order to increase mechanical properties, hydrophilicity, cell adhesion and osteogenicity. *In vitro* the scaffold microstructure was investigated with Environmental Scanning Electronic Microscopy (ESEM) analysis and micro tomography, while mechanical properties were investigated by means compression tests. In addition, cell attachment and growth within the three-dimensional scaffold inner structure were validated using human osteosarcoma cell lines (SAOS-2 and MG-63). Standard ISO *in vivo* biocompatibility studies were carried out on model animals, while bone regenerations in humans were performed to assess the efficacy of the product. All results from *in vitro* to *in vivo* investigations are here reported, underlining that this scaffold promotes bone regeneration and has good clinical outcome.

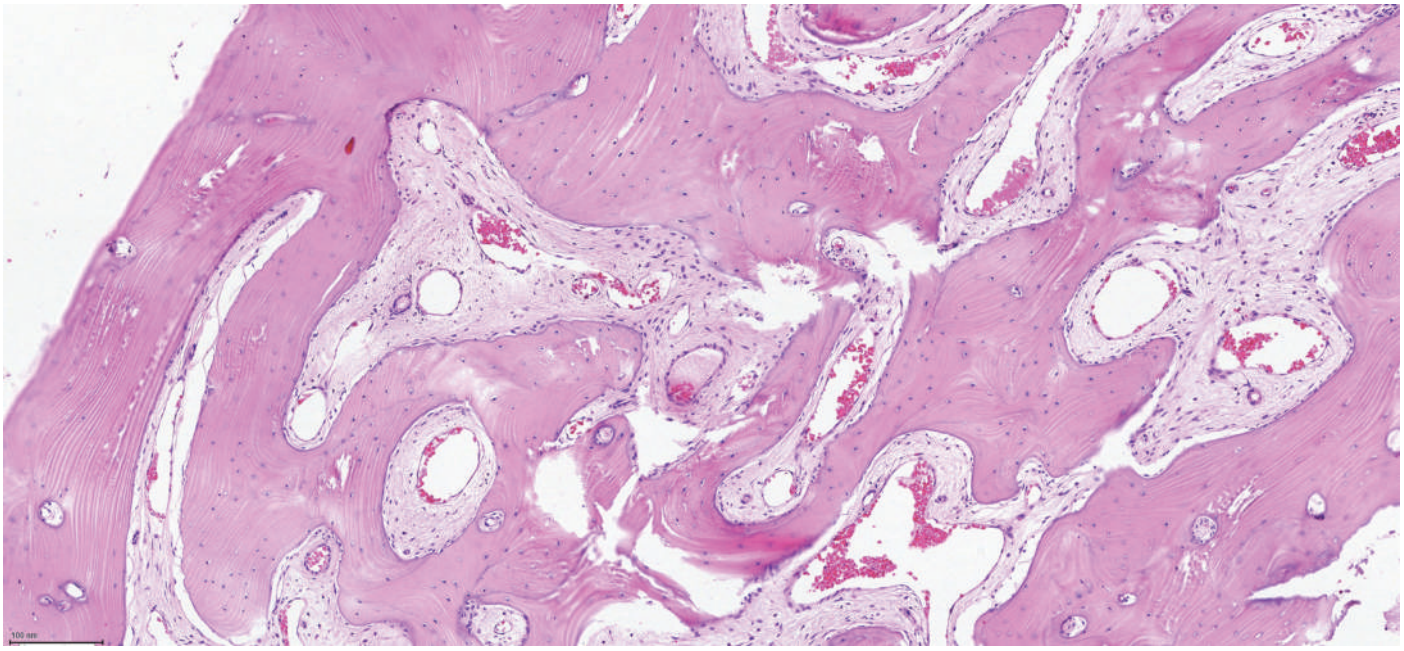

Figure 4: H/E stained histological slice from SmartBone® on Demand™ graft, 2.5 years post-surgery; the graft is completely substitute and the osteogenesis has formed a lamellar bone with cement lines; a lot of osteocytes inside the lacunae and a good angiogenesis are evidenced. Image taken from [Grecchi, 2014].

3

Mechanism of Action

3.1 REMODELLING OF SMARTBONE®

SmartBone® integration into the natural bone, and hence its resorption, is driven by its being progressively substituted with healthy living bone from host: it is, indeed, important to underline the key role of remodeling, hence the capability of SmartBone® to be substituted by healthy living bone.

This is a key feature of SmartBone® and one of its major innovative claims, also with respect to competing grafts. Here, moreover, lies one of the keys to understanding the mechanism of action of SmartBone® [Pertici, 2010; Grecchi, 2014; Pertici, 2014; Pertici, 2015; Zollino, 2015; Secondo, 2017; D'Alessandro, 2017; Roato (1), 2018; Cingolani (1), 2018; Cingolani (2), 2018 Mandelli, 2018]. SmartBone® graft soaks up blood, thus starting microcoagulation to occur inside the graft itself and hence enhancing graft integration [D'Alessandro, 2017; Mandelli, 2018; Stacchi, 2018].

The first weeks are then needed for cellular colonization of the graft, which is also enhanced by the presence of gelatine that offers a viable environment for cells to spread onto; meanwhile, this time lag is also necessary for the degradation of the thin polymeric film, which progressively fades away leaving mineral structure for cells to consolidate and promote the formation of new living bone (also by means of formation of new vessels); the following couple of months are needed for the integration of the graft with the native patient bone, thanks also to vascularization and new bone formation inside the graft.

Human histological studies provided very robust confirmation, with clinical evidences, on this action mechanism, offering a greatly detailed insight also on new bone formation supported by SmartBone® [Pertici, 2010 ; Grecchi, 2014; Pertici, 2014, Pertici, 2015; Zollino, 2015; Secondo, 2016; D'Alessandro, 2017; Mandelli, 2018; Roato(1), 2018; Stacchi, 2018; Facciuto, 2019].

The choice of a bovine-derived mineral matrix is driven by the very high similarity with the human one [Datta, 2006]. The adding of resorbable polymers serves not only to increase the mechanical performances but also to protect the mineral fraction from the very initial post-surgical inflammation and finally to sustain bone formation.

The adding of gelatine to the polymeric thin film serves to provide immobilized biomolecules containing the RGD (Arg-Gly-Asp) sequence, which promotes cell adhesion and hence sparks the formation of new bone.

SmartBone® undergoes complete substitution via remodelling process: it shows about 35-40% substitution at about 4-6 months (averaged considering key factors *e.g.* surgical site, patient sex and age, *etc.*) which proceeds till 60-70% substitution in *ca.* 1 year, up to complete substitution with no evidences of residuals after *ca.* 2 years.

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Bovine bone matrix/poly(L-lactic-co-ε-caprolactone)/gelatin hybrid scaffold (SmartBone®) for maxillary sinus augmentation: A histologic study on bone regeneration

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ABSTRACT

The ideal scaffold for bone regeneration is required to be highly porous, non-immunogenic, biostable until the new tissue formation, bioresorbable and osteoconductive. This study aimed at investigating the process of new bone formation in patients treated with granular SmartBone® for sinus augmentation, providing an extensive histologic analysis. Five biopsies were collected at 4–9 months post SmartBone® implantation and processed for histochemistry and immunohistochemistry. Histomorphometric analysis was performed. Bone-particle conductivity index (BPCi) was used to assess SmartBone® osteoconductivity.

At 4 months, SmartBone® (12%) and new bone (43.9%) were both present and surrounded by vascularized connective tissue (37.2%). New bone was grown on SmartBone® (BPCi = 0.22). At 6 months, SmartBone® was almost completely resorbed (0.5%) and new bone was massively present (80.8%). At 7 and 9 months, new bone accounted for a large volume fraction (79.3% and 67.4%, respectively) and SmartBone® was resorbed (0.5% and 0%, respectively). Well-oriented lamellae and bone scars, typical of mature bone, were observed. In all the biopsies, bone matrix biomolecules and active osteoblasts were visible. The absence of inflammatory cells confirmed SmartBone® biocompatibility and non-immunogenicity. These data indicate that SmartBone® is osteoconductive, promotes fast bone regeneration, leading to mature bone formation in about 7 months.

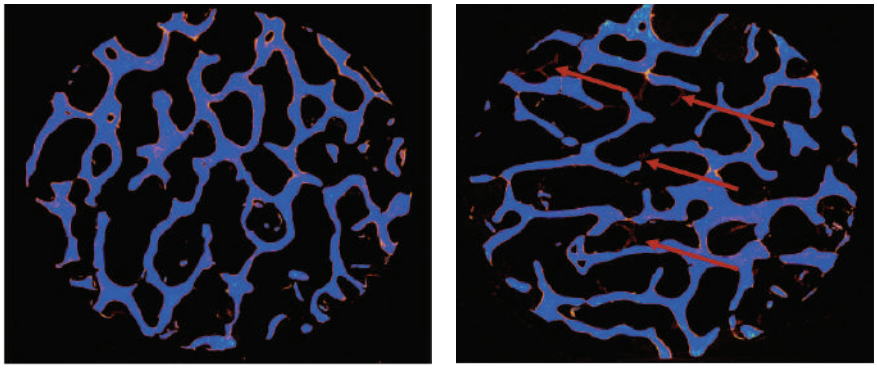
3.2 CELLULAR EXPLANATION OF SMARTBONE® REMODELING MECHANISM

IBI devoted important resources into the detailed investigation of SmartBone® integration mechanism. Driven by human histological results, IBI committed to deeply investigate the very initial phases of SmartBone® integration and had, hence, developed a reliable *in vitro* model reproducing the first 60 days post-grafting. Essential issue in model development was the choice of the cell population to be used, aiming at best reproducing the natural *in vivo* environment faced by grafted SmartBone®. Literature suggested the use of non-cultured fraction of adipose tissue-derived stem cells [Roato (1), 2018].

Adipose tissue-derived stem cells (ASCs) are a promising tool for the treatment of bone diseases or skeletal lesions, thanks to their ability to potentially repair damaged tissue. One of the major limitations of ASCs is represented by the necessity to be isolated and expanded through *in vitro* culture; thus, a strong interest was generated by the adipose stromal vascular fraction (SVF), the non-cultured fraction of ASCs. SVF is a heterogeneous cell population, directly obtained after collagenase treatment of adipose tissue.

SVF has hence a high potential as model cell type in assessing bone graft performances in vitro assays. We demonstrated [Roato (1), 2018] that SVF cells plated on SmartBone® expressed their osteoinductive potential. Moreover, we observed an increasing area of new tissue over time, with and also without osteointegration media!

These data proved the dynamics of bone remodeling supported by SmartBone® during the very early phase post-surgical grafting. Furthermore, these results strongly support an innovative idea for the use of adipose SVF and SmartBone® to promote tissue regeneration and repair, also thanks to an easier cell management preparation that allows a potentially larger use in clinical applications [Roato (2), 2018].



SmartBone® Stromal Vascular Fraction (SVF)

Figure 5: adipose-derived Stromal Vascular Fraction (SVF) cultured on SmartBone® promoted the formation of new trabeculae also in in vitro model. Images taken from [Roato(1), 2018].

Hindawi
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Research Article

Adipose-Derived Stromal Vascular Fraction/Xenohybrid Bone Scaffold: An Alternative Source for Bone Regeneration

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Adipose tissue-derived stem cells (ASCs) are a promising tool for the treatment of bone diseases or skeletal lesions, thanks to their ability to potentially repair damaged tissue. One of the major limitations of ASCs is represented by the necessity to be isolated and expanded through *in vitro* culture; thus, a strong interest was generated by the adipose stromal vascular fraction (SVF), the noncultured fraction of ASCs. SVF is a heterogeneous cell population, directly obtained after collagenase treatment of adipose tissue. In order to investigate and compare the bone-regenerative potential of SVF and ASCs, they were plated on SmartBone®, a xenohybrid bone scaffold, already used in clinical practice with successful results. We showed that SVF plated on SmartBone, in the presence of osteogenic factors, had better osteoinductive capabilities than ASCs, in terms of differentiation into bone cells, mineralization, and secretion of soluble factors stimulating osteoblasts. Indeed, we observed an increasing area of new tissue over time, with and without OM. These data strongly support an innovative idea for the use of adipose SVF and bone scaffolds to promote tissue regeneration and repair, also thanks to an easier cell management preparation that allows a potentially larger use in clinical applications.

3.3 RADIOLOGICAL ASSESSMENT OF SMARTBONE® INTEGRATION AND REMODELING OVER TIME

Assessing remodeling of SmartBone®, and above all integration, is an essential surgical need as it helps the surgeon to evaluate the best timing to further proceed with the treatment and go further with implants placement. Typically, histological sampling is a non-commonly available tool in daily practice, where on the other hand radiographic imaging is routinely performed.
The rule of a thumb in assessing bone reliability to receive dental implants is density, evaluated by means of radiographic opacity. Briefly, one of major causes of opacity is the mineral fraction: the denser is the more opaque.

Importantly, opacity of grafted SmartBone® changes with time: it is a real indicator of bone regeneration and a measurable parameter to monitor remodeling!

Other mineral biomaterials, both of natural origin and artificial are very opaque because they are dense. However, it must be pointed out that the counter-effect of this high density is the very low resorption and the poor capability to sustain remodeling: using these materials bone, indeed, heals by simply "growing around" mineral granules. Moreover, standard xenograft treatment foresees the use of high temperature processes that also change the material mineral crystal structure, making them denser, hence more opaque, but also less resorbable [Piattelli, 1999; Sartori, 2003]. Last, but not least, these types of grafts are usually very weak from a mechanical point of view and hence can easily be "compacted" (since they are in small granules which behave as powder-like). The more you compact them, the more opaque they become, the more they become stable and the less they resorb [Carusi, 2016].

As seen before, IBI philosophy underneath SmartBone® design is exactly the opposite: a bone graft that is not too dense, not too compact as it must conduct cells within it and support an effective remodeling. SmartBone® mineral fraction is designed to be as similar as possible to human bone, particularly to young human bone [Kuhn, 2008], which is less dense and hence less opaque: this allows blood, cells and micro vessels to colonize it, growing on the polymeric film attaching to RGD-fragments from gelatin, progressively degrade the polymeric film, find the mineral matrix and start remodeling it into new healthy bone that can become mature and robust healthy bone in due time.

To obtain this, SmartBone® has the adequate open and interconnected porosity, that leads to a not-too-dense material, hence poorly opaque immediately after grafting. Moreover, given the most important claim of complete remodeling, the mineral crystal matrix comes from bovine bones (*i.e.* most similar to human one) but not high temperature treated because it must not be changed into a stable mineral structure that the body cannot remodel! This essential feature means that the material is initially poorly opaque. Microgranules size is important too: the overall performances of granules are ensured exactly thanks to their structure: they are tough and can hence not be compressed too much, again resulting in poor opacity but in a very supportive micro-environment for regeneration!

3.4 CONCLUSION

Osteoinduction is the process by which osteogenesis is induced. It is a phenomenon regularly seen in any type of bone healing process. Osteoinduction implies the recruitment of immature cells and the stimulation of these cells to develop into pre-osteoblasts. Osteoinduction is a part of the so-called remodeling process over a bone graft, *i.e.* the replacement of graft by new bone tissue. This is supported by health bone physiologic processes which occur in the adult skeleton to maintain bone mass.

Overall, all levels of investigations on SmartBone® have recorded the occurrence of this sequence of phenomena. Indeed, from a clinical point of view SmartBone® integration can be briefly described as follows: the graft very easily soaks up large amounts of blood, thus starting micro coagulation to occur inside the graft itself and hence strongly enhancing graft integration (as far as the local micro coagulation sparkles a chemical cascade that is essential for patient native cells ingrowth into the graft); the first weeks are then needed for cellular colonization of the graft, which is also enhanced by the presence of gelatine (offering RGD-end as site-specific terminals for adhesion via linking with integrins from cells, as widely known from literature back from the '90s [Yamamoto, 1995; Ruoslahti, 1996; Duong, 1998; Rodan, 1998] that offers a viable environment for cells to spread onto; meanwhile, this time lag is also necessary for the degradation of the thin polymeric film, which progressively fades away leaving mineral structure for cells to consolidate and promoting the formation of new living bone (also by means of formation of new vessel); following months are needed for the integration of the graft with the native patient bone, due also to vascularization and new bone formation inside the graft.

Studies have also proven that SmartBone® sustains the anatomically selective remodeling: even if SmartBone® is an homogeneous dense spongy bone graft, it undergoes progressive remodeling supporting the formation of either cancellous or cortical new bone according to the site specific anatomical selective recruitment [Ghiretti et al. 2020; Grottoli et al. 2019].

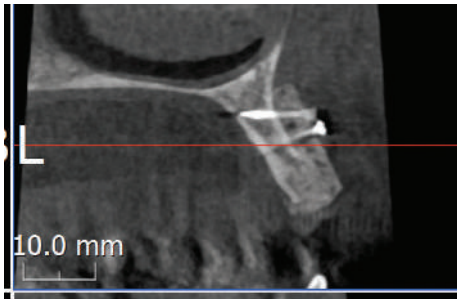


Figure 6: CBTC section immediately after op.

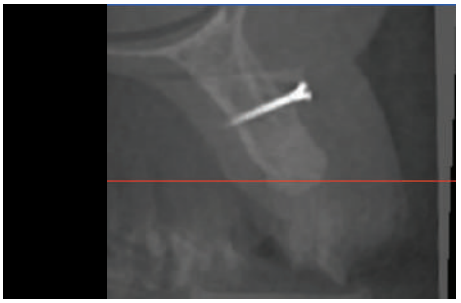


Figure 7: CBTC section immediately after 6 months.

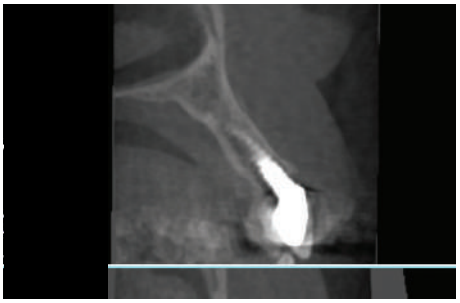
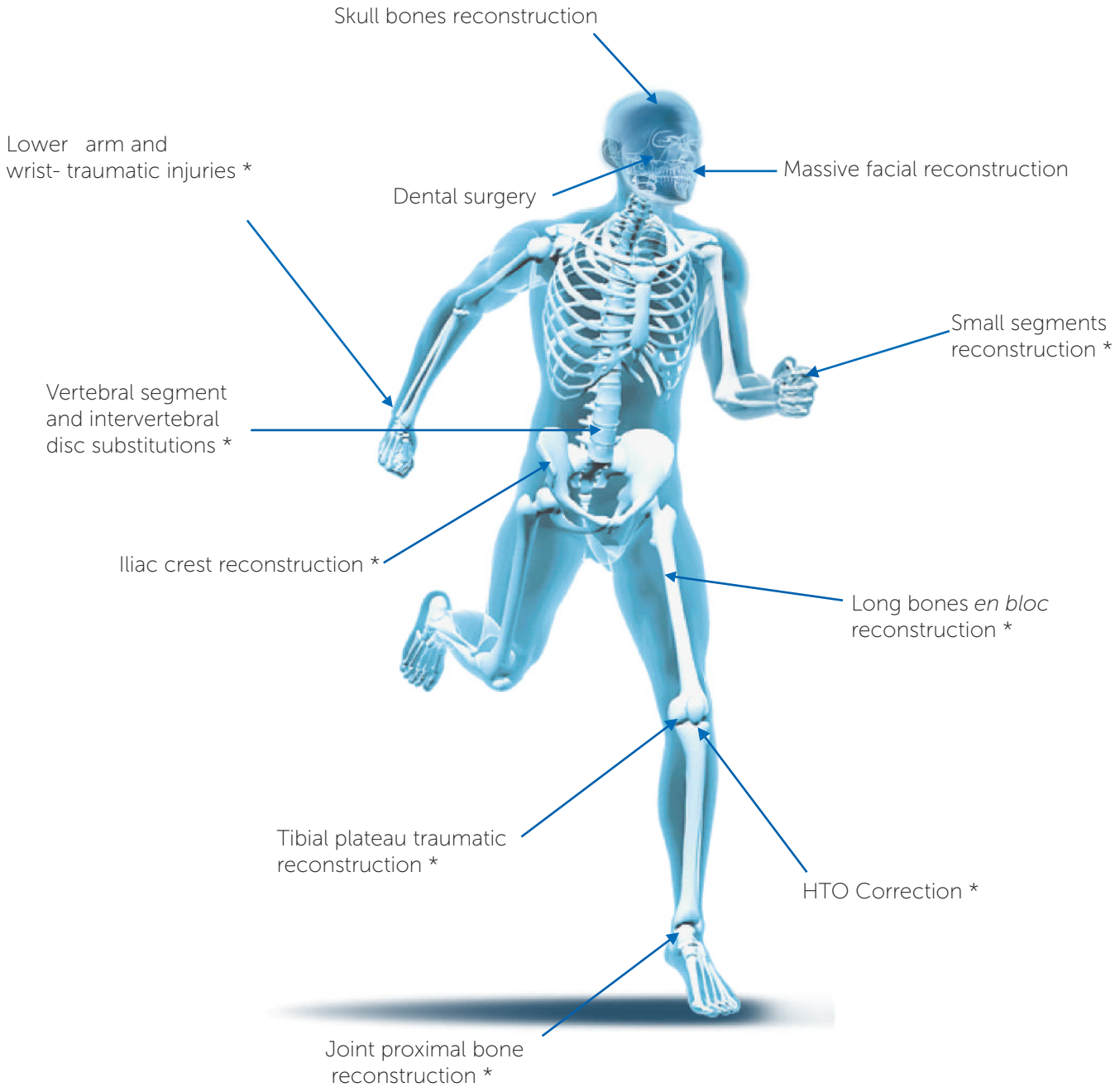


Figure 8: CBTC section immediately after 20 months.

Courtesy of Dr. R. Ghiretti

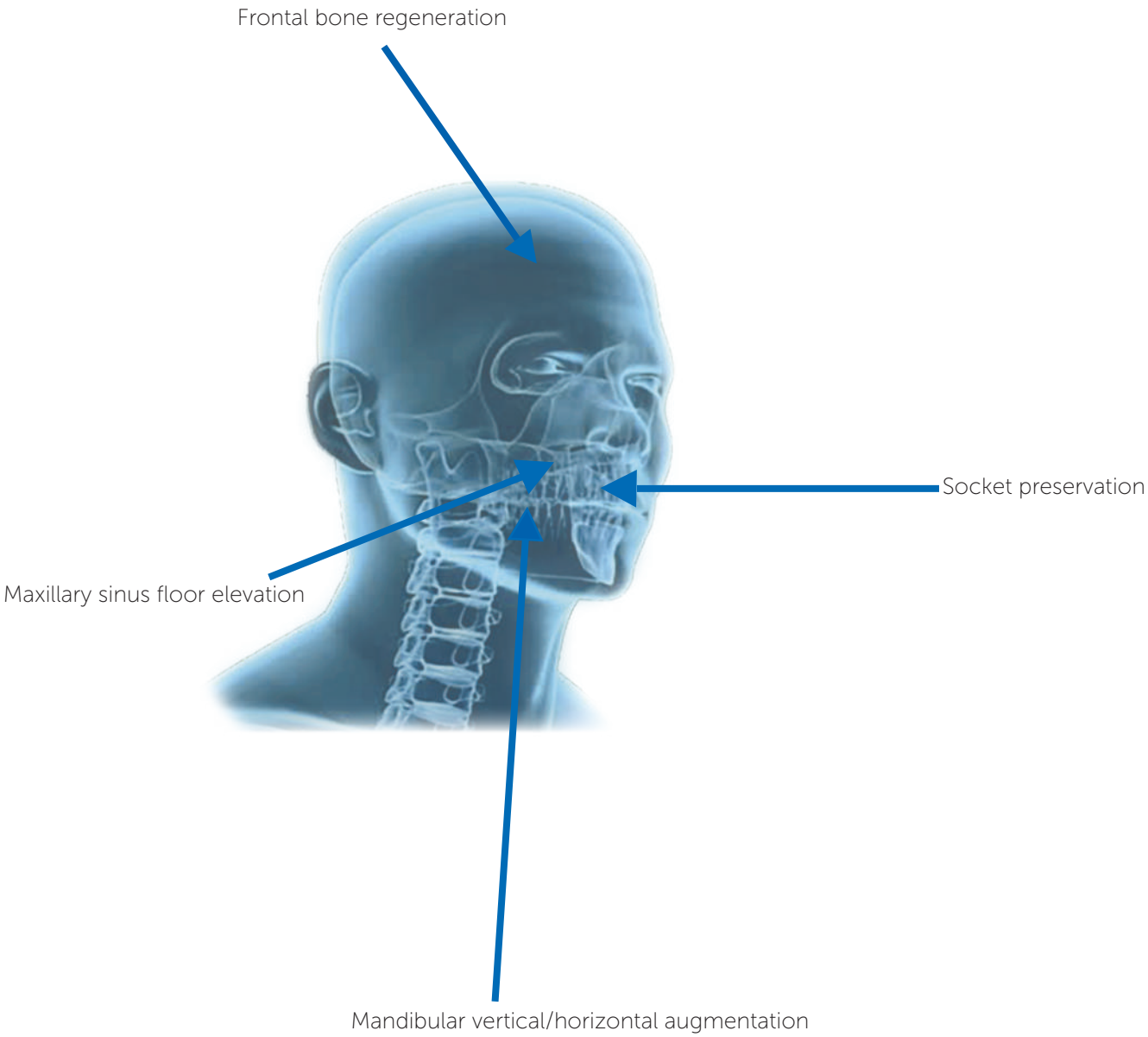


* Indications out of scope of present document.

4

Clinical indications

4.1 WHERE SMARTBONE® CAN BE USED



SmartBone® is a bone substitute, intended to be used for reconstruction surgeries and for bone regeneration/augmentation: it is intended for filling bone defect and for bone augmentation. SmartBone® is intended for professional use only. It should be used by trained surgeon, *e.g*. orthopaedic surgeons, neurosurgeons, plastic surgeons, oral and maxillofacial surgeons and trained dentists.

The patient population consist of adults (age 18+, skeletally mature subjects) with bone defects.

General principles of surgical use must be observed, while using SmartBone®. The product is to be used in a sterile environment (surgical theatre). The general principles of sterile handling, using sterile surgical instruments and patient medication must be followed when using SmartBone®.

The duration of use SmartBone® is of long term: SmartBone® integration into the natural bone and, hence, its resorption is driven by its being progressively substituted with healthy living bone from host (remodelling process of resorbable bone graft). The device is a sterile and single use.

In oral surgery SmartBone® is used in:

- Regeneration of periodontal bone defects;
- Regeneration of extraction alveoli;
- Regeneration of cavities between the alveolar wall and immediate implants;
- Vertical and Horizontal alveolar ridge augmentation;
- Sinus lift floor elevation;
- Alveolar ridge augmentation at implant sites with sufficient residual bone and a good blood supply.

4.2 CONTRAINDICATONS

- Do not use SmartBone® where there are infected wounds.
- Do not use SmartBone® in patients with known allergies to collagen and its derivatives.

As a matter of experience from clinical practice and similarly to any bone grafting procedures, surgeons should be restrained in using SmartBone® in the following cases, due to higher risks for complications and side-effects:

- acute bacterial inflammation, either systemic of the bone and the surrounding tissues (*e.g.* in case of acute or chronic osteomyelitis) and in the surgical area or in the immediate area surrounding it;
- severe, non-regulated metabolic diseases (such as *e.g.* severe diabetes mellitus, osteomalacia, or hyperparathyroidism, *etc.*);
- highly dosed long-term cortisone therapy;
- on-going treatment with gluco- and mineral-corticoids and with agents affecting calcium metabolism (*e.g.* calcitonin).
- immunosuppressed patients with severe organ dysfunction (*e.g.* of the liver or kidneys).

Certain medication can also influence bone healing and regeneration processes, *e.g.* bisphosphonates.

4.3 PATIENT POPULATION

Adult male and female patients that have reached skeletal maturity with edentulous areas or bone defects. Do not treat patients who have not reached skeletal maturity with SmartBone®. Do not treat pregnant or lactating women with SmartBone®.

Patient medical history should be properly investigated prior to SmartBone® grafting.

Patient should be excluded if they present with a medical condition that would contraindicate dental surgery or interfere with the wound healing process:

- Acute sinusitis;
- Sinus infection;
- Uncontrolled diabetes;
- Uncontrolled hypertension;
- Active chemotherapy.

Increased failure rates should be expected in patients exhibiting risk factors such as systemic disease causing wound healing problems, heavy smoking, increased periodontal susceptibility, poor bone density and extreme atrophy [Bornstein, 2008] and Vitamin D deficiency or high LDL or low HDL cholesterol levels [Choukroun, 2014].

4.4 SHAPES AND SIZES

SmartBone® is available in a wide variety of shapes and dimensions, to best and most easily meet surgeons common needs. Shapes are available in different sizes which were specifically designed to allow simpler, easier and faster surgical procedures and, hence, guaranteeing better results and a higher safety for patients!

smartbone® Microchips

SMG251025	0.25 - 1 mm	0.25 g
SMG251005	0.25 - 1 mm	0.5 g
SMG251010	0.25 - 1 mm	1 g
SMG251020	0.25 - 1 mm	2 g
SMG102005	1 - 2 mm	0.5 g
SMG102010	1 - 2 mm	1 g
SMG102020	1 - 2 mm	2 g

smartbone® Block

SMB011005	7 x 7 x 7 mm
SMB011010	10 x 10 x 10 mm
SMB011020	10 x 10 x 20 mm
SMB011030	10 x 20 x 20 mm
SMB011110	14 x 12 x 6 mm
SMB011130	14 x 12 x 8 mm
SMB011160	14 x 12 x 12 mm
SMB011190	14 x 12 x 24 mm
SMB011310	16 x 14 x 6 mm
SMB011330	16 x 14 x 8 mm

smartbone® Plate

SMP013010	3 x 25 x 15 mm
SMP013040	4 x 10 x 10 mm

5

Dental use of smartbone®

5.1 SINUS ELEVATION

The implant success is strictly related to the quantity and quality of bone where the implant is to be placed.

This problem is especially magnified in the posterior maxilla where ridge resorption and sinus pneumatization, compounded with a poor quality of bone, are often encountered [Helmy, 2017]. Bone atrophy in the maxilla is a physiological process which accelerates in case of tooth extractions.

The procedure of choice to restore this anatomic deficiency is maxillary sinus floor elevation (sinus lift). In 1980, Dr. Philip Boyne was the first to describe the technique in lifting the maxillary sinus membrane to increase bone volume in order to place dental implants where there is insufficient residual bone crest.

The basic concept of this technique is to graft bone tissue in the sinus cavity without altering the physiology of the nasal cavity [Toffler, 2012].

Millions operations to lift the maxillary sinus for implants placement have been performed throughout the world and the sinus grafting has become a predictable method to increase the vertical bone height.

Several techniques and approaches can be used to raise the sinus pavement and allow for new bone to form.

There are two main techniques, the classic lateral antrostomy (lateral window osteotomy, LWO) and the more conservative crestal approach (osteotome-mediated sinus floor elevation, OMSFE).

Lateral approach allows for a greater amount of bone augmentation to the atrophic maxilla but requires a larger surgical access. The crestal approach is minimally invasive but permits only a limited augmentation [Helmy, 2017].

Many clinical considerations must be taken into account in order to perform a sinus elevation, see Table 2. Advanced imaging technologies greatly enhance planning and execution of bone augmentation procedures. Cone Beam Computerized Tomography (CBCT) technology provides an increased accuracy, less morbidity for the patient and decreased surgical and restorative chair time by improving results.

Sinus Floor Elevation (SFE) technique	Sinus Floor Elevation (SFE) technique 2	Sinus Floor Elevation (SFE) technique 3	Sinus Floor Elevation (SFE) technique 4	Sinus Floor Elevation (SFE) technique 5	Sinus Floor Elevation (SFE) technique 6
1. Staged lateral window osteotomy (LWO)	single or multiple molar/premolar	4 mm or less	≥ 7 mm	moderate to severe	N/A
2. LWO simultaneous implant placement	single molar	5-6 mm	≥ 6 mm	moderate to severe	≥ 7 mm
3. Crestal core elevation (CCE)	Multiple molar/ premolar	3-6 mm	4-6 mm	mild to severe	≥ 8 mm
4. Osteotome-mediated sinus floor elevation (OMSFE) with simultaneous implant placement	single molar/ premolar	5-6 mm	5-6 mm	mild to moderate	≥ 8 mm
	single molar/ premolar	≥ 6 mm	2-5 mm	mild to severe	≥ 5 mm
	single molar/ premolar	5 mm	3-4 mm	minimal	≥ 6.5 mm (implant body ≥ 4.5 mm)
	multiple tooth sites	4-5 mm	2-5 mm	minimal to moderate	≥ 6 mm

Table 2: Sinus lift clinical indication; adapted from [Toffler, 2012].

5.1.1 SINUS ELEVATION CLINICAL APPROACHES

A. SINUS ELEVATION WITH LATERAL APPROACH

This technique comprises the creation of an access to the maxillary sinus via a window through the lateral bone window. A mucoperiosteal trapezoidal flap is raised after a midcrestal horizontal incision.

The mucoperiosteal flap is elevated so as to expose the lateral bone aspect of the maxillary sinus.

The osteotomy in the superior part of the window is carried out with a partial thickness approach so as to make the infraction of the window easier. A minimum size is requested in order to have a comfortable access and for filling with graft material.

The extent of the bone window to the sinus is marked by drilling with a medium size round bur (or using piezo). Dissection is performed carefully in order to avoid sinus membrane perforation using a periosteal elevator placed to the posterior/superior part of the created cavity prior to its filling with grafting material [Zollino, 2015].

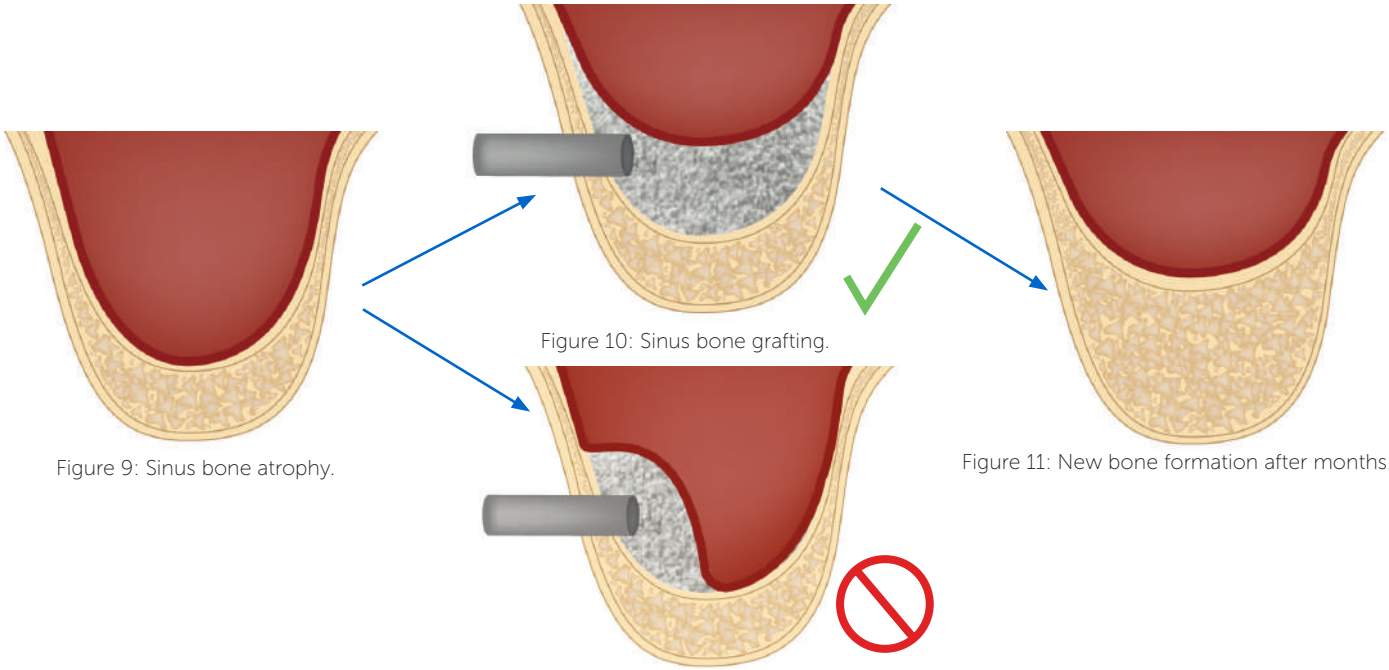


Figure 9: Sinus bone atrophy.

Figure 10: Sinus bone grafting.

Figure 11: New bone formation after months.

Figure 10a: the membrane MUST raised completely

Indian J Stomatol 2015;6(2):59-62

Positioning of a Contextual Implant Along with a Sinus Lift with Smartbone® Microchips of Composite Heterologous-Synthetic Bone

Ilaria Zollino[1], Giorgio Carusi[2,3], Francesco Carinci[1], Giuseppe Perale[3,4]

Abstract

The present case reports the success rate after 8 months of follow-up in a sinus pneumatization case with maxillary sinus floor cortical bone loss due to 2.5 dental agenesis. Rehabilitation including the opportunity to insert a contextual implant during maxillary sinus lift surgery was planned, using SmartBone® Microchips heterologous bone inserted into the maxillary sinus. The newly developed bone substitute was designed starting from bovine bone derived mineral matrix, reinforced with bioresorbable aliphatic polymers and cell nutrients. SmartBone® Microchips showed a tight contact with the new bone and neither gaps nor fibrous tissues at the interface. No inflammation or foreign body reaction were observed, and these findings support the good biocompatibility of SmartBone® Microchips composite material. Moreover, new bone, thanks to its mechanical properties, consented to fix screw in combination with maxillary sinus floor elevation for a dental implant.

Keywords: Implant; case report; sinus pneumatisation; sinus lift; SmartBone® Microchips.

Introduction

Since the first use of sinus grafting implant placement in the atrophic posterior maxilla, sinus grafting has become a predictable method to increase vertical bone height. The first graft material suggested for the reconstruction of bone defects was autografts bone. Theoretically, autografts bone possesses the pre-requisite properties for the successful incorporation of a grafting material and for bone healing, thanks to it being both osteoconductive and osteoinductive. So, it is considered the gold standard graft for bone reconstruction. The limitations of using autografts bone grafts concern the size of the donor site and risks of morbidity due to demanding surgery. Factors to be taken into account when choosing the donor site are the amount of bone required, the type (cortical vs. cancellous) of bone needed, the recipient site, and the expected biological behaviour (neovascularization and resorption). Donor sites can be extraoral or intraoral. The iliac crest, the calvaria, the ribs and the tibia are the most commonly described extraoral donor sites in the literature. Mandibular symphysis, mandibular ramus, infrazygomatical crest and maxillary tuberosity have been suggested as different intraoral donor sites.[1]

In order to simplify bone reconstruction by avoiding donor site surgery, increased surgical cost, limited amount of material, possible rapid bone resorption, and patient discomfort, the use of bone substitutes is obviously an attractive alternative. Several bone substitutes of biological and synthetic origins are available: biological ones can be allografts, i.e., from other humans or xenografts, i.e., from other species than humans (bovine derived hydroxyapatite). Fresh or untreated allograft are limited in use due to the presence of antigens, which may affect the immune response and trigger a rejection response. As with xenografts, allografts proteins are extracted for reasons of immunological safety. As a consequence, the osteoinductive properties disappear and the graft can only work as an osteoconductive scaffold.[2]

The current focus, thus, is on xenografts vs. synthetic devices: naturally derived materials provide structures extremely similar to living tissues such as stimulating a specific cellular response, which sometimes supersedes the advantages of synthetic polymers. Xenografts may also reduce the stimulation of chronic inflammation or immunological reactions and toxicity, often detected with synthetic polymers and minerals (such as e.g., bioglasses and bioceramics).[3]

On the other side, materials science, in conjunction with bio- and nano-technologies, can satisfy these requirements by developing novel grafting devices. In particular, bioresorbable scaffolds, as key artificial devices widely used in tissue engineering, aim to provide a desirable microenvironment that allows neo-tissue to be generated properly for repairing and replacing damaged tissues or organs. Indeed, synthetic polymers can be tuned in terms of composition, rate of degradation, mechanical and chemical properties.[3,4]

For all these reasons, the goal of the current approach was to combine the biocompatibility and tissue integration of natural materials with the possibility to tune mechanical and physical properties typical of synthetic ones: composite grafts best mimic the real nature of healthy human bone, being rigid and elastic, compact but porous, dense but viable to cells and vessels.

A newly developed bone substitute, named SmartBone® (briefly SB), was design following a new concept of composite approach, starting from bovine bone derived mineral matrix, reinforced with bioresorbable aliphatic polymers and RGD-containing peptide fragments as cell nutrients. In this case report the SmartBone® Microchips, 1-2 mm in diameter, were used to achieve a sinus lift surgery with the placement of a contextual implant screw.

Case report

A 43-year-old male patient (smoker) was referred to private practitioner for implant-supported prosthesis in a sinus

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B. TRANSCRESTAL SINUS ELEVATION APPROACH

Transcrestal sinus floor elevation (tSFE), which was first proposed by Tatum (1986), has been introduced as a more conservative and minimally invasive alternative to the lateral approach.

In this procedure, an osteotomy is performed through the residual crest and the sinus floor using various devices, such as osteotomes, specially designed burs, ultrasonic instruments, or combinations of the above.

After obtaining the fracture of the sinus floor, Schneiderian membrane is indirectly elevated by progressive increments of biomaterial, or by hydrodynamic pressure or by the implant itself, according to the different techniques [Stacchi, 2018].

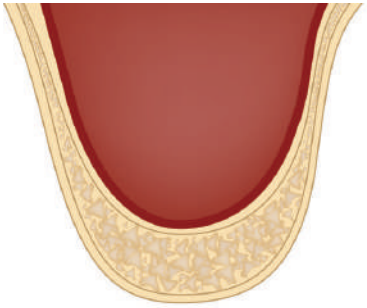

Figure 12: Sinus bone atrophy.

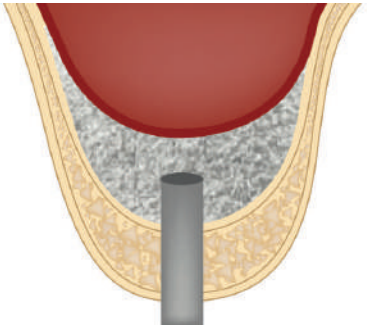

Figure 13: Sinus bone grafting.

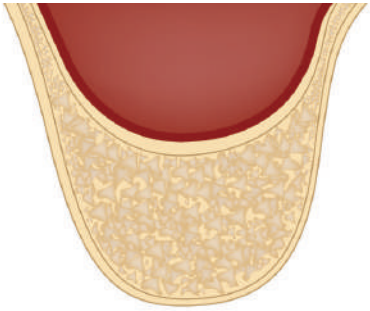

Figure 14: New bone formation after months.

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ORIGINAL RESEARCH

WILEY CLINICAL ORAL IMPLANTS RESEARCH

New bone formation after transcrestal sinus floor elevation was influenced by sinus cavity dimensions: A prospective histologic and histomorphometric study

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Abstract

Objective: The aim of this multicenter prospective study was to analyze clinically and histologically the influence of sinus cavity dimensions on new bone formation after transcrestal sinus floor elevation (tSFE).

Material and Methods: Patients needing maxillary sinus augmentation (residual crest height <5 mm) were treated with tSFE using xenogeneic granules. Six months later, bone-core biopsies were retrieved for histological analysis in implant insertion sites. Bucco-palatal sinus width (SW) and contact between graft and bone walls (WGC) were evaluated on cone beam computed tomography, and correlations between histomorphometric and anatomical parameters were quantified by means of forward multiple linear regression analysis.

Results: Fifty consecutive patients were enrolled and underwent tSFE procedures, and forty-four were included in the final analysis. Mean percentage of newly formed bone (NFB) at 6 months was 21.2 ± 16.9%. Multivariate analysis showed a strong negative correlation between SW and NFB (r^2 = .793) and a strong positive correlation between WGC and NFB (r^2 = .781). Furthermore, when SW was stratified into three groups (<12 mm, 12 to 15 mm, and >15 mm), NFB percentages (36%, 13% and 3%, respectively) resulted significantly different.

Conclusions: This study represented the first confirmation based on histomorphometric data that NFB after tSFE was strongly influenced by sinus width and occurred consistently only in narrow sinus cavities (SW <12 mm, measured between buccal and palatal walls at 10-mm level, comprising the residual alveolar crest).

KEYWORDS
histomorphometry, osteotomes, sinus floor elevation, sinus width, transcrestal

5.1.2 SINUS ELEVATION CLINICAL PROCEDURE

- Evaluate the oral epithelium of the gum, which must be well keratinized.
- It is suggested making an incision a few millimeters above the muco-gingival junction from the canine eminence anteriorly to the zygomatic buttress posteriorly. Elevate the mucoperiosteal flap from the incision buccally/superiorly and create a oval window in the canine fossa with the help of 4 mm, 6 mm chisels and mallet. Remove muscle fibers, using a dissector, and incise a muco-periodontal flap (Figure 15).
- Proceed with a blunt dissection of the muco-periodontal flap and elevate it in distal direction to access the bone Figure 16).
- Use a drill to incise a bone window; be careful not to perforate the Schneider membrane (if necessary, fix the perforation with a resorbable membrane). If this should happen, cover with a collage membrane if the perforation is small. Instead if the damage on the Schneider membrane is large you have to stop the surgery, close the flap and wait 9 months for a new surgery.
- Proceed with a blunt dissection of the membrane in both distal and apical directions
- Using SmartBone® Microchips, fill the newly-formed bone cavity between the floor of the maxillary sinus and the Schneider membrane (Figure 17).
- It's always a good practice to hydrate SmartBone® Microchips exclusively with patient's blood.

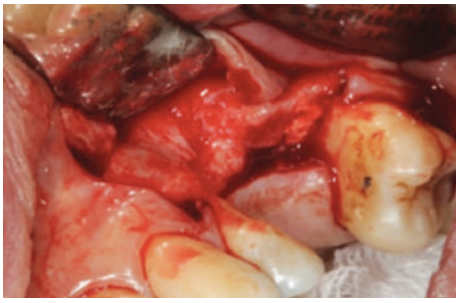

Figure 15: Skeletization of the bone defect.

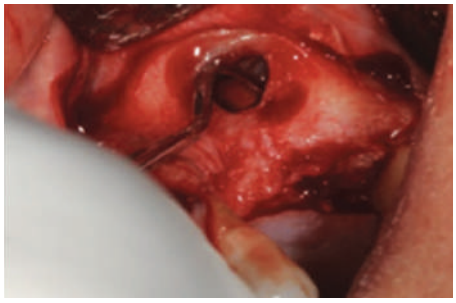

Figure 16: Blunt dissection of the muco-periodontal flap

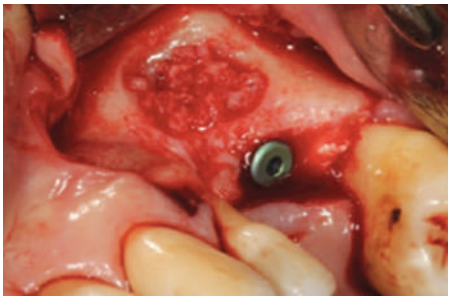

Figure 17: Bone cavity filled with SmartBone® Microchips.

These instructions are for educational purposes only. Surgical techniques may vary depending on the clinical operator.

Courtesy of Prof. Dr. G. Carusi

- Cover the surgical area with a resorbable membrane to stabilize the platelet, bovine pericardium membrane is suggested (Figure 18).
- Suture the flaps (Figure 19).
- Once SmartBone® is placed, close the tissue with stitches. Implants can be placed 6-8 months later in order to ensure a good regenerated bone. Before placing the implant, it is always a good practice to proceed with specific clinical evaluation using radiography/Computerized Tomography (CT) scan.

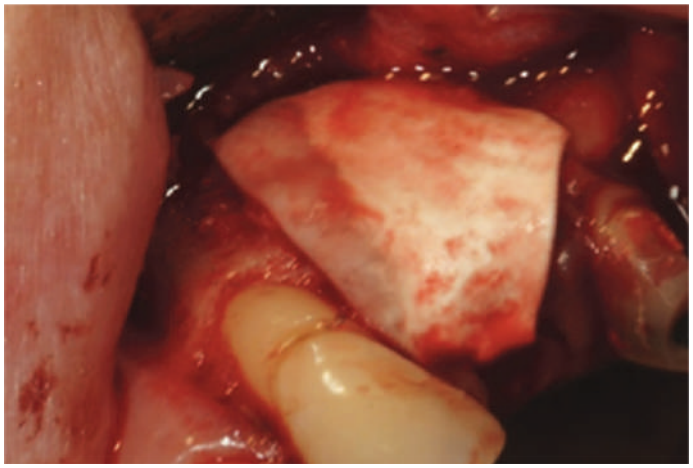

Figure 18: Surgical area cover by resorbable membrane.

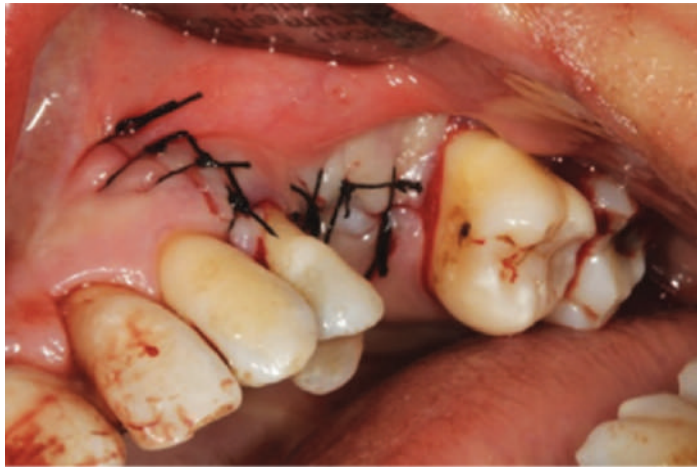

Figure 19: Sutures.

These instructions are for educational purposes only. Surgical techniques may vary depending on the clinical operator.

Courtesy of Prof. Dr. G. Carusi

5.1.3 CLINICAL CASES

CASE 1 - SINUS LIFT

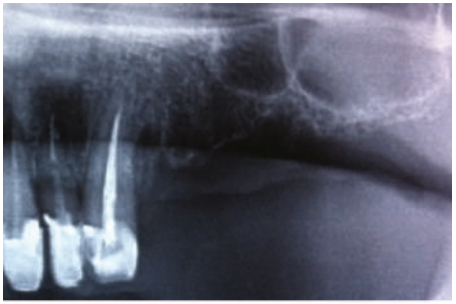

Figure 20: X Rays of the initial condition.

Physician:
Prof. Dr. D. Epistatus and
Prof. Dr. G. Carusi

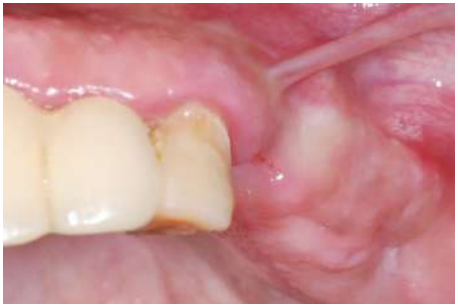

Figure 21: Soft tissue initial condition.

Patient:	Male, 36 years old, good initial health condition.
Surgical anatomic site:	24-25-26.
Pre-surgical clinical situation:	sinus pneumatization with loss of jaw cortical pavement bone due to edentulism.
Surgical procedure:	sinus lift and vertical bone augmentation using SmartBone® Microchips (1 - 2 mm).

SURGERY

SmartBone® Microchips application both for sinus lift and vertical bone augmentation

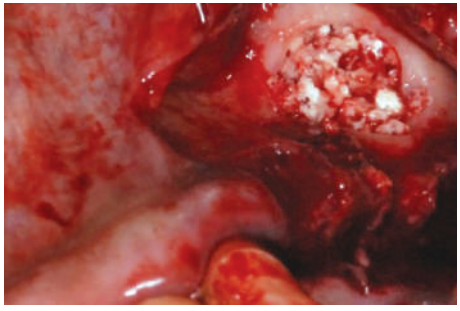

Figure 22: SmartBone® Microchips bone grafting.

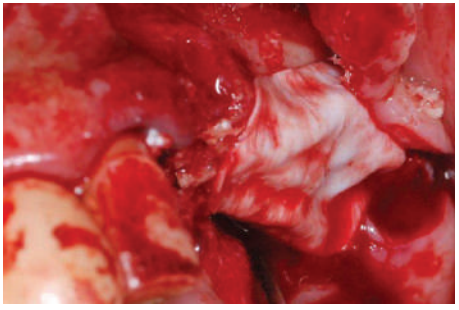

Figure 23: Surgical site.

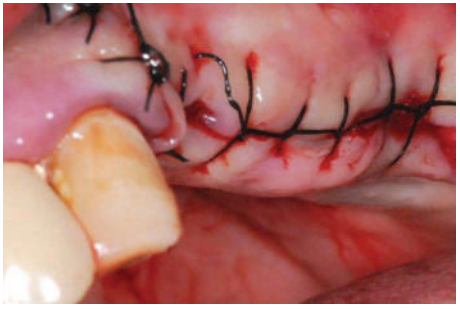

Figure 24: Suture.

Courtesy of Prof. Dr. D. Epistatus and Prof. Dr. G. Carusi

FOLLOW-UP FROM 2 TO 4 MONTHS

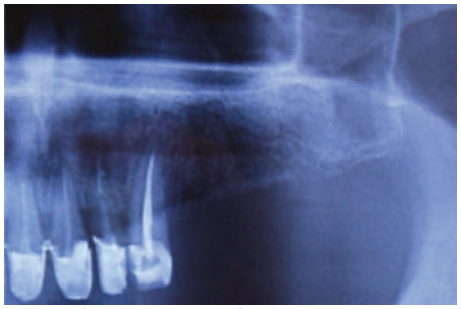

Figure 25: Follow-up 2 months: everything proceeds properly.

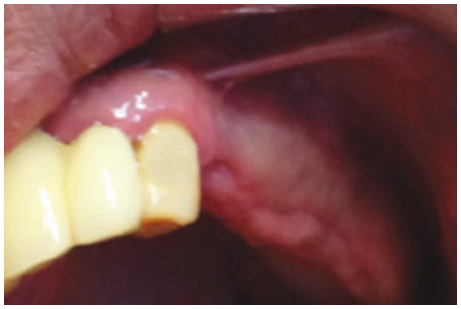

Figure 26: Follow-up 2 months: everything proceeds properly.

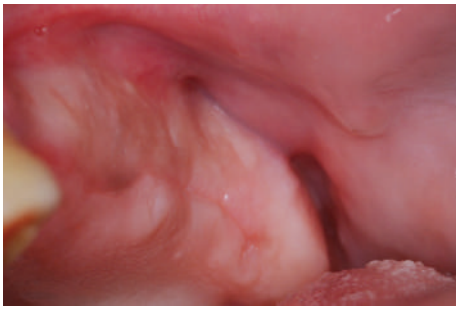

Figure 27: Follow-up 4 months: good bone regeneration for the placement of three implants.

ANALYSIS 4 MONTHS

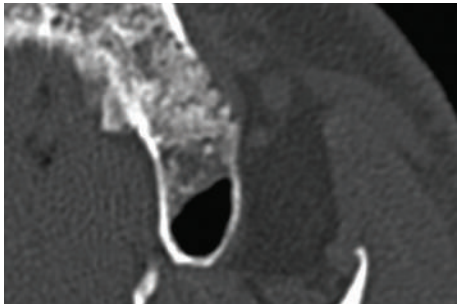

Figure 28: Bone density; axial view: average bone density 500 HU, adequate for the placement of three implants.

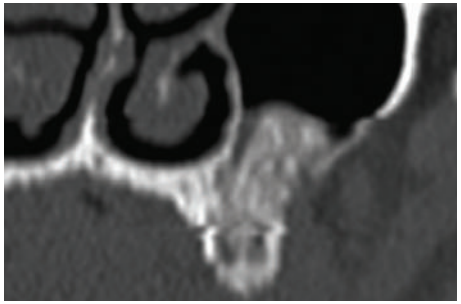

Figure 29: Bone density; coronal view: average bone density 500 HU, adequate for the placement of three implants.

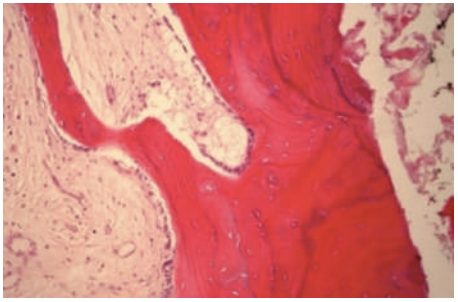

Figure 30: Histological analysis.

FOLLOW-UP FROM 1 YEAR TO 3 YEARS

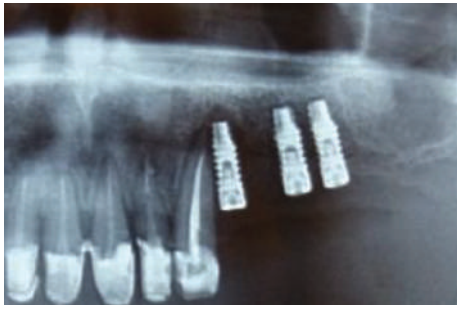

Figure 31: Follow-up 1 year.

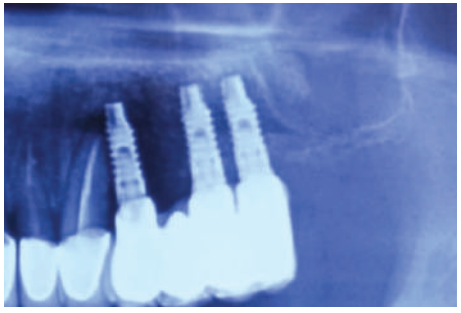

Figure 32: Follow-up 2 years.

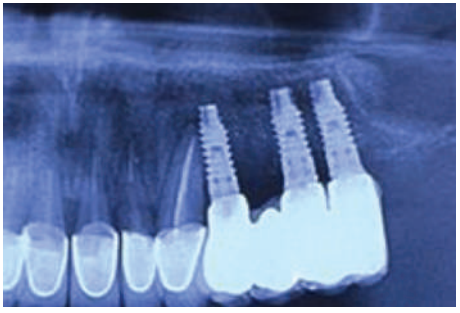

Figure 33: Follow-up 3 years.

Courtesy of Prof. Dr. D. Epistatus and Prof. Dr. G. Carusi

CASE 2 - SINUS LIFT

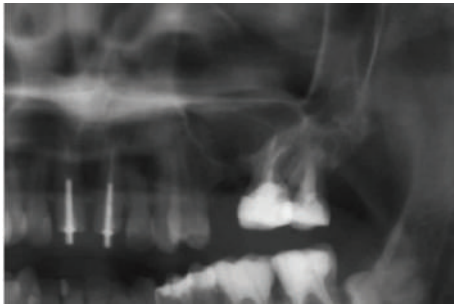

Figure 34: Initial condition: loss of jaw cortical pavement bone due to edentulism.

Physician:
Dr. R. Pezzoli

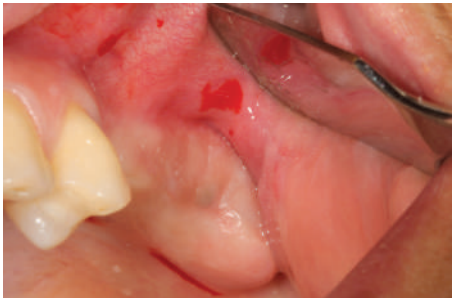

Figure 35: Soft tissue of the initial condition.

Patient:

Female, 46 years old, good initial health condition.

Surgical anatomic site:

25.

Pre-surgical clinical situation:

sinus pneumatization with loss of jaw cortical pavement bone due to edentulisminus lift with SmartBone® Microchips (0,25 - 1 mm).

SURGERY

SmartBone® Microchips in the sinus cavity

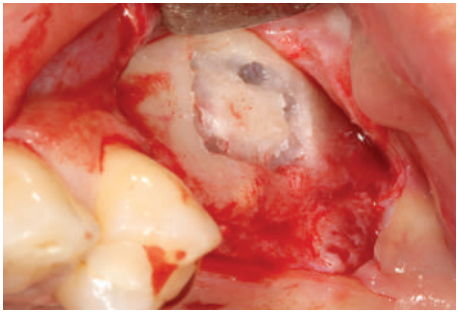

Figure 36: Lateral window.

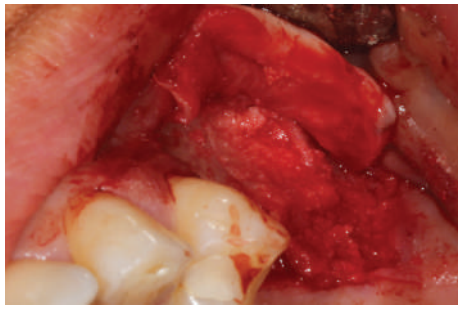

Figure 37: Bone grafting using SmartBone® Microchips.

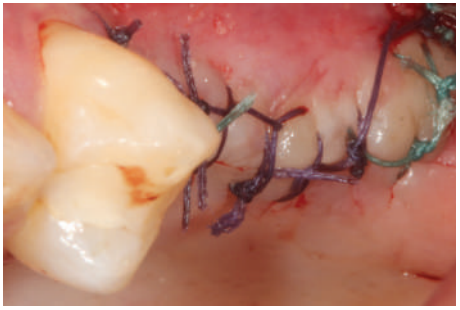

Figure 38: Suture.

Courtesy of Dr. R. Pezzoli

CHECK-UP AFTER SURGERY

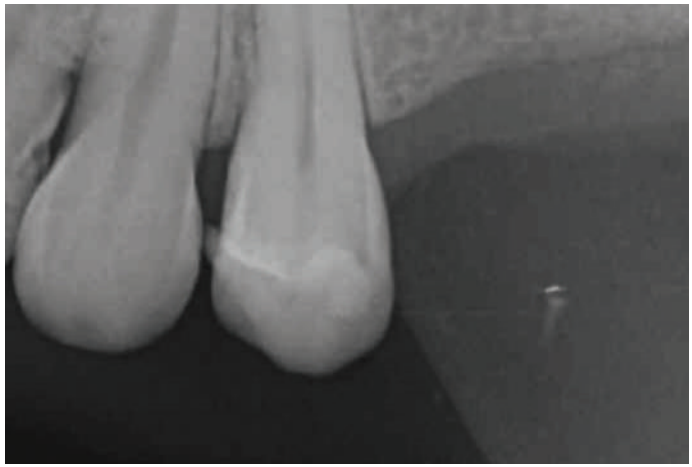

Figure 39: Check-up 3 days after surgery: everything is proceeding well.

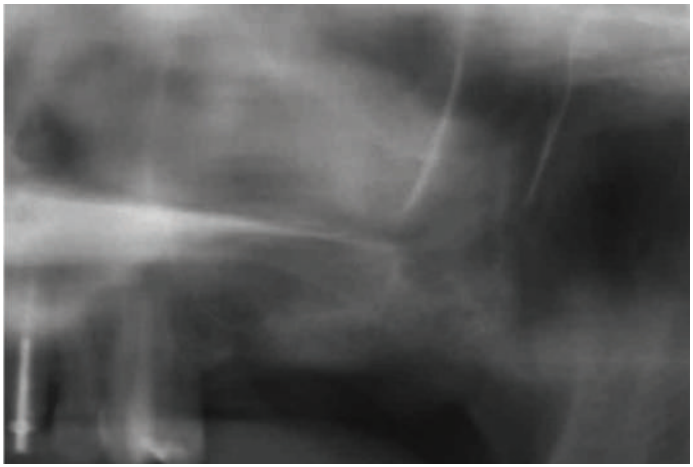

Figure 40: Check-up 15 days after surgery: everything is proceeding well.

FOLLOW-UP FROM 4 MONTHS TO 1 YEAR

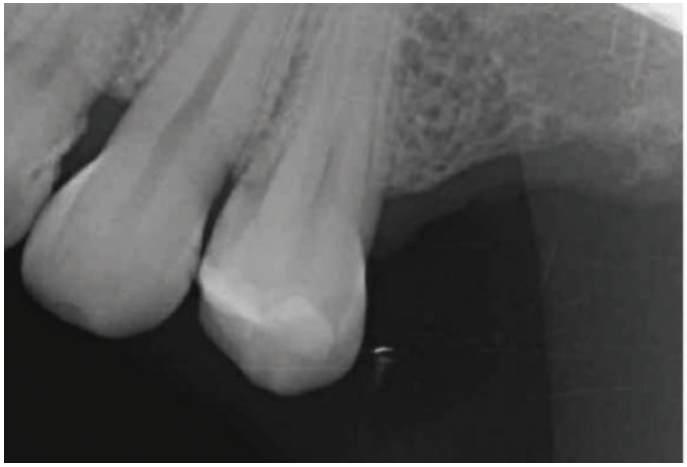

Figure 41: Follow-up 4 months: good integration of SmartBone® suitable for the placement of two implants.

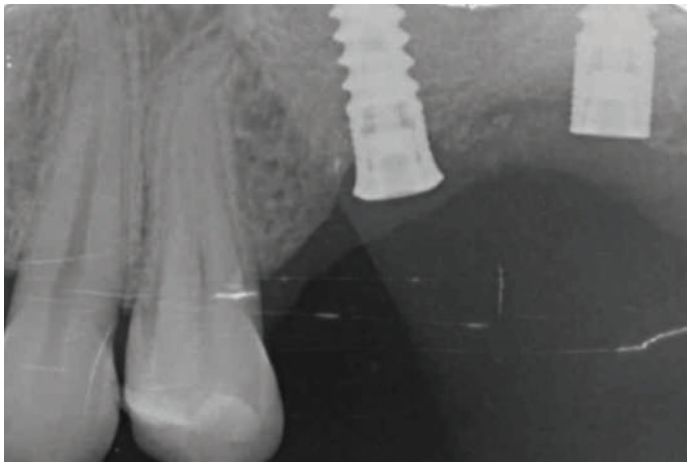

Figure 42: Follow-up 1 year: good bone formation and volume maintenance.

Courtesy of Dr. R. Pezzoli

CASE 3 - SINUS LIFT

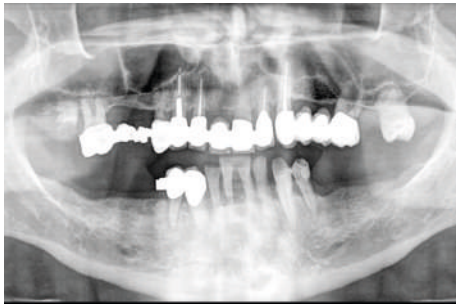

Figure 43: X-Rays panoramic view of the initial condition.

Physician:
Dr. B. Fraschini

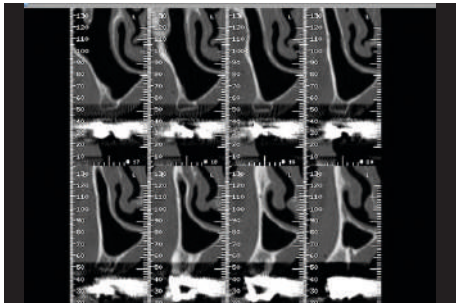

Figure 44: CBCT cross sections of the initial situation, sinus bone atrophy.

Patient:	Male,62 years old, good initial health situation, no smoker.
Surgical anatomic site:	14-15-16
Pre-surgical clinical situation:	sinus pneumatization with loss of jaw cortical pavement bone due to edentulism.
Surgical procedure:	sinus lift using SmartBone® Block with Microchips (0,25 - 1 mm) and implant placement.

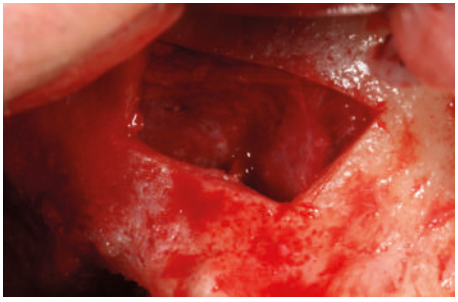

Figure 45: Vestibular window for the sinus elevation procedure.

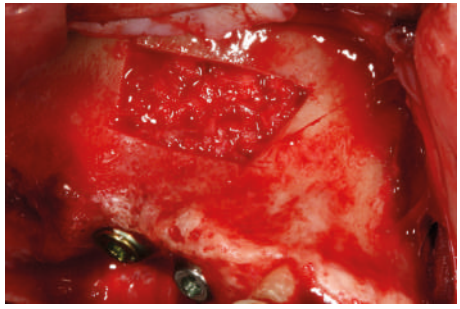

Figure 46: The defect is filled with 0,25-1 mm microchips and it has been place 2 implants.

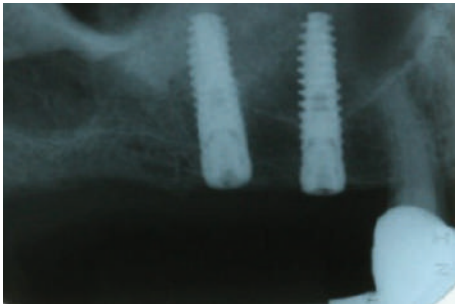

Figure 47: Final result after some months.

Courtesy of Dr. B. Fraschini

CASE 4 - SINUS LIFT

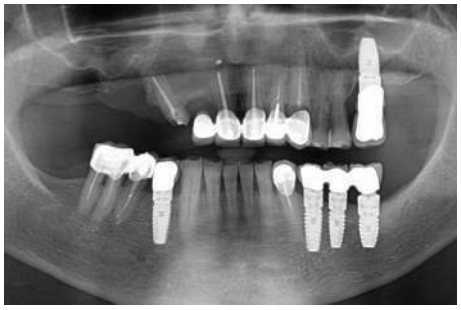

Figure 48: X-Rays of the initial condition.

Physician:
Dr. F. Secondo

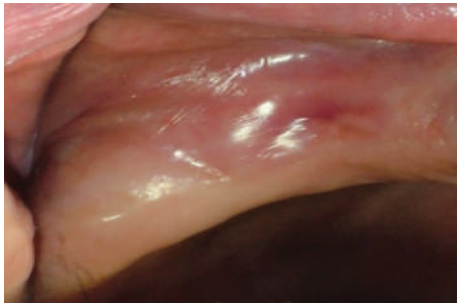

Figure 49: Soft tissue initial condition.

Patient:	Female, 73 years old, good initial health condition.
Surgical anatomic site:	14-15-16.
Pre-surgical clinical situation:	sinus pneumatization with loss of jaw cortical pavement bone due to edentulism.
Surgical procedure:	sinus lift using SmartBone® Block with Microchips (0,25 - 1 mm) and implant placement.

SURGERY

SmartBone® Block is placed to fix the implant in the sinus cavity

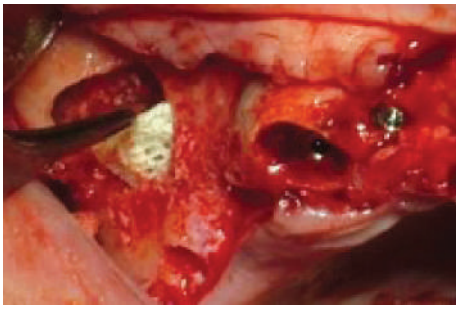

Figure 50: SmartBone® Block placement.

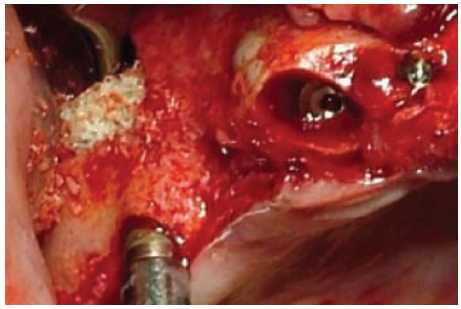

Figure 51: Implant fixation through the block in the sinus cavity.

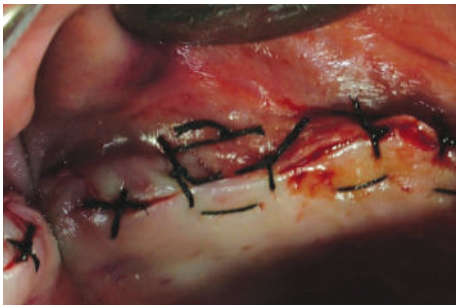

Figure 52: Suture.

Courtesy of Dr. F. Secondo

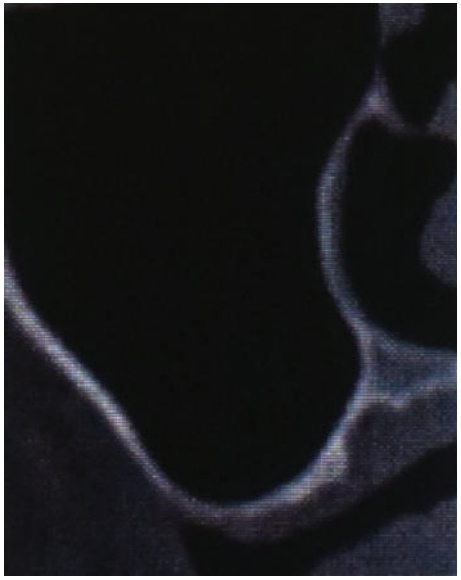

Figure 53: Drawing of the sinus cavity.

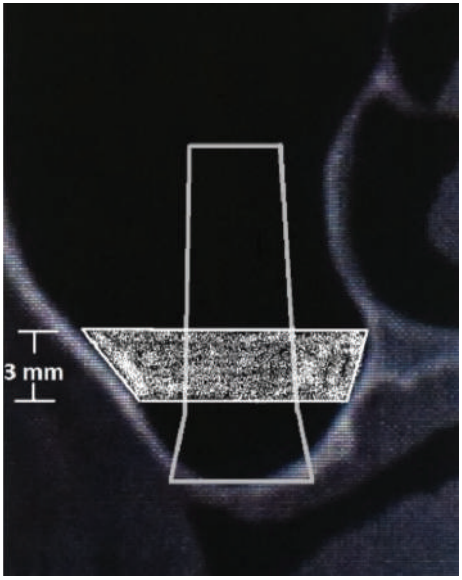

Figure 54: Drawing of the implant positioning through the 3 mm Block thickness.

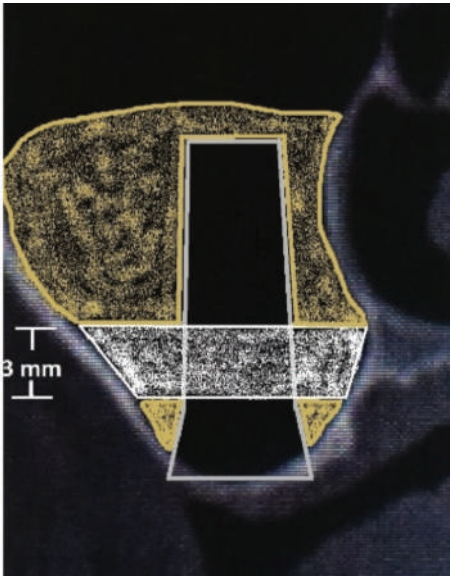

Figure 55: Drawing of the final sinus restoration.

The SmartBone® Block is shaped accordingly with the stereolithographic model in a sterile environment.

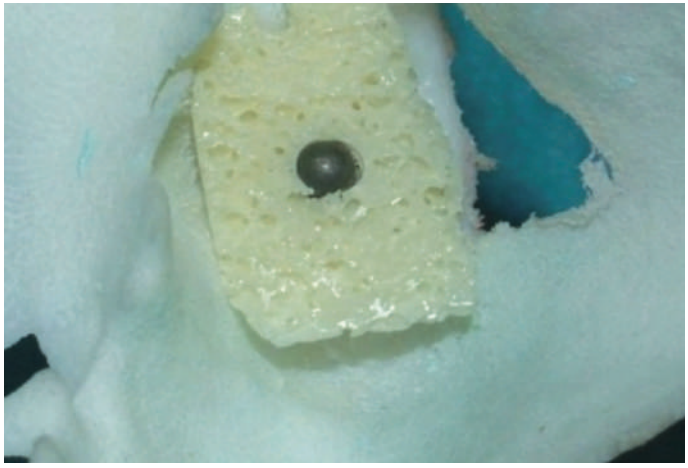

Figure 56: SmartBone® Block placed upon the stereolithographic model.

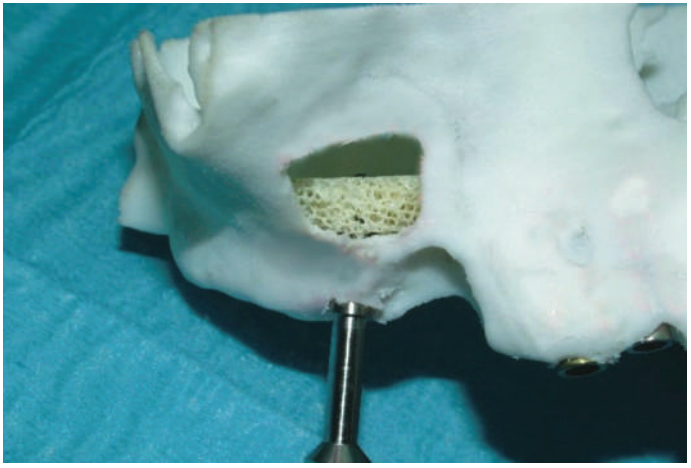

Figure 57: Simulation of the implant placement through the Block to the stereolithographic model.

Courtesy of Dr. F. Secondo

CHECK-UP AFTER SURGERY AND FOLLOW-UP FROM 6 MONTHS TO 10 MONTHS

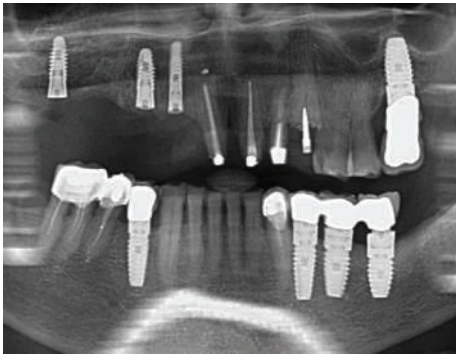

Figure 58: Check-up after surgery: the surgery was well performed.

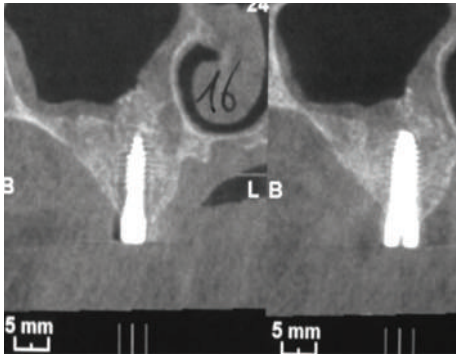

Figure 59: Follow-up 6 months: the new bone has a very good quality also around the implant and the entire bone volume was maintained.

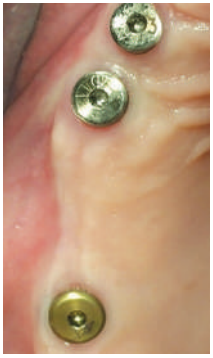

Figure 60a: 9 months.

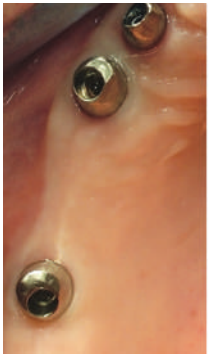

Figure 60b: 9 months.

Aesthetically good gum contour and good bone augmentation suitable for the loading with the final prosthesis.

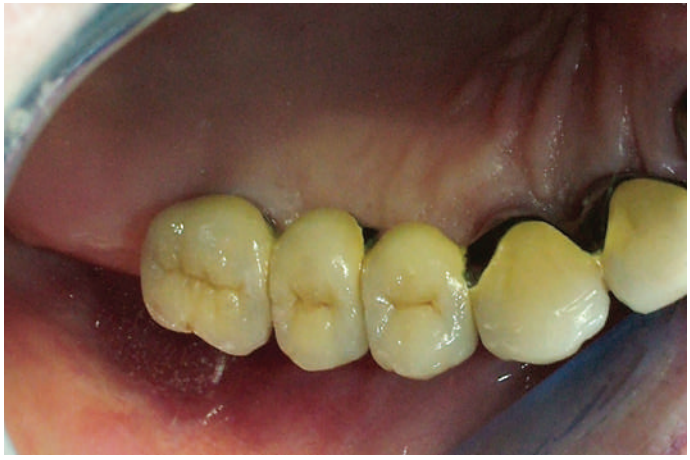

Figure 61: 10 months.

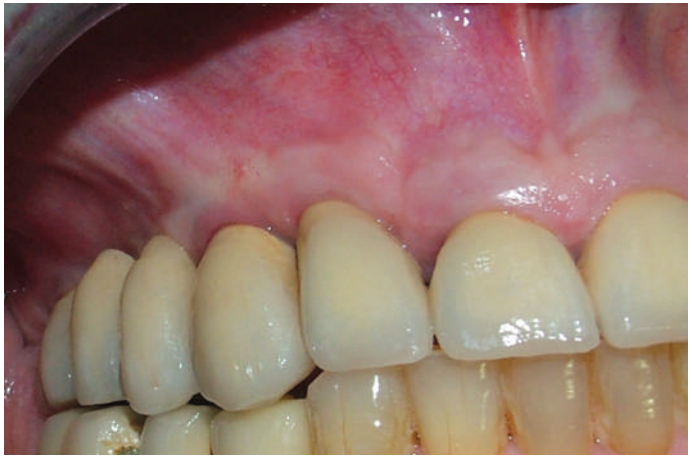

Figure 62: 10 months.

Courtesy of Dr. F. Secondo

POSITIONING OF A CONTEXTUAL IMPLANT ALONG WITH A SINUS LIFT ANCHORED WITH A BLOCK OF HETEROLOGOUS BONE

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[2] *Industrie Biomediche Insubri SA, Mezzovico-Vira, Switzerland*
[3] *Department of Morphology, Surgery and Experimental Medicine, University of Ferrara, Ferrara, Italy*
[4] *Department of Innovative Technologies, University for Applied Science and Art of Southern Switzerland, Manno, Switzerland*
[5] *Department of Medicine and Surgery, University of Milano "Bicocca", Monza, Italy*

SUMMARY

During a sinus lift procedure the main requirement in order to position an implant is to have a maxillary sinus floor cortical bone thick enough to guarantee a primary stability in the implant inserted. In this way, the healing process is facilitated and osseointegration of the titanium surface may occur simultaneously, thus reducing the waiting time for the engraftment of the implant into the body. Unfortunately, these conditions are not always present. Hence, the need of developing an alternative approach that could simultaneously allow to perform sinus floor elevation along with an implant placement.

Here we present the case of a 62-year-old patient that requires implant-prosthetic rehabilitation from 1.2 to 1.6 at diagnosis. In this study, we reported a novel application derived from the use of a heterologous bone scaffold (SmartBone@) in a sinus lift procedure. We showed the successful implant along with sinus lift with SmartBone@, both at the time of the surgery and after follow-up of the patient at 10 months from the implant. The possibility to perform simultaneously the contextual implant along with sinus lift dramatically reduced the waiting time for the patient of minimum 5-6 months required for osseointegration of the grafted biomaterials, before performing the implant procedure. This surgery represents an advance both in terms of medical technique and as life-benefit for the patient.

Key words: implants, case report, sinus pneumatization, sinus lift, heterologous bone, SmartBone®.

5.2 HORIZONTAL/VERTICAL AUGMENTATION

Resorption of alveolar bone is a common clinical problem which can be a physiologic or a pathologic process (Figure 59).

The deformities and defects may occur as a result of tooth loss due to extraction, advanced periodontal diseases or trauma, long term use of removable appliances, dehiscence and fenestration defects, developmental defects/clefts, congenitally missing teeth and odontogenic cysts and tumors.

When minimum dimensions for implant placement are not present in alveolar process, it is necessary to augment the size of the ridge.

This can be achieved by using different methods and materials. The goal of each method is to replace the alveolar process and to have enough bone for the implant placement [Deshpande, 2014] (Figure 60).

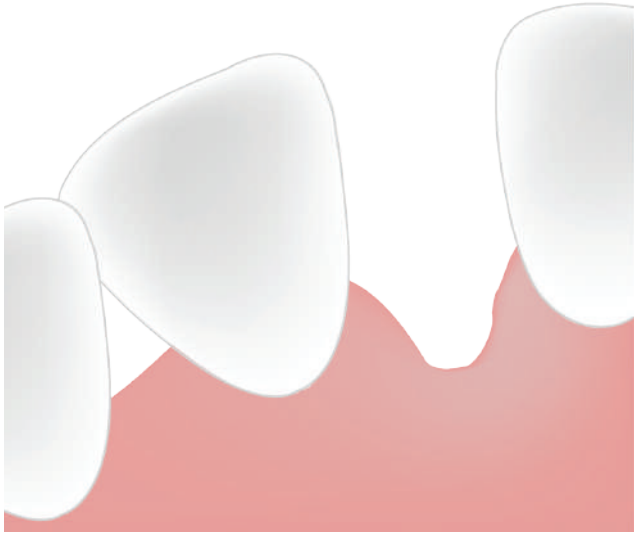

Figure 63: Bone defect.

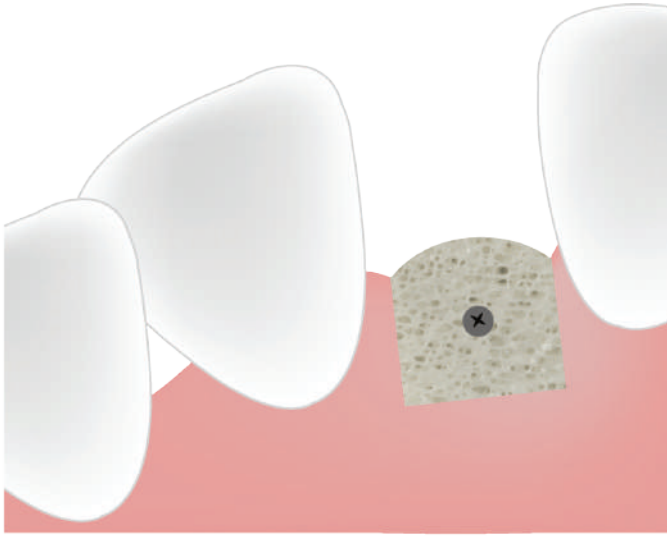

Figure 64: Bone area replaced by SmartBone® graft.

5.2.1 HORIZONTAL/VERTICAL AUGMENTATION PROCEDURE

- Evaluate the oral epithelium of the gum, which must be well keratinized.
- Perform a surgical incision on the crest of the bottom right arch.
- Remove muscle fibers, using a dissector, and incise a muco-periodontal flap, only in the area where the bone block is inserted, because apically a partial thickness has to be performed in order not to have tension on the flaps during the closure (Figure 61).
- Proceed with a blunt dissection of muco-periodontal flap and elevate it in distal direction to access the bone.
- Perform an intramedullary canalization to let the blood flow towards the surgical area; SmartBone® is highly hydrophilic and absorbs blood quickly. The platelet promotes cellular colonization of the biomaterial, in particular by the mesenchymal stem cells that promote the osteogenic process (Figure 62).

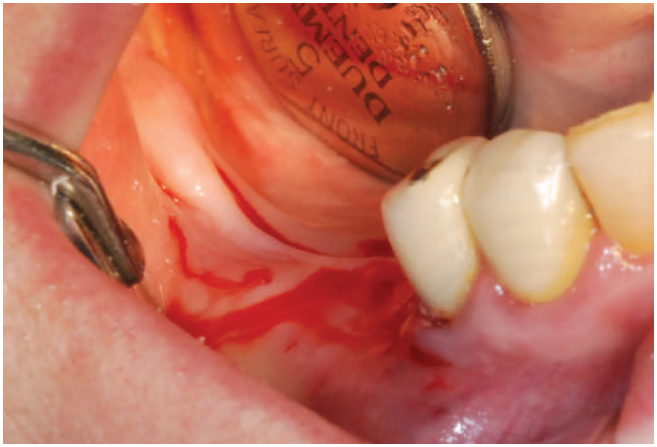

Figure 65: Bone defect.

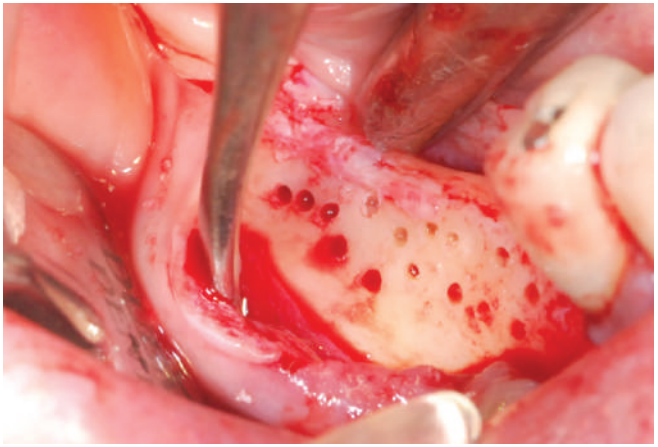

Figure 66: Intramedullary canalization of the recipient site.

- Cut and shape SmartBone®. Mechanical tools are suggested. If modelling is peformed by drill or Piezo, it is preferable to maintain a cold environment by using a sterile water spray in order not to overheat the biomaterial, because this could modify its biomechanical properties (do not use saline solution). If SmartBone® is shaped intensely, its polymeric coating could be widely compromised and a partial resorption could be observed during the first inflammation period (Figures 63 and 64).

These instructions are for educational purposes only. Surgical techniques may vary depending on the clinical operator.

Courtesy of Prof. Dr. G. Carusi

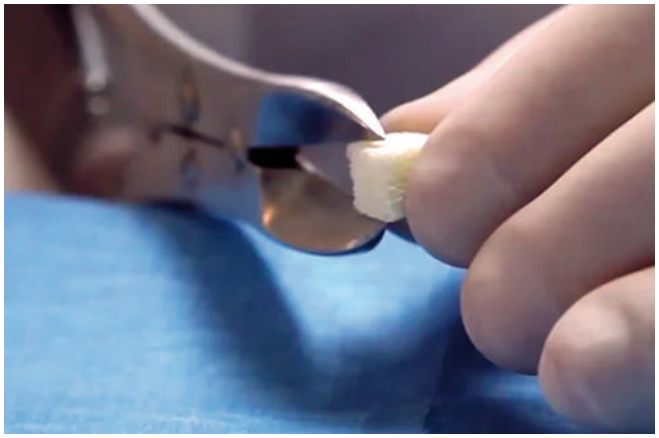

Figure 67: Shaping of the SmartBone® graft.

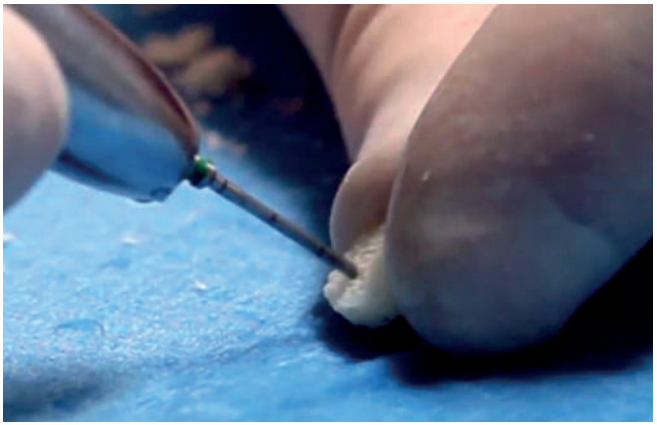

Figure 68: shaping of the SmartBone® graft.

- Place the block in its anatomic seat. Do not overfill the surgical area in order to avoid creating any tension on the flaps. Thanks to its polymeric coating, SmartBone® is not reabsorbed during the first healing/osteo-integration period. If it is preferred to add extra material, 5-10 % extra-volume should not be exceeded (Figure 65).
- It's always a good practice to hydrate the SmartBone® blocks exclusively with patient's blood.
- Fix the block with osteo-synthesis screws in order to obtain perfect stability (Figure 66).
- Cover the surgical area with a resorbable membrane to stabilize the platelet, bovine pericardium is suggested (Figure 67).

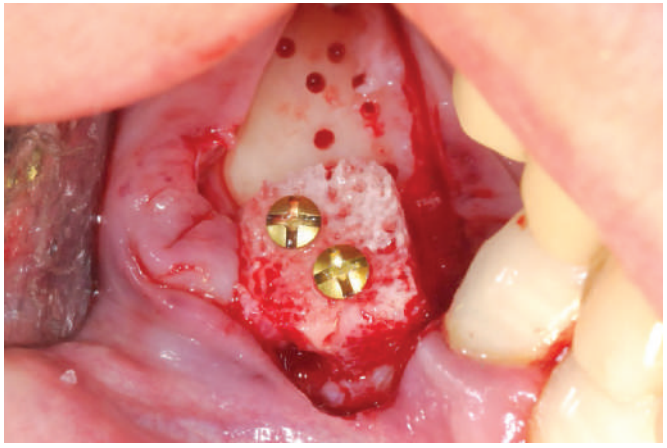

Figure 69: SmartBone® Block fixation.

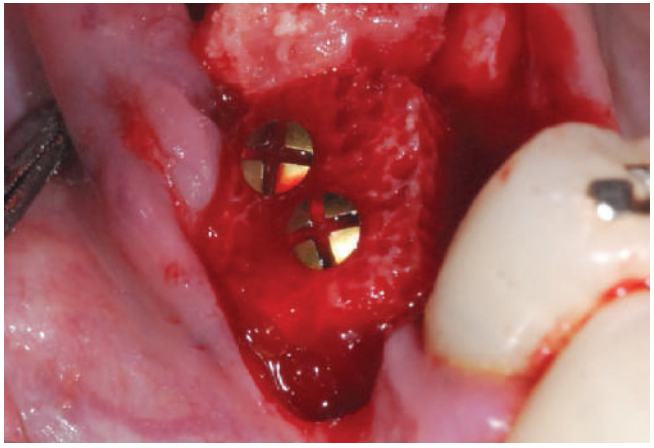

Figure 70: Wettability of SmartBone®.

These instructions are for educational purposes only. Surgical techniques may vary depending on the clinical operator.

Courtesy of Prof. Dr. G. Carusi and Dr. R. Pezzoli

- Suture the flaps.
- Evaluate the passive mobilization of the flap, already performed previously with the partial apical thickness, and if needed ease/loose the apical part better, to guarantee a passive coverage of the graft and the membrane without any tension. It is preferred to use at least 2 horizontal mattress sutures, to enable the contact between the connective wall of the opening flaps, avoiding eventual epithelial migration, and use single sutures after complete closure of the flaps. The closure must be perfect without leaving any opening space (Figure 68).
- After 6-8 months, it is possible to proceed with the implant placement; however, each individual case needs critical clinical evaluation.

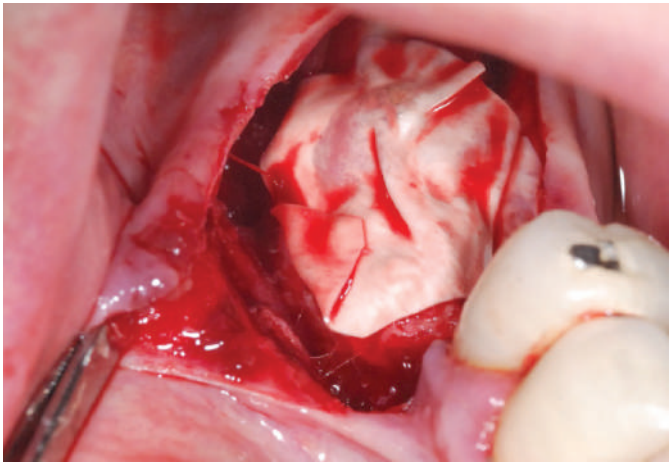

Figure 71: Surgical area cover by resorbable membrane.

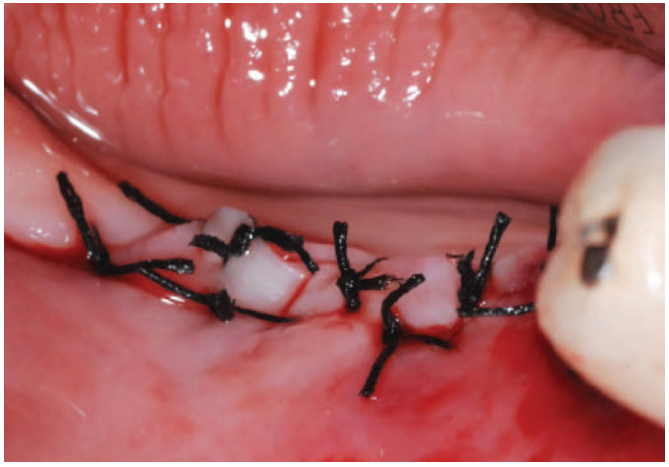

Figure 72: Sutures.

These instructions are for educational purposes only. Surgical techniques may vary depending on the clinical operator.

Courtesy of Prof. Dr. G. Carusi

5.2.2 CLINICAL CASES

CASE 5 - HORIZONTAL/VERTICAL AUGMENTATION

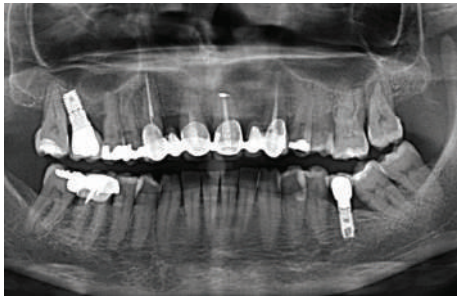

Figure 73: X Rays of the initial condition.

Physician:
Dr. F. Mandelli

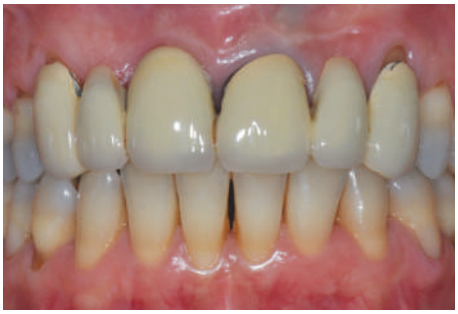

Figure 74: Initial condition.

Patient:	Female, 51 years old, good initial health condition.
Surgical anatomic site:	upper jaw area 11-12-13-21-22-23.
Pre-surgical clinical situation:	bone atrophy.
Surgical procedure:	horizontal bone augmentation with SmartBone® Microchips (0,25-1 mm) and immediate loading.

SURGERY

Bone augmentation around the implants and immediate loading.

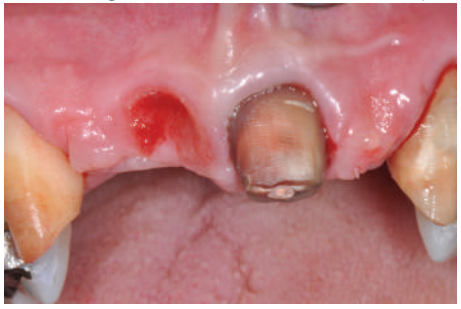

Figure 75: Bone defect.

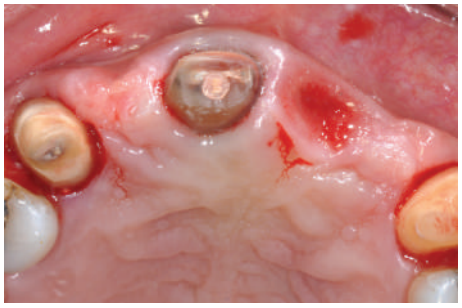

Figure 76: Bone defect.

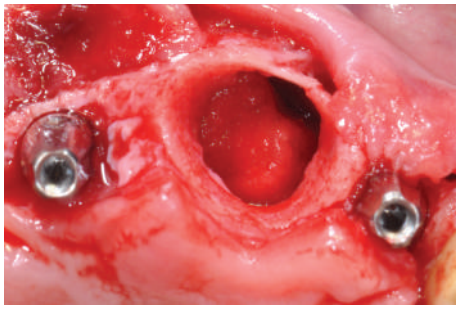

Figure 77: Bone defect.

Courtesy of Dr. F. Mandelli

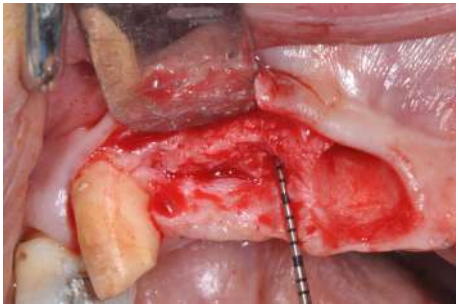

Figure 78: Bone defect.

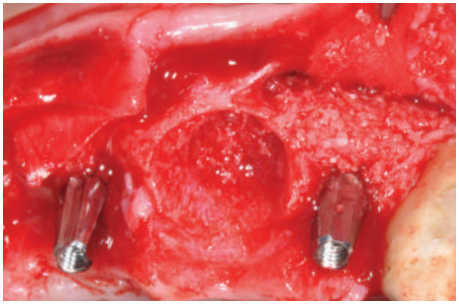

Figure 79: Implant placement and bone grafting.

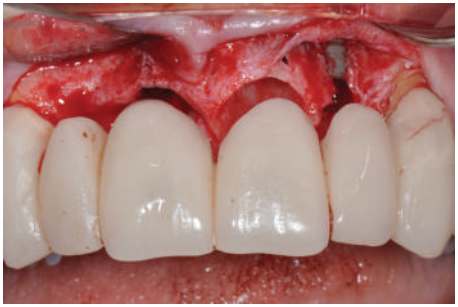

Figure 80: Restoration with immediate load.

FOLLOW-UP

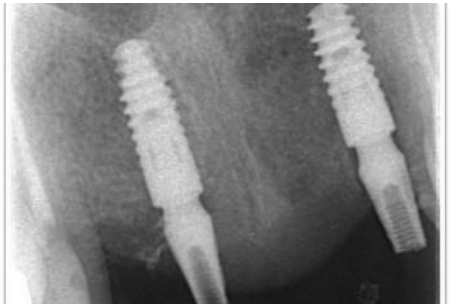

Figure 81: Check-up 10 days after surgery: everything is proceeding well.

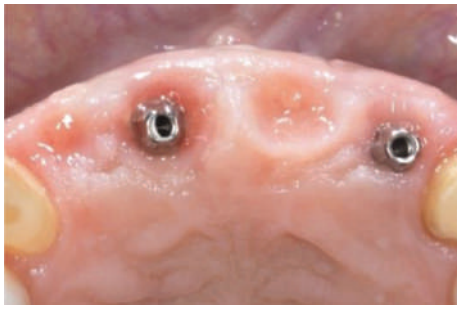

Figure 82: Follow-up 3 1/2 months after surgery: good keratinized tissue.

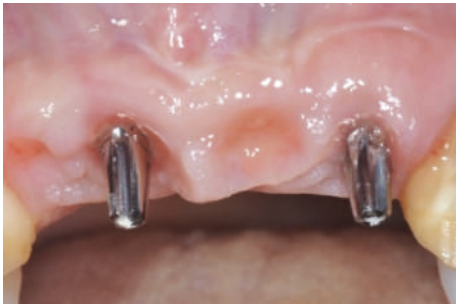

Figure 83: Check-up 3 1/2 months after surgery: good keratinized tissue.

FOLLOW-UP FROM 6 MONTHS TO 6 YEARS

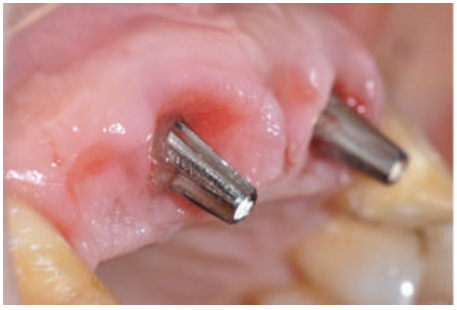

Figure 84: Follow-up 6 months: successful bone augmentation in the pontic area.

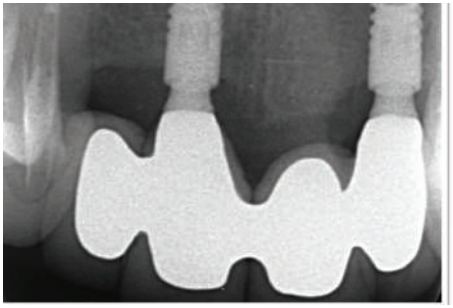

Figure 85: Complete osteointegration of soft and hard tissue.

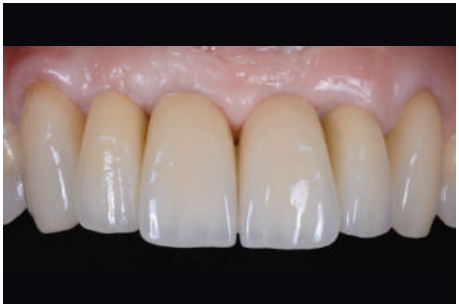

Figure 86: Follow-up 6 years: complete osteointegration and maturation of soft and hard-tissues.

Courtesy of Dr. F. Mandelli

CASE - HORIZONTAL/VERTICAL AUGMENTATION

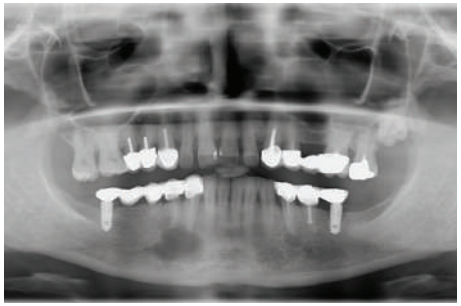

Figure 87: CBCT scan of the initial situation

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Physician:
Dr. R. Ghiretti

Patient: Female, 59 years old.

Surgical anatomic site: 34-36.
Pre-surgical clinical situation: Radicular fracture and peri-implantitis
Surgical procedure: Horizontal bone augmentation with SmartBone®

RADIOLOGICAL IMAGES PRE AND POST SURGERY:

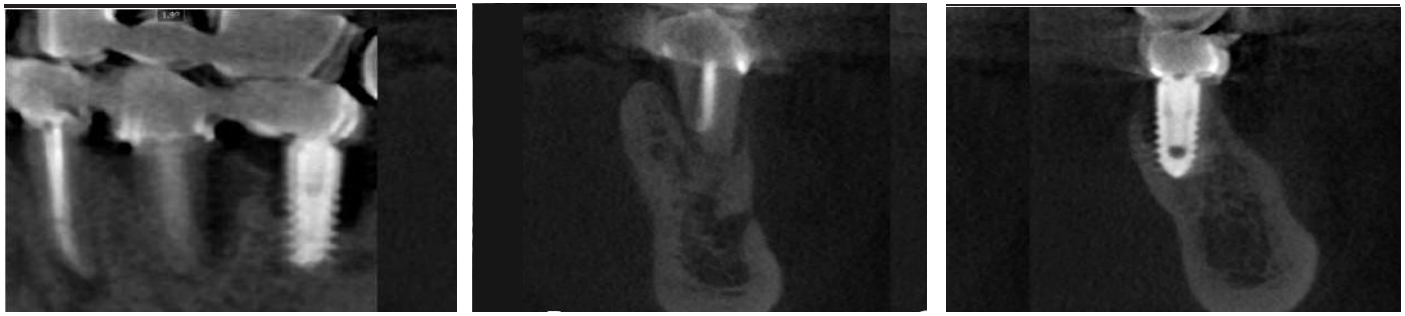

Figure 88: CBCT Scan before surgery shows severe impairment of Region 35 caused by radicular fracture and accentuated peri-implantitis around fixture in Region 3.

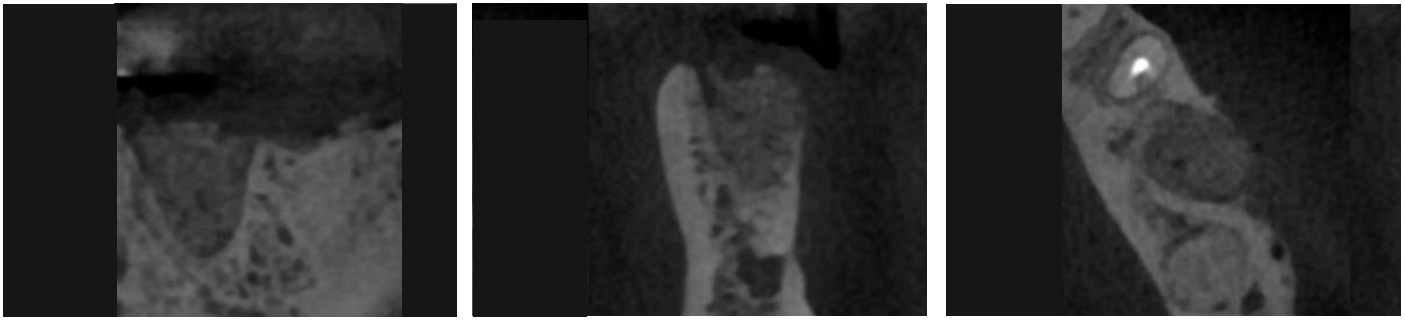

Figure 89: Post op X-Ray in sagittal and axial projection, and cross-sections of Regions 35 and 36.

Courtesy of Dr. R. Ghiretti

FOLLOW-UP 4 MONTHS

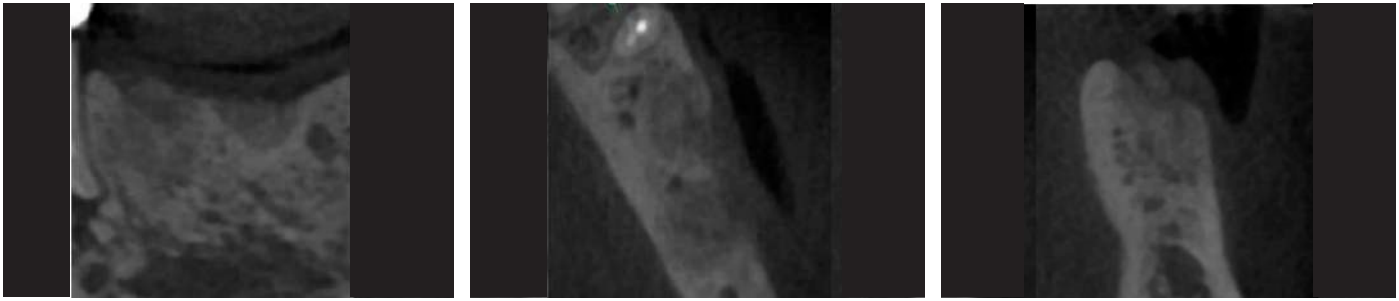

Figure 90: X Ray after 4 Months demonstrates a good bone regenration.

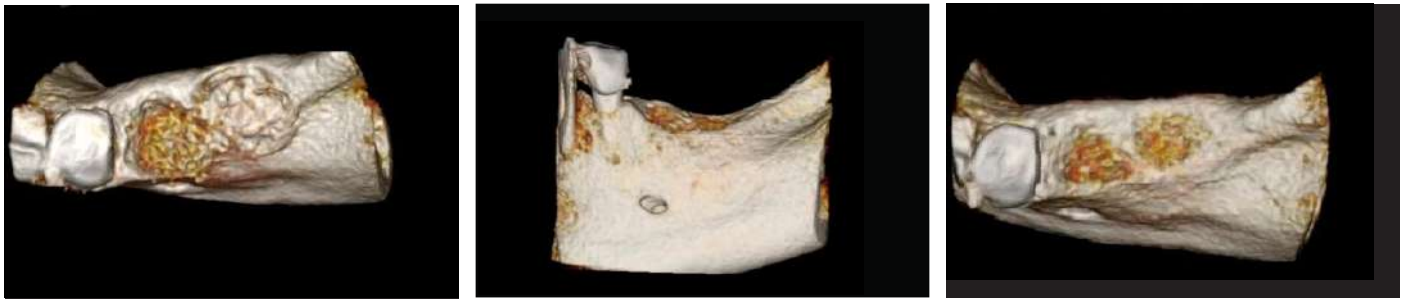

Figure 91: 3d Rendering in sagittal and axial views taken from CBCT (left) during postoperative period and (right) 4 Months after the regenerative surgery prove a excellent bone quality.

FOLLOW-UP 3 YEARS

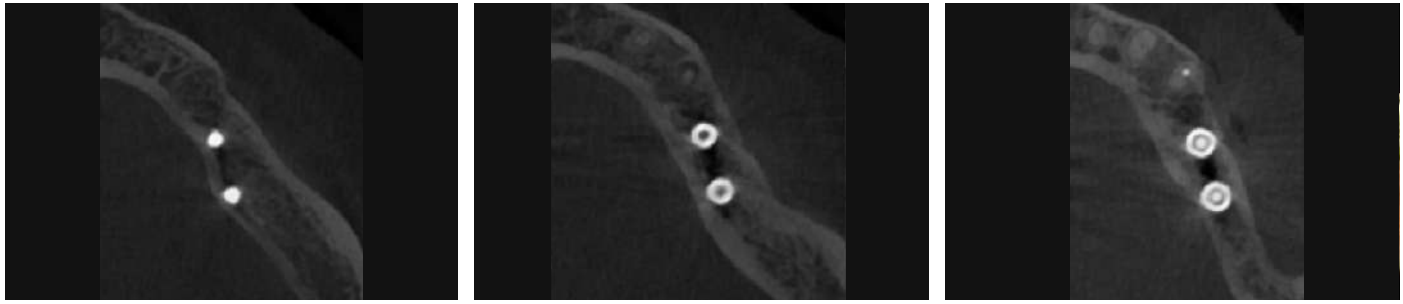

Figure 92: Good final result.

Courtesy of Dr. R. Ghiretti

applied sciences

MDPI

Case Report

Clinical Case Employing Two Different Biomaterials in Bone Regeneration

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3 Faculty of Biomedical Sciences, University of Southern Switzerland (USI), Via G. Buffi 13, 6900 Lugano, Switzerland
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check for updates

Abstract: The case of a 59-year-old woman lacking bone in the lower left side of her mandible, and treated with two different biomaterials for bone regeneration, is reported here. Specifically, two different anatomical sites damaged by two different pathologies were studied: a radicular fracture and peri-implantitis. The sites were treated via xenograft bone substitute and calcium phosphosilicate, respectively. Follow-up evaluations showed that the two different methodologies employing different materials in the same organism undergoing the same metabolic processes achieved the same good results. This represents a significant change in current surgical strategies for the dental region: instead of focusing on a single gold-standard technique, it is possible to follow a hybrid approach by adapting the biomaterial and the protocol used to the specificities of the defect.

Keywords: bone grafts; xenograft; calcium phosphosilicate; CGF

1. Introduction

Mandibular augmentations are surgical procedures that often require the use of bone grafts. This way, after a period of recovery to enable osteointegration, correct implant positioning is possible. In general, they are more complicated than maxillary-bone augmentations because of the thicker cortical layer of the patient's residual bone, which limits blood supply and overall graft integration.

The gold-standard approach involves autologous (cortical and medullar) bone harvested from the patient [1,2]. This ensures limited probability of rejection [3], but still carries inherent risks, particularly with regard to the comorbidity of the harvest site. In general, this grafting technique relies on two major concepts: the "diamond" (or regenerative pentagon) and the "organic room" [4]. The resulting protocol, which is very common and effective in orthopedic practice, entails that all biological activities occurring during osteointegration are confined to a vital, aseptic, mechanically stable, sealed environment (the "room") [4]. Of course, such an environment is difficult to prepare in a more hostile region like the oral. Indeed, surgeons usually have to operate under local anesthesia in a much more contaminated environment. Moreover, application sites are often less surgically accessible, are in contact with moving structures (e.g., the jaw, tongue, and cheeks), and the soft tissue at the sites can be fragile and difficult to utilize for the proper coverage and final sealing of the hypothetical organic room (tissue expanders are, in fact, seldom used in this kind of surgery). This leads to a long postoperative period and subsequent reconstruction of bone-regeneration materials that have been under strain from the patient's unavoidable chewing activity. As a matter of fact, an appropriate

CASE 5 - HORIZONTAL/VERTICAL AUGMENTATION

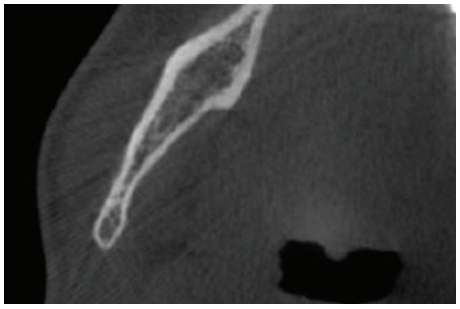

Figure 93: Start point CBCT scan axial view.

Physician:
Dr. M. Martini

Patient: Male, 42 years old.

Surgical anatomic site: 44-45.
Pre-surgical clinical situation: Mandibula bone atrophy.
Surgical procedure: Horizontal bone augmentation with SmartBone® Block.

SURGERY

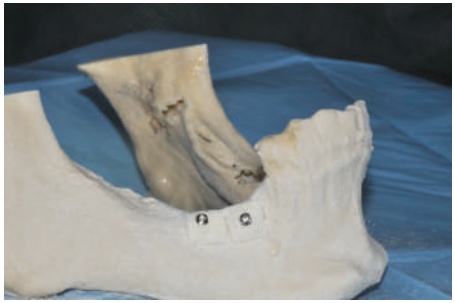

Figure 94: Bone graft appearance at the end of shaping.

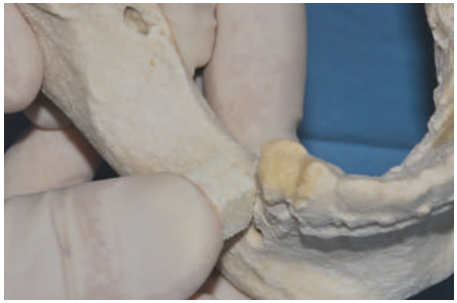

Figure 95: SmartBone® Block shaped on a stereolytographic model.

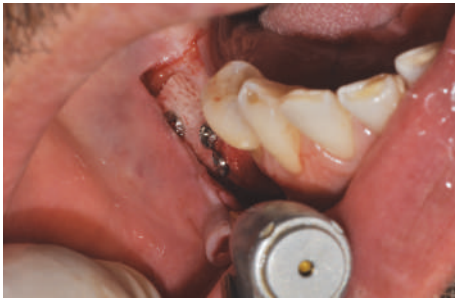

Figure 96: Clinical status upon fixing the graft on the mandible.

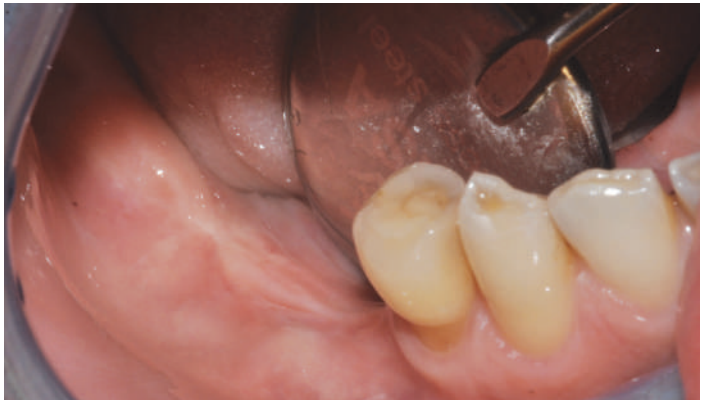

Figure 97 : Healing after 3 months.

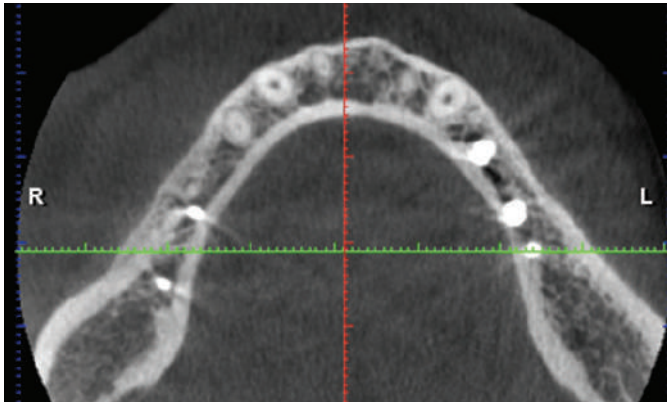

Figure 98: CBCT scan after 4 months.

Courtesy of Dr. M. Martini

IMPLANT PLACEMENT

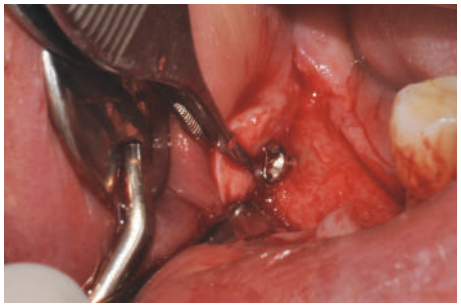

Figure 99: Second stage surgical procedure.

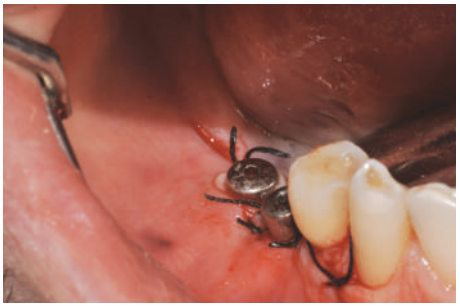

Figure 100: Healing abutment placement.

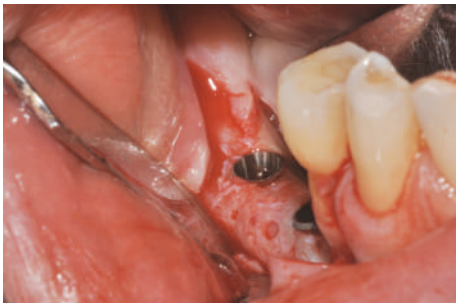

Figure 101: Implant placement in same session.

HISTOLOGICAL ANALYSIS

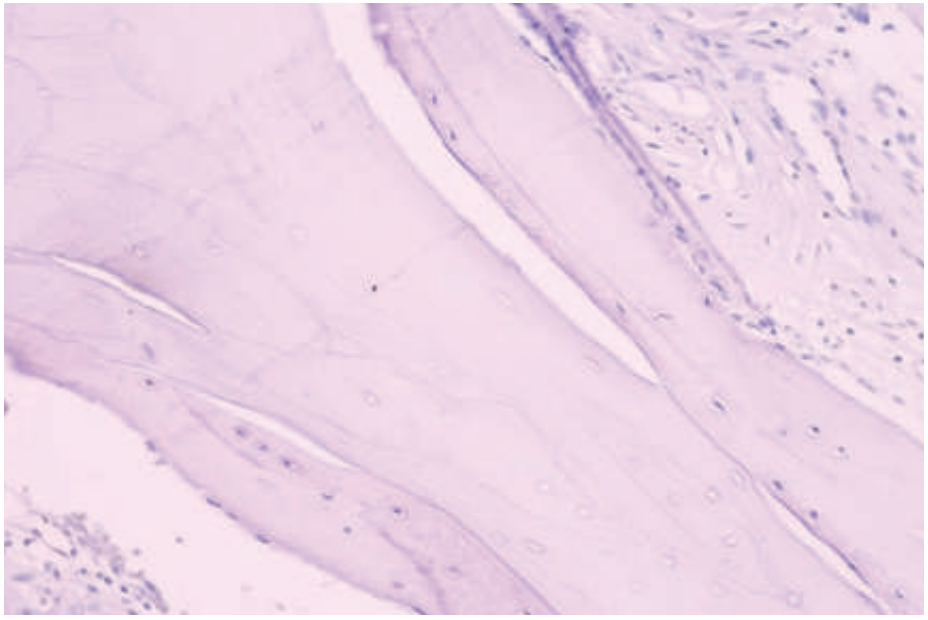

Figure 102: Histology - New young bone tissue with osteocytes in lacunae and with a good lamellar structure.

Courtesy of Dr. M. Martini

CASE 6 - HORIZONTAL/VERTICAL AUGMENTATION

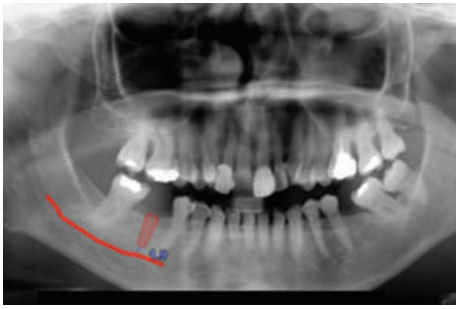

Figure 103: X-Rays of the initial condition.

Physicians:
Dr. J. Hrkal

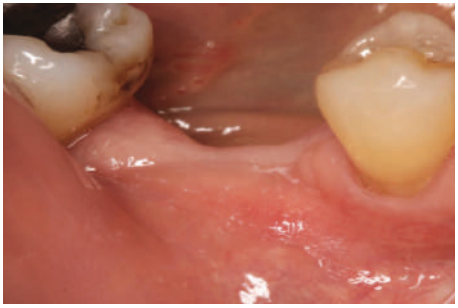

Figure 104: Soft tissue of the initial condition.

Patient:	Female, 58 years old.
Surgical anatomic site:	Loc. 46, horizontal atrophy, horizontal bone - 3,0 mm, vertical - 2,7 mm.
Surgical procedure:	SmartBone® Block + SmartBone® Microchips.

RADIOLOGICAL IMAGES PRE AND POST SURGERY:

Augmentation loc. 46 – SmartBone® Block 10x10x4 mm + SmartBone® Microchips (0,25 - 1,0 mm) + PRFG.

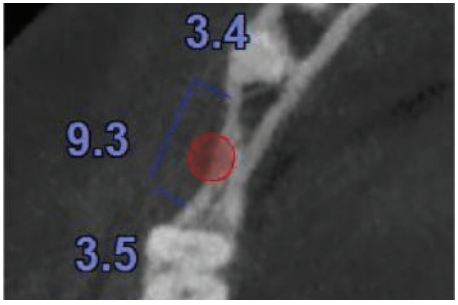

Figure 105: CBCT section of the defect.

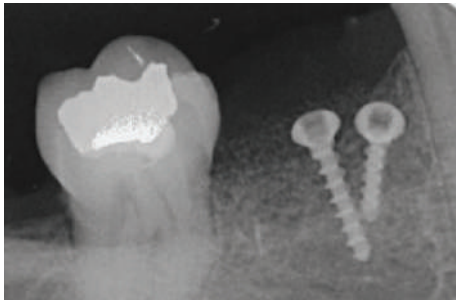

Figure 106: Follow-up 1 month.

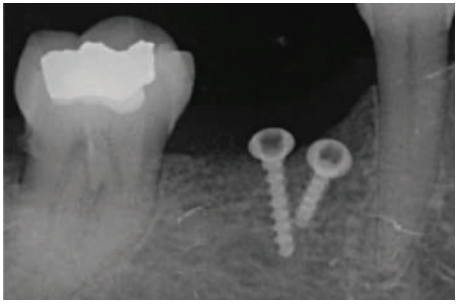

Figure 107: Follow-up 6 months.

Courtesy of Dr. J. Hrkal

FOLLOW-UP 7 MONTHS

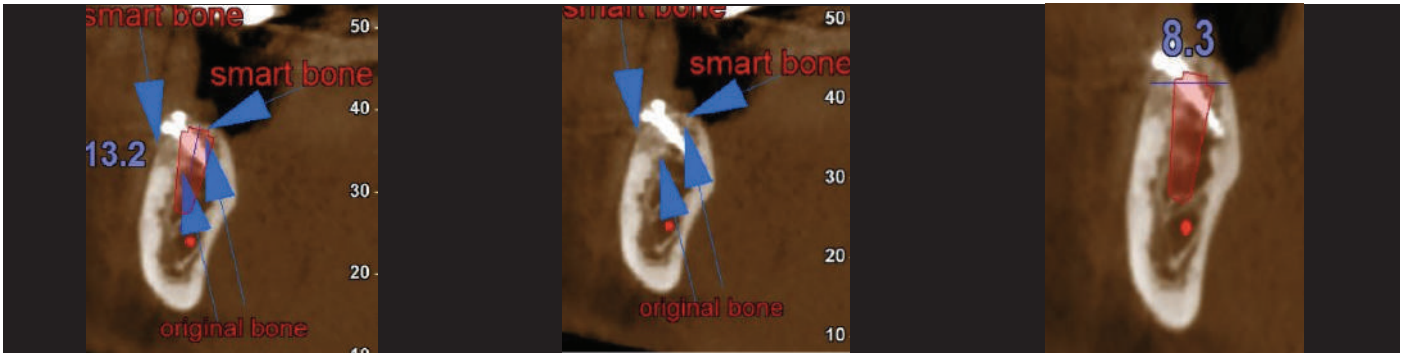

Figure 108: Control CB CT post 7 months.

IMPLANT PLACEMENT

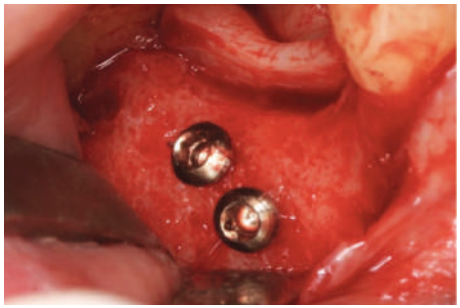

Figure 109: Bone quality 10 months after augmentation.

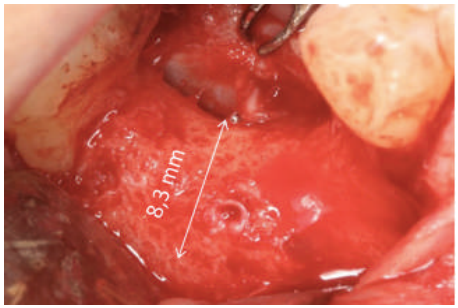

Figure 110: Height increased after 10 months after augmentation.

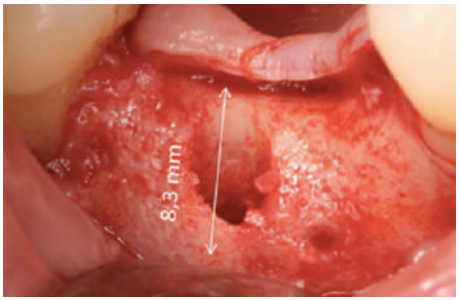

Figure 111: Depth increased after 10 months after augmentation.

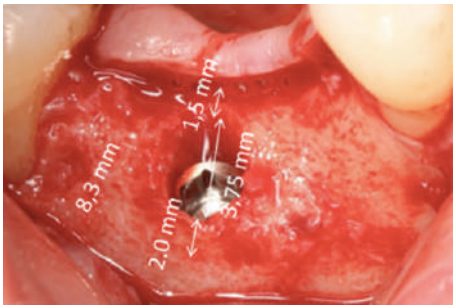

Figure 112: Bone increased after 10 months and implant placement.

Courtesy of Dr. J. Hrkal

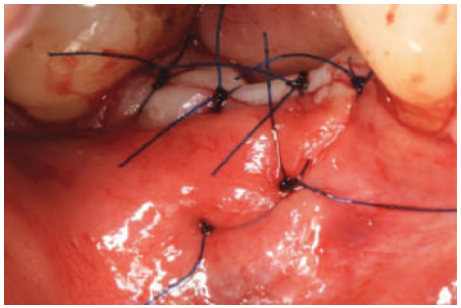

Figure 113: Suture.

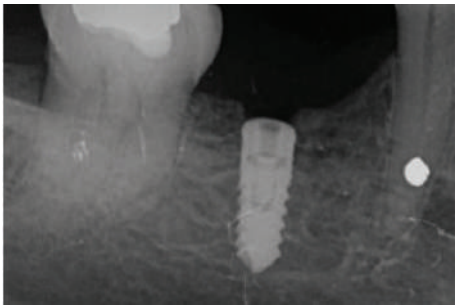

Figure 114: X-Rays after implant placement.

CASE 7 - HORIZONTAL/VERTICAL AUGMENTATION

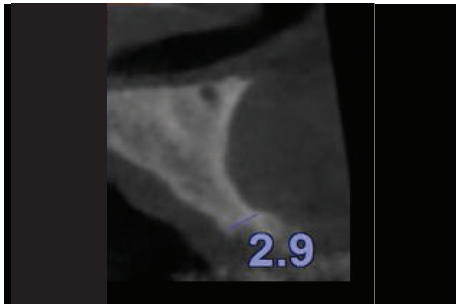

Figure 115: X-Rays of the initial condition.

Physician:
Dr. J. Hrkal

Patient: Male, 63 years old.

Surgical anatomic site: Loc. 21-22.
Surgical procedure: Augmentation with SmartBone®
Block 10x10x3 mm + SmartBone®
Microchips + Collagen membrane.

SURGERY

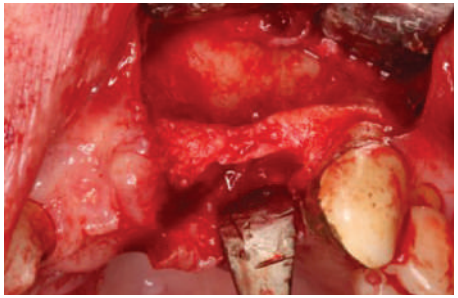

Figure 116: Bone defect.

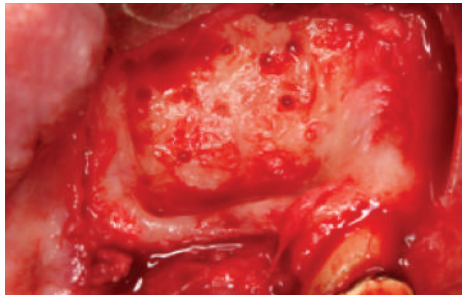

Figure 117: Recipient site.

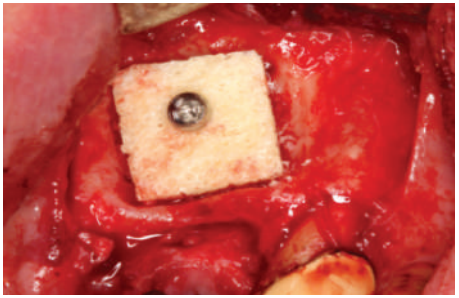

Figure 118: Positioning SmartBone® Plate.

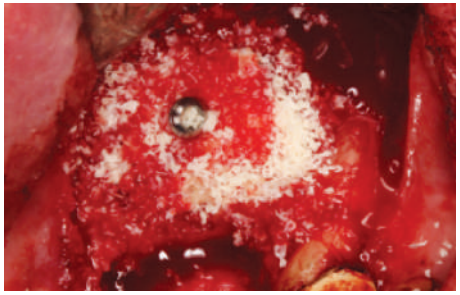

Figure 119: SmartBone® microchips all over the place.

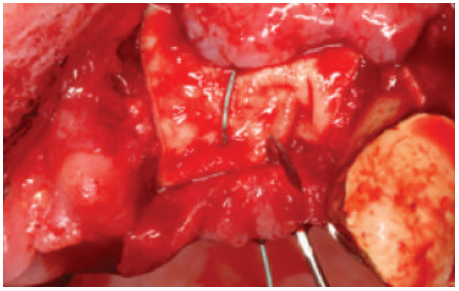

Figure 120: Surgical area covered by collagen membrane.

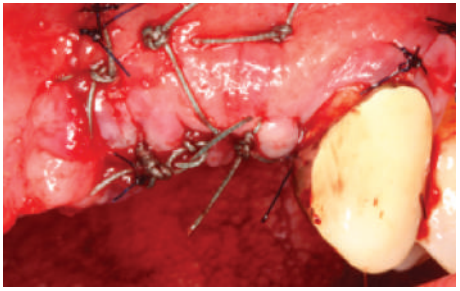

Figure 121: Suture.

Courtesy of Dr. J. Hrkal

FOLLOW-UP

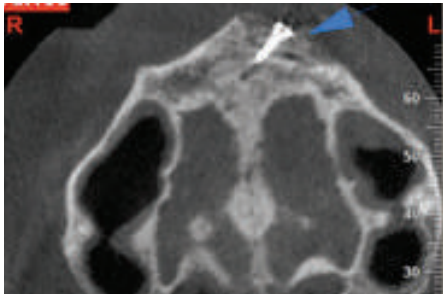

Figure 122: Check-up immediately after surgery.

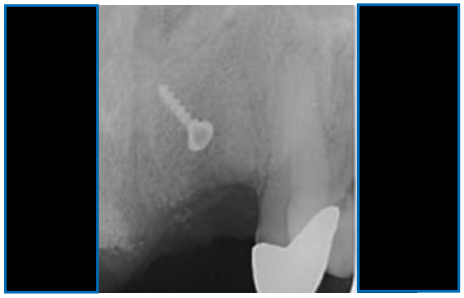

Figure 123: Follow-up 3 months post op.

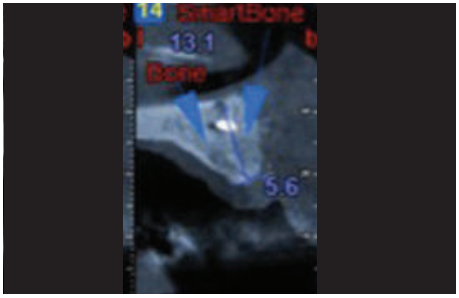

Figure 124: CBCT section 8 months post op.

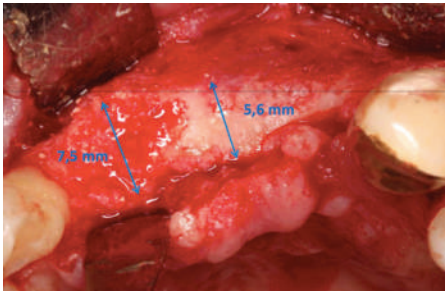

Figure 125: Follow-up 8 months - bone augmentation.

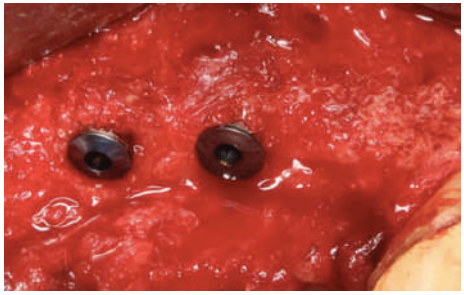

Figure 126: Implant placement.

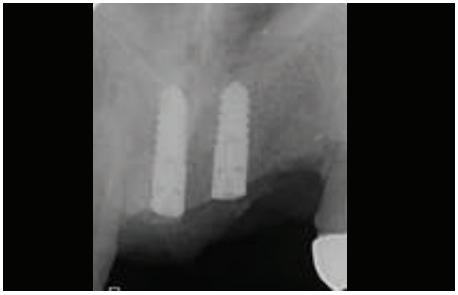

Figure 127 a: X-Rays of the final result 8 months after bone augmentation.

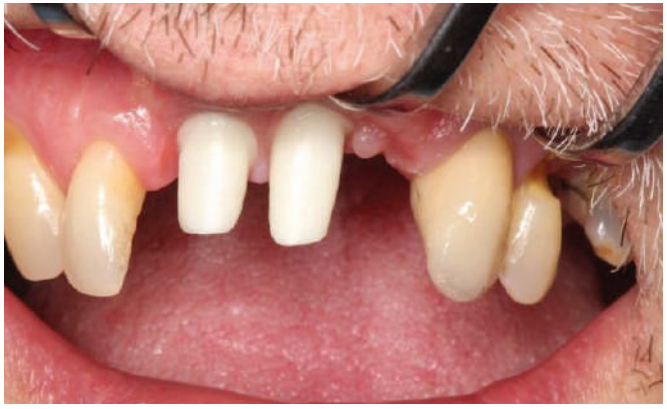

Figure 127 b: final restoration.

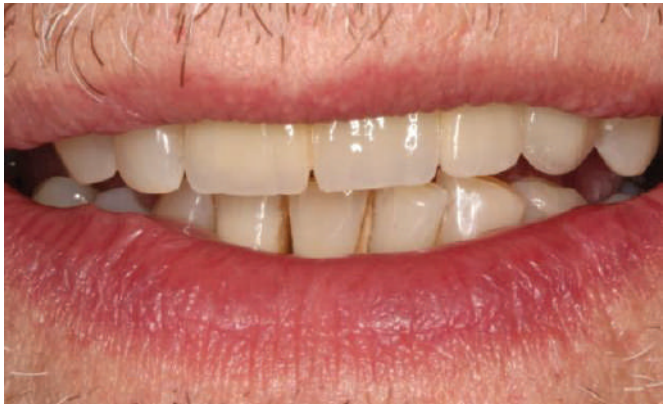

Figure 127 c: final restoration.

Courtesy of Dr. J. Hrkal

CASE 8 - HORIZONTAL/VERTICAL AUGMENTATION

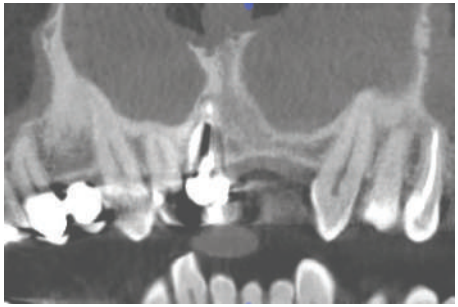

Figure 128: X-Rays of the initial condition.

Physician:
Dr. R. Ghiretti

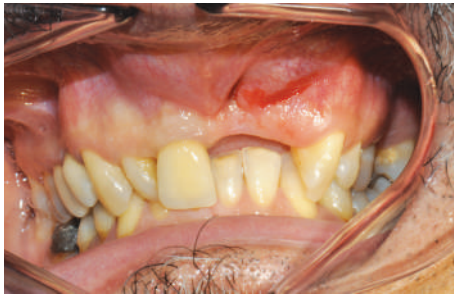

Figure 129: General condition of the bone atrophy.

Patient:	Male, 46 years old.
Surgical anatomic site:	21, 22.
Pre-surgical clinical situation:	Bone loss due to traumatic event
Surgical procedure:	SmartBone® Block augmentation.

SURGERY

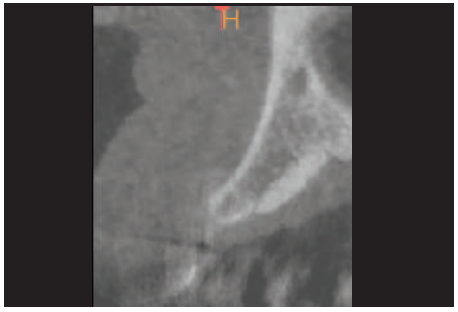

Figure 130: Bone atrophy region 21-22.

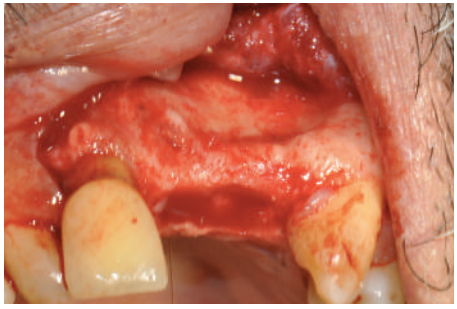

Figure 131: Skeletonization of the surgical area.

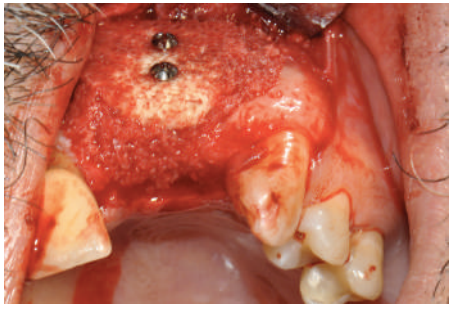

Figure 132: SmartBone® Plate placement and fixation. Surrounding area coverd with SmartBone® Microchips mixed with CGF.

Courtesy of Dr. R. Ghiretti

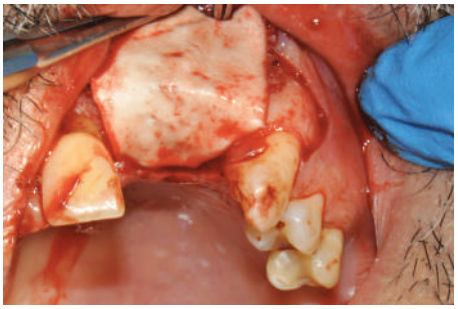

Figure 133: Collagen membrane placement.

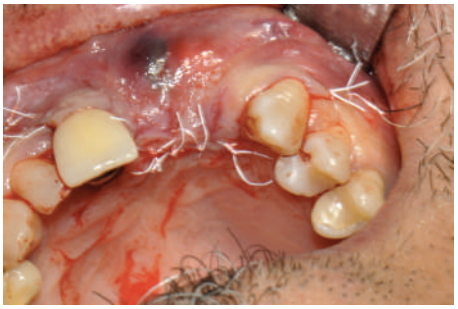

Figure 134: Suture in PTFE.

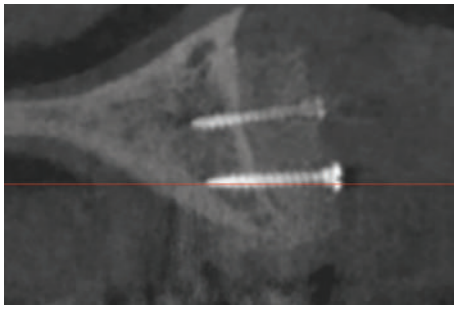

Figure 135: CBCT Check.

FOLLOW-UP AT 6 MONTHS AND IMPLANT PLACEMENT AT 10 MONTHS

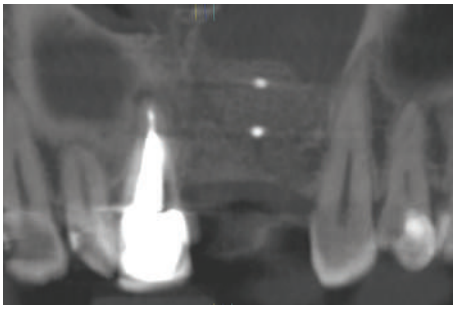

Figure 136: Follow-up 6 months.

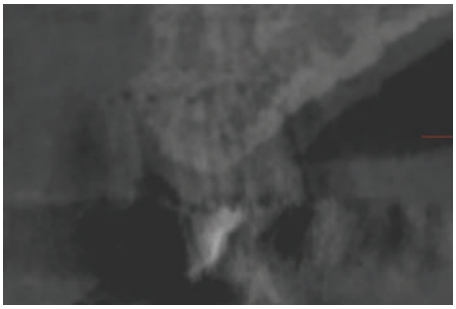

Figure 137: Follow-up 6 months.

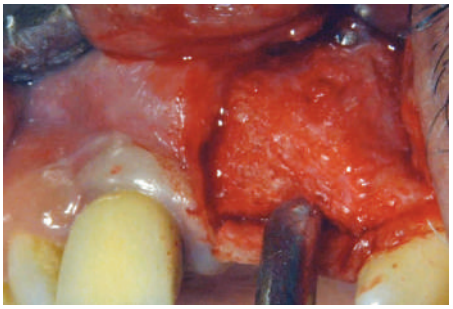

Figure 138: Follow-up 10 months.

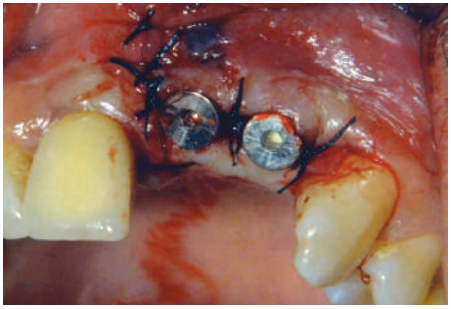

Figure 139: Follow-up 10 months.

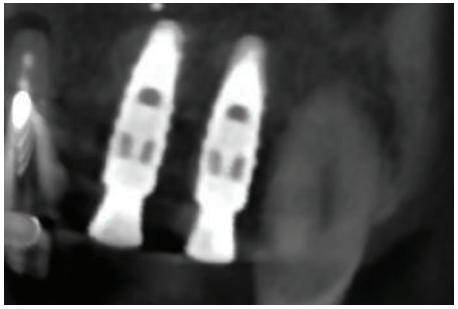

Figure 140: Follow-up 10 months.

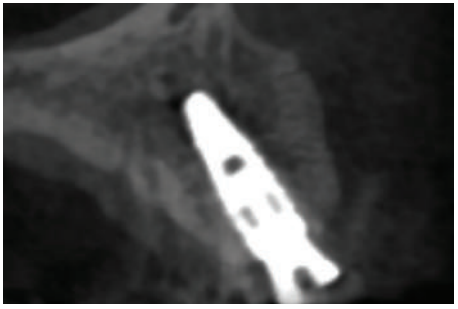

Figure 141: Follow-up 10 months.

Courtesy of Dr. R. Ghiretti

CASE 4 - HORIZONTAL/VERTICAL AUGMENTATION

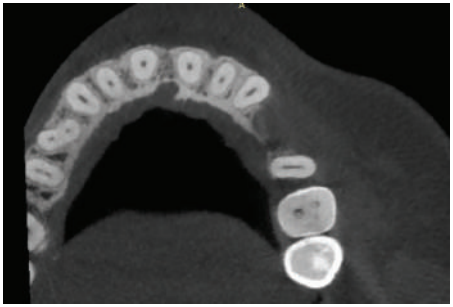

Figure 142: CBCT of the initial condition.

Physician:
Dr. J. L. Latorre Valenzuela

Patient: Female, 37 years old, no smoker, anemia.

Surgical anatomic site: 24.

Pre-surgical clinical situation: severe resorption, horizontal/vertical augmentation with SmartBone® Block.

SURGERY

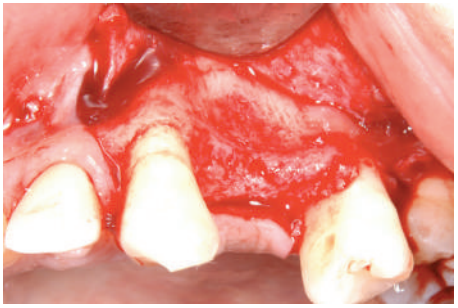

Figure 143: Skeletization of the surgical site.

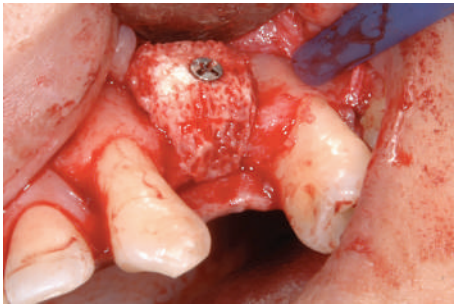

Figure 144: Perfect fitting of the graft during fixation, which was hand-molded by the physician from a block

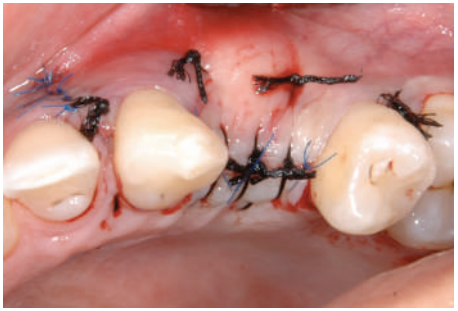

Figure 145: Sutures.

IMPLANT PLACEMENT AFTER 8 MONTHS

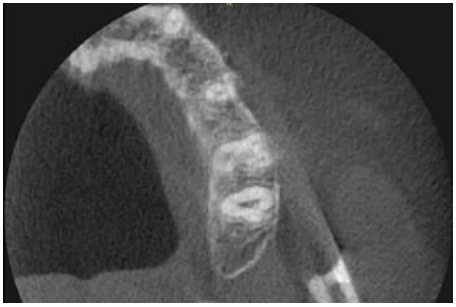

Figure 146: CBCT section.

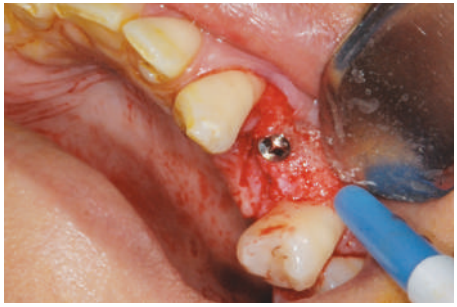

Figure 147: Implant placement.

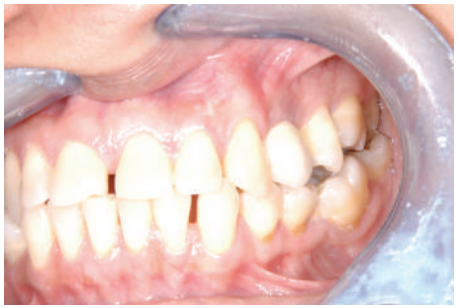

Figure 148: Final restoration.

Courtesy of Dr. J. L. Latorre Valenzuela

CASE 4 - HORIZONTAL/VERTICAL AUGMENTATION

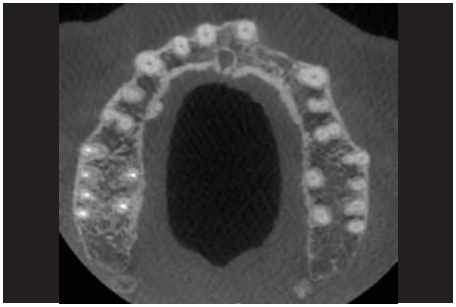

Figure 149: CBCT of the initial condition.

Physician:
Dr. J. L. Latorre Valenzuela

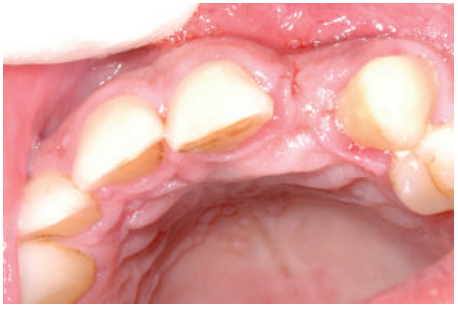

Figure 150: Initial condition of the tissues.

Patient:	Male, 41 years old
Surgical anatomic site:	21.
Pre-surgical clinical situation:	horizontal/vertical augmentation with SmartBone® Block.

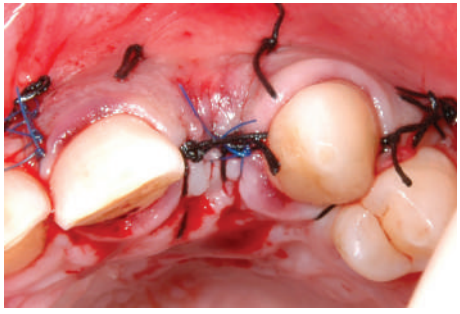

Figure 151: Suture.

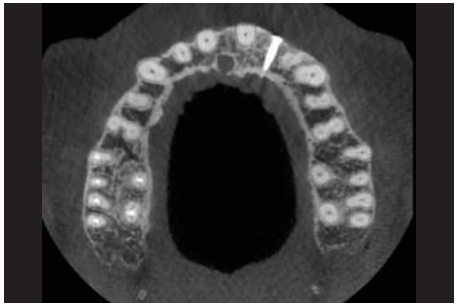

Figure 152: Follow-up 10 months after surgery.

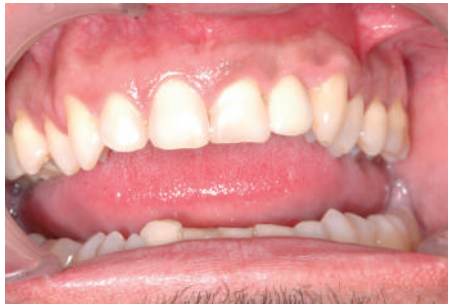

Figure 153: Final result

Courtesy of Dr. J. L. Latorre Valenzuela

5.3 SOCKET PRESERVATION

After teeth extraction, resorption of the alveolar ridge is a prevedibile result. The reduction is in terms of loss of height and width. The width occurs primarily on the buccal side of the edentulous ridge, creating a potential esthetic problem for prosthetic or implant dentistry.

Using socket preservation techniques, it is possible to preserve the height and width of the edentulous ridge.

The use of a bone replacement graft alone results in some preservation of alveolar height and width. The use of a barrier membrane plus a bone replacement graft has been shown to be superior to the sole bone graft or the barrier membrane alone.

The factors that are critical for the preservation of the alveolar ridge at the time of tooth extraction are the extraction technique and the flap design. A traumatic extraction technique should be used with attempts to preserve all of the remaining alveolar bone adjacent to the tooth.

The elevation of buccal lingual flaps, which are often needed in the extraction of badly broken-down teeth, will result in some loss of adjacent papillae height.

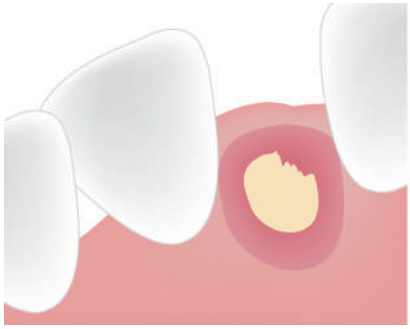

Figure 154: Bone defect after extraction.

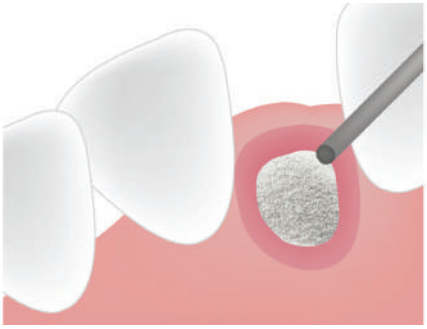

Figure 155: Bone grafting.

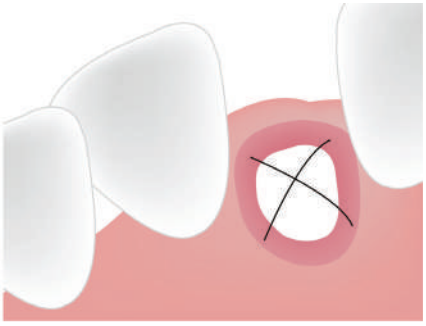

Figure 156: Membrane and sutures.

CLINICAL AND HISTOLOGICAL EVALUATION OF SOCKET PRESERVATION USING SMART-BONE®, A NOVEL HETEROLOGOUS BONE SUBSTITUTE: A CASE SERIES STUDY

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[1] *Private Practice, Milano, Italy*
[2] *Industrie Biomediche Insubri SA (IBI SA), Mezzovico-Vira, Switzerland*
[3] *Creative Engineering Design Area, The Biorobotics Institute, Scuola Superiore Sant'Anna, Pontedera (PI), Italy*
[4] *Department of Surgical, Medical, Molecular Pathology and Emergency Medicine, University of Pisa, Pisa, Italy*
[5] *Centre for Integrative Biology (CIBIO), University of Trento, Trento, Italy*

SUMMARY

Objectives. The aim of this case series study was to evaluate, clinically and histologically, the performances of a novel composite xenohybrid bone substitute.

Methods. Ten non-restorable teeth were extracted and socket preservation was performed with a bovine heterologous graft enriched with collagen and resorbable biopolymers (SmartBone®). The socket was covered with a collagen membrane firmly sutured. After five months of healing, implant site was prepared by means of a trephine bur and a dental implant was inserted. Specimens were sent for histological analysis. After three months of healing, patients received a provisional restoration followed by a definitive crown.

Results. All socket preservations healed uneventfully and, after five months, it was possible to insert implants with no additional bone augmentation procedures. All placed implants osseointegrated successfully and were in function after a minimum follow-up period of 30 months.

Conclusions. The tested biomaterial confirmed good clinical performance and, even if left exposed to the oral cavity covered with a collagen membrane, did not show signs of infection. Further research is desirable with a larger sample and variations of socket preservation technique to better understand the potential of this novel bone substitute.

Key words: socket preservation, biomaterial, heterologous, histological, dental implants, bone substitute.

5.3.1 SOCKET PRESERVATION PROCEDURE

- Evaluate the oral epithelium of the gum, which must be well keratinized. Soft tissues must be in proper conditions in order to guarantee a stable suturing.
- Perform the extraction by separating the tooth in two or more fragments with a surgical bur and a high-speed handpiece. This procedure allows to minimize soft and hard tissue trauma (Figure 135).
- To keep intact soft tissue architecture and vascularization don't perform a flap incision. Bone regeneration starts from the bottom of the alveoli and the healing process ends at the extremity of the alveolar process. After the bone grafting in order to stimulate the vascularization and the volume maintenance it is recommended to cover the alveoli by periosteum. The soft tissue management must be decided according to clinical standard surgical procedures.
- Fill the socket using SmartBone® Microchips mixed with patient's blood. It is recommended the use of a membrane. It could be the periosteum (as active membrane) or a bioresorbable membrane that it helps for the soft tissue healing (Figure 136).
- Once SmartBone® is placed, close the soft tissue with sutures. Implants can be placed 5-6 months later in order to ensure a good regenerated bone.
- Before placing the implant, it is always a good practice to proceed with specific clinical evaluation using CBCT scan.

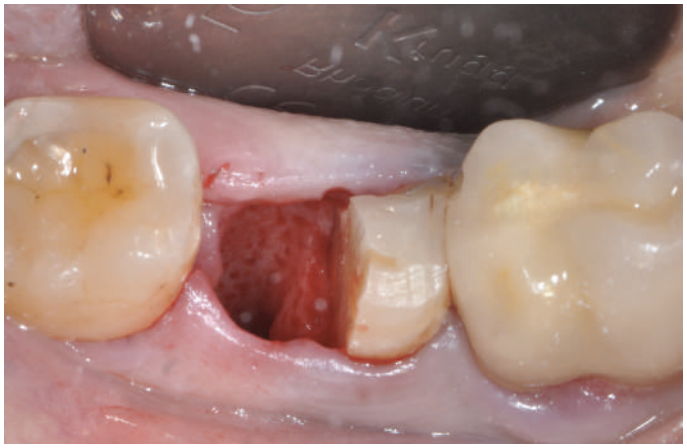


Figure 157: Tooth fragments extration.

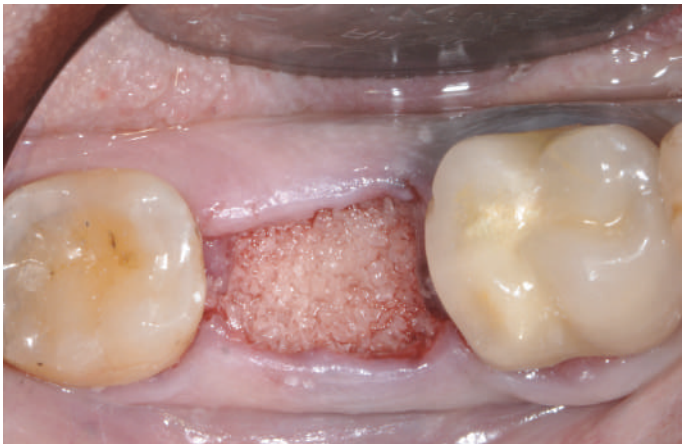


Figure 158: Socket filled with SmartBone® Microchips.

These instructions are for educational purposes only. Surgical techniques may vary depending on the clinical operator.

Courtesy of Dr. F. Mandelli

5.3.2 CLINICAL CASES

CASE 9 - SOCKET PRESERVATION

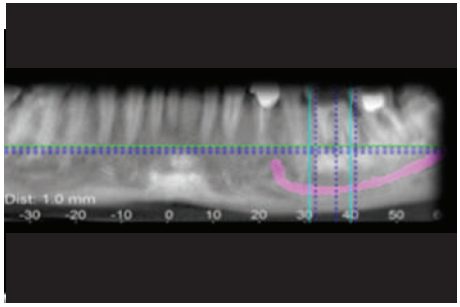


Figure 159: X-Rays of the initial condition.

Physician:
Dr. Mahesh Lanka

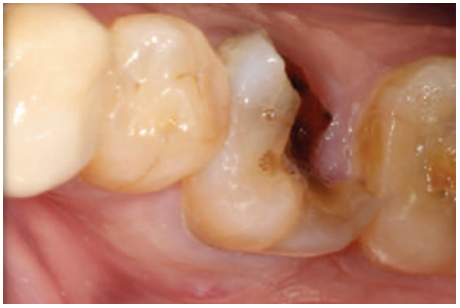


Figure 160: Non restorable molar.

Patient:

Female, 50 years old.

Surgical procedure:

was advised a socket bone graft with delayed implant placement as the tooth was very wide and the periapical infection too differed immediate implant placement.

SURGERY

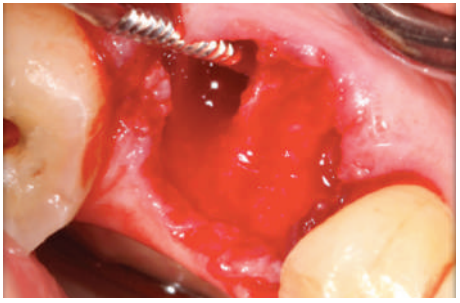


Figure 161: The tooth was gently extracted, the socket curetted thoroughly with a buck file.

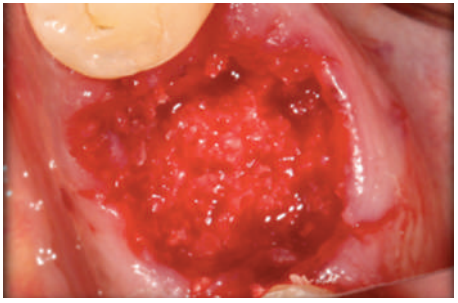


Figure 162: The socket was filled with SmartBone® Microchips.

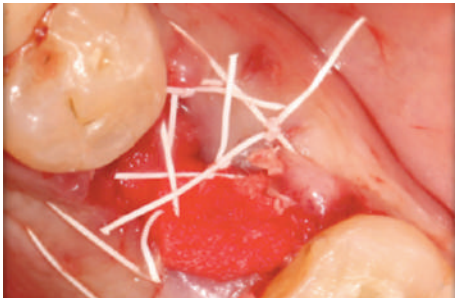


Figure 163: The wound was closed with 3-0 cytoplast sutures and a resorbable collagen.

Courtesy of Dr. Mahesh Lanka

FOLLOW-UP 5 MONTHS

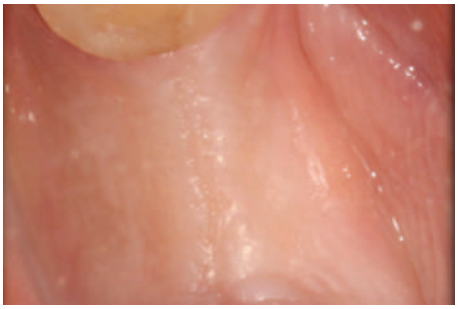


Figure 164: Follow-up 5 months - clinical view.

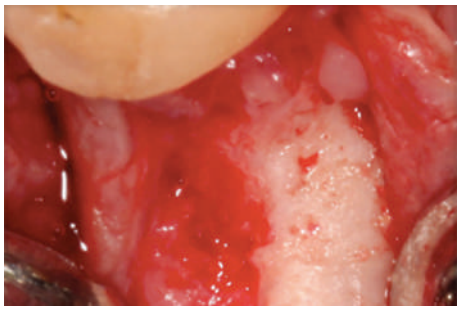


Figure 165: The grafted site has appeared to be well vascularised.

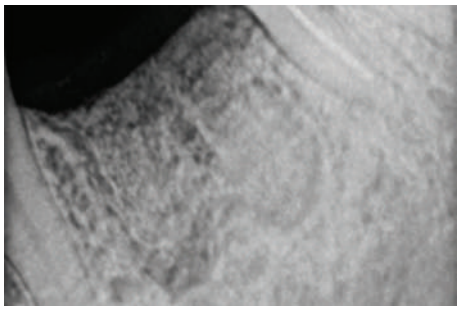


Figure 166: Follow-up 5 months - clinical view.

IMPLANT PLACEMENT

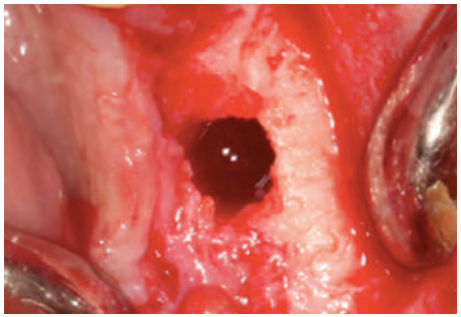


Figure 167: It has been harvested a bone sample for histological examination.

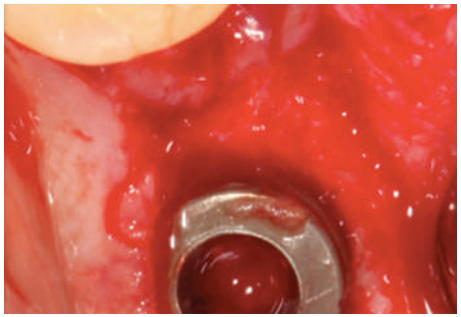


Figure 168: A 5/11.5 dm implant was inserted at 50 ncm.

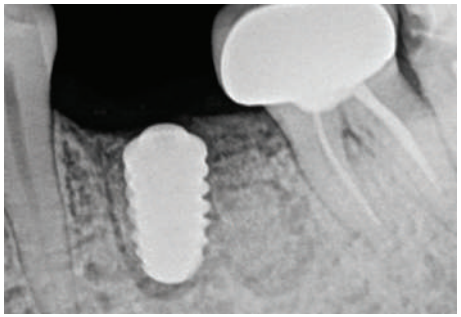


Figure 169: Immediate post operation X-Rays showing the implant in grafted bone.

ANALYSIS FROM 5 TO 18 MONTHS

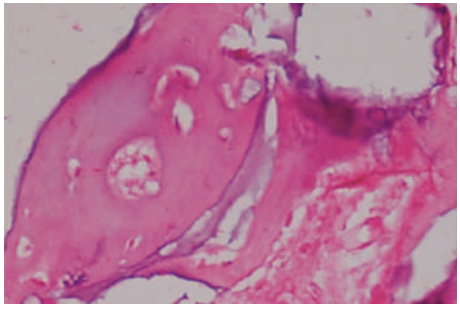


Figure 170: Histological analysis.

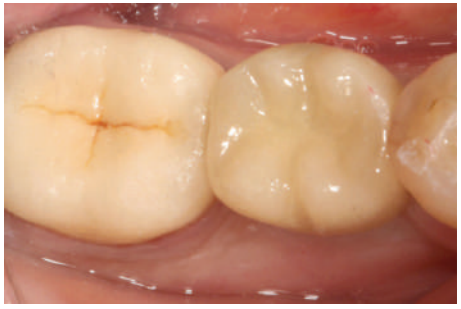


Figure 171: Final prosthesis.

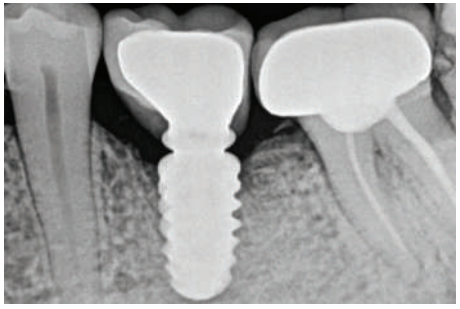


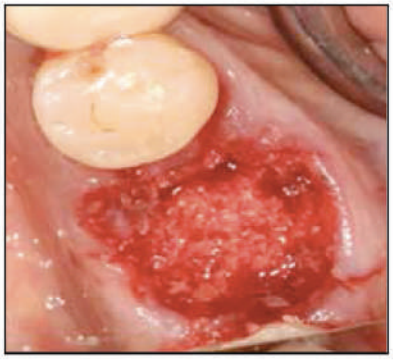
Figure 172: Recall radiograph at 18 months showing complete maturation of the grafted socket.

Courtesy of Dr. Mahesh Lanka

Socket Preservation Using a Small Particulate Xenograft: A Case Report

Dr. Lanka Mahesh[1] • Dr. Devich Aran Shetty[2] • Dr. Sagrika Shukla[3]

Abstract



Soon after tooth extraction a cascade of bone remodeling starts which result in bone resorption. Procedures such Socket Seal Surgery can be employed to pre - serve future implant site. There are various grafts which can used for the same purpose. The best method to observe a graft's healing is surgical re-entry and or histopathology. The aim of this Case Report is to document the use of Smart - bone® xenograft for socket preservation. After 5 months of healing, histopathological core sam - pling revealed good osteoconduction of the graft.

KEY WORDS: Socket preservation, bone graft, xenograft

1. Private practice, New Delhi, India
2. Principal Professor and Department Head, Oral Pathology, ITS Dental College, Ghaziabad UP, India
3. Private practice, New Delhi, India

CASE 10 - SOCKET PRESERVATION

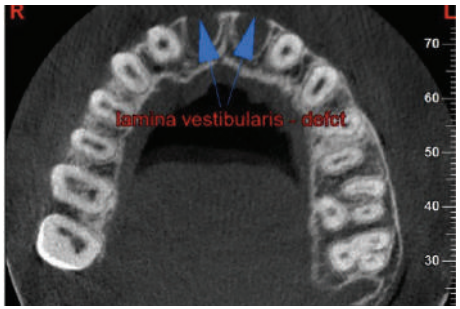


Figure 173: CBCT image of the initial condition.

Physician:
Dr. J. Hrkal

Patient:	Male, 19 years old.
Surgical anatomic site:	11, 21
Surgical procedure:	defect lamina vestibularis, fracture lamina palatinalis.

SURGERY

Treatment plan:

Augmentation – Ridge preservation loc. 11,21- SmartBone® Microchips (1 - 2 mm) Collagen membrane + PRFG.

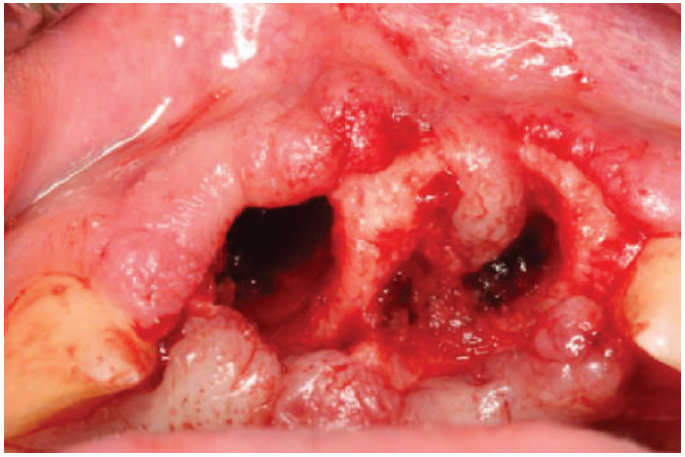


Figure 174: Soft tissue of the initial condition.

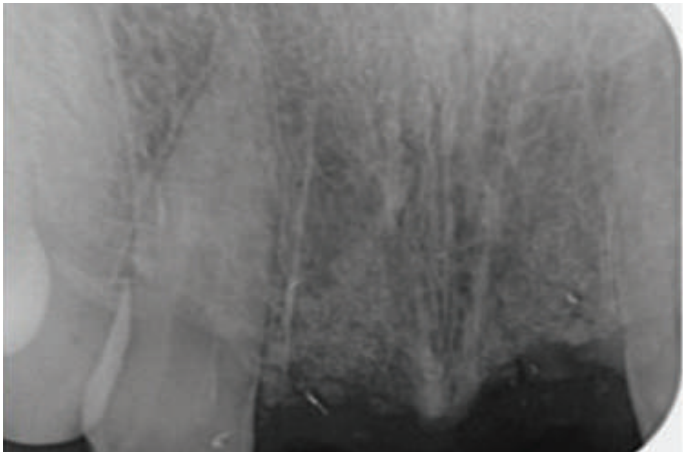


Figure 175: X-Rays image of the initial condition.

Courtesy of Dr. J. Hrkal

FOLLOW-UP AFTER 5 MONTHS

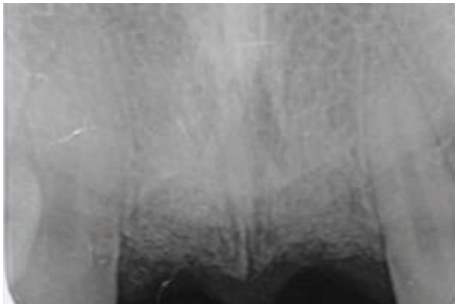


Figure 176: X-Rays image 5 month post op.

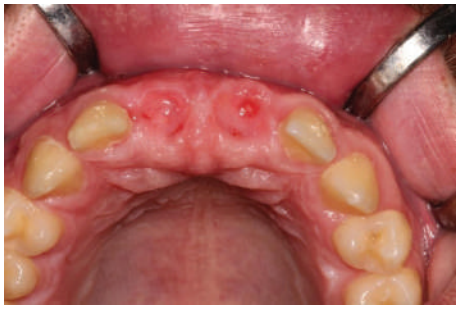


Figure 177: Full arch.

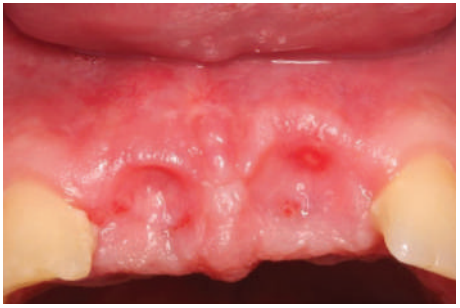


Figure 178: Emergence profile.

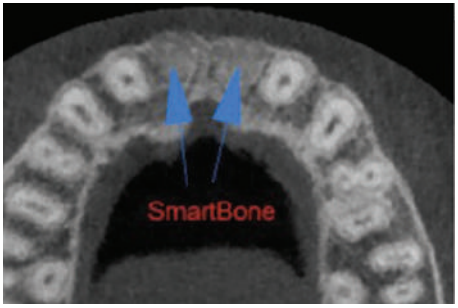


Figure 179: CBCT image after 5 months.

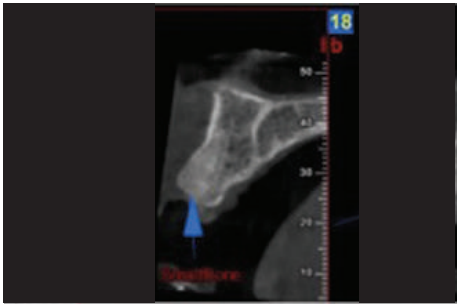


Figure 180: CBCT section 5 months post op.

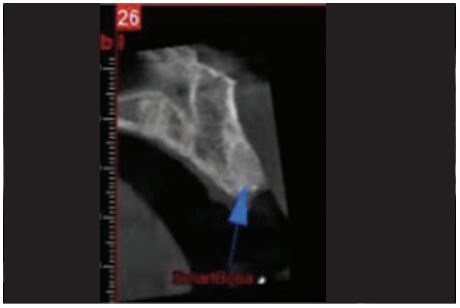


Figure 181: CBCT section 5 months post op.

IMPLANTATION

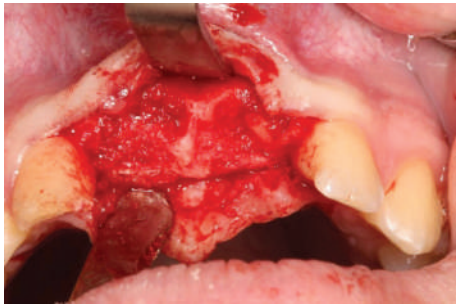


Figure 182: Implant placement after 7 months of the bone quality.

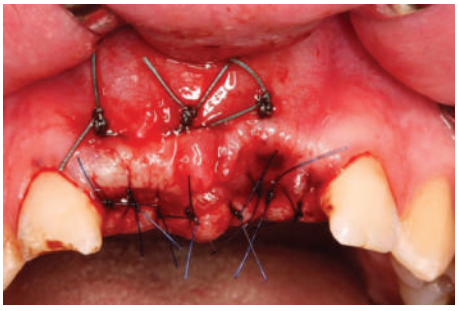


Figure 183: Implant placement after 7 months of the bone augmentation.

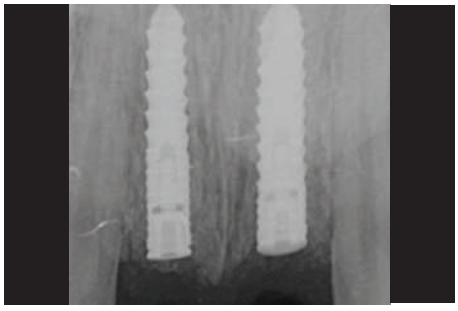


Figure 184: X-Rays of the implant placement.

Courtesy of Dr. J. Hrkal

5.4 FAILURE MANAGEMENT PROTOCOL

DIAGNOSTIC APPROACH

Advanced imaging technologies greatly enhance planning and execution of bone augmentation procedures. CBCT technology provides an increased accuracy, less morbidity for the patient and decreased surgical and restorative chair time by improving results [Sonic, 2012].

PATIENT MEDICAL HISTORY

Patient are excluded if they present with a medical condition that would contraindicate dental surgery or interfere with the wound healing process:

- Infection;
- Uncontrolled diabetes;
- Uncontrolled hypertension;
- Active chemotherapy;
- Radiotherapy.

Increased failure rates should be expected in patients exhibiting risk factors such as systemic disease causing wound healing problems, heavy smoking, increased periodontal susceptibility, poor bone density and extreme atrophy [Bornstein, 2008] and Vitamin D deficiency or high LDL or low HDL cholesterol level [Choukroun, 2014].

COMPLICATIONS

Perforation of the Schneiderian membrane.
It is observed that the percentage of perforation of the Schneiderian membrane during the sinus floor elevation when it is simultaneous placed an implant by using a crestal approach is from 0% to 25% [Ferrigno, 2006]. Membrane lacerations can be attributed to thin sinus membrane, sinus septa, aggressive use of osteotome, drills or large increments of grafting material. Stops may be attached directly to the osteotome to limit the extent of apical displacement. Sinus infection, even if treated early with antibiotics, destroys the grafting augmentation and implant success. It's recommended to avoid the grating placement where a perforation is confirmed or even only suspected.

After a CBCT post-operative control it is possible to verify the distribution of the grafting material. If the grafting material is homogenous with a crown shape you can understand that there is no perforation of the membrane. Instead the irregular distribution of the grafting material is index of membrane perforation. It is forbidden once a perforation is detected to add grafting material and it is suggested to place membrane (collagen, PRF) gently apically and close the soft tissue. The PRF membrane can provide protection for the sinus membrane, and in case of perforation, the fibrin matrix can aid in the wound closure [Diss, 2008]. Once a perforation of the Schneiderian membrane is detected, it is suggested to abort and repeat the procedure after at least 3 months.

LACK OF PRIMARY STABILITY BEFORE IMPLANT PLACEMENT

The primary stability is a fundamental prerequisite for a correct implant placement [Javed, 2006]. During the torque must be evaluated the primary stability and immediately stop the implant placement if there are evidences of lack of primary stability. Micromovements can compromise the osteointegration of the grafted material bringing fibrous tissue around the implant with a consequent of fibrointegration it is suggested to abort and repeat the procedure after months.

The primary stability is not only related to the bone around the implant but also to the design of the implant itself. For the implant placement it is important to follow the correct clinical protocol of the implant producer.

FIBROUS TISSUE PRESENTS IN THE BONE GRAFT DURING THE INTEGRATION PROCESS

If you have evidence not to have new bone formation but a mix with fibrous tissue not stable for the implant placement, don't proceed with implant placement and wait more months to ensure to have enough bone to have primary stability. If this doesn't happen even after months there are 2 options to solve the problem. Choose a short implant if you have at least a residual bone stable or repeat the grafting surgery cleaning the fibrous tissue. Be sure to respect the clinical protocol of the bone manufacturer.

LACK OF SECONDARY STABILITY TIME AFTER IMPLANT PLACEMENT

The lack of osteointegration is normally detected within 20 days post op. It is not a synonymous of a failure of the osteointegration process since it can also occur during implant placement without adding grafting material. Rarely it can be also observed during prosthetic rehabilitation maneuvers even after few months and it is appreciated in implants with a strong aggressive morphology. In this case the primary stability can mask the lack of osseointegration.

However, implants not well integrated can be highlighted by slight rotation movements. Osseointegrated implants show a different rotation. An implant rotation around bone is completely different from an implant rotation in fibrous tissue. If there are cases of lack of osseointegration, it is possible to proceed applying a new, larger caliber fixture, immediately of course if this is allowed from the anatomical conditions, otherwise after 3-4 months, allowing the new bone tissue to colonize and fill the residual vacuum generated from the implant expulsion.

BONE GRAFT LOSS DURING THE REGENERATION PERIOD

Don't proceed with implant placement if you don't have enough bone to have the primary stability. Complete the restoration only if you have enough bone to place an implant otherwise repeat the grafting surgery. Be sure to respect the clinical protocol of the bone manufacturer.

DEHISCENCE ON THE SOFT TISSUE

NO INFLAMMATION

If there is no inflammation, check soft tissue status, if you can see clearly already the granulation tissue under the dehiscence keep the patient under observation and under antibiotic therapy. it's also possible not to re-close the tissue. If you are not sure about the granulation tissue, it's suggested to perform again the sutures in order to close the dehiscence. Remember not to have tension on the tissue in order to have a correct healing. Keep the patient under observation during the first 2 weeks. Wait months in order to have the bone graft completely integrated.

LOCALIZED INFLAMMATION

If there is inflammation, remove the compromised bone part, clean the surrounding area using antibiotics and close again the soft tissue. It is suggested to keep the patient under observation during the first 2 weeks. Wait months in order to have the bone graft completely integrated.

HEAVY INFLAMMATION/FISTULA

Open and remove the infected graft, proceed with an antibiotic therapy, consider to insert antibiotic in granules also in the local cavity. Wait some months by keeping the patient under control in particular during the first 3 weeks. Wait months before re-doing the grafting augmentation.

CASE REPORT

10.5005/jp-journals-00000-0000

Management of a Failed Implant Site with Guided Bone Regeneration, Reimplantation, and Root Submergence Technique

[1]Nitika Poonia, [2]Hilde Morales, [3]Lanka Mahesh

ABSTRACT

A patient with failed implant in relation to 44 was being referred to the dental office. Site 44 was reimplanted with AB Dent dental implants, and guided bone regeneration was done with Smartbone® bone graft and resorbable collagen membrane. Root submerged technique was followed in relation to 45. One year postoperative follow-up shows stable bone levels in relation to 44, 45, and 46.

Keywords: Bone regeneration, Crown, Dental Implant.

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Conflict of interest: None

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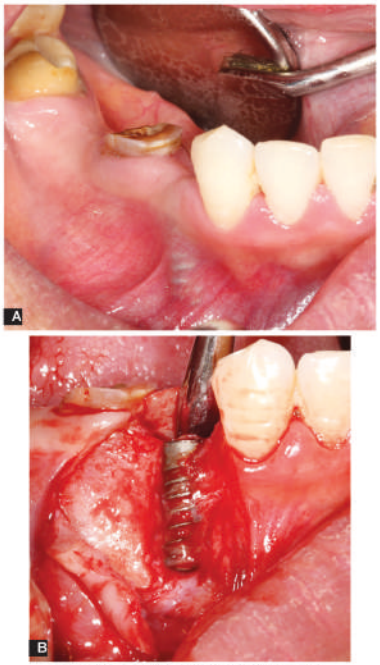


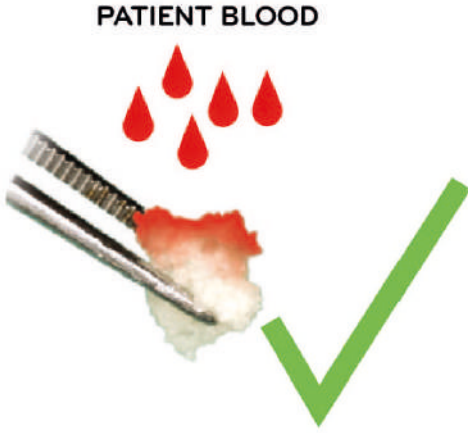
Figs 1A and B: Failed implant w.r.t. 44

DON'T

DO

DON'T

DO



6

Tip's, Tricks, Do's, Dont's

6.1 SINUS ELEVATION REMEMBERS

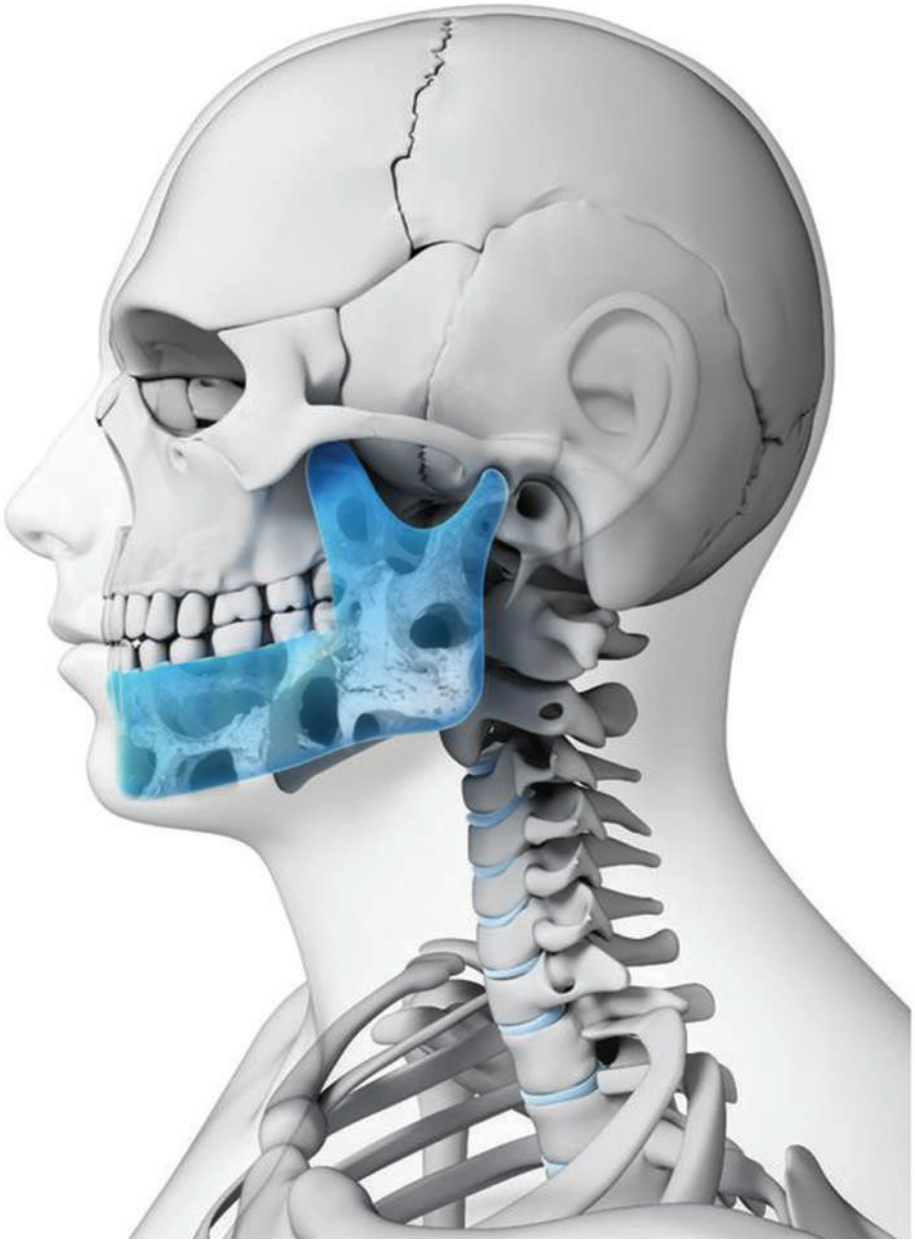
Remember:

- The amount of bone used will vary, but usually several millimeters of bone are added above the jaw.
- The main risk of a sinus lift is that the sinus membrane could be punctured or torn.
- Please pay attention not to perforate the Schneider membrane.
- Consider to elevate correctly the Schneider membrane.
- For placing the implant during the bone augmentation it is necessary to have a sufficient thickness of residual cortical bone in the maxillary sinus floor in order to have a good primary stability.
- Do not mix/dip SmartBone® in saline solution.
- It's not recommended to use SmartBone® Granules (2- 4 mm) in oral applications.

6.2 HORIZONTAL/VERTICAL AUGMENTATION REMEMBERS

Remember:

- Drill: it is preferable to maintain a cold environment by using a sterile water spray in order to not overheat the biomaterial, as this could modify its biomechanical properties. If SmartBone® is shaped/drilled intensely, its polymeric coating is widely compromised and a partial resorption could be observed during the first inflammation period.
- Prepare the receiving site well, properly expand soft tissues and properly microdrill native bone.
- Ensure a tight contact to host bone appropriate graft shaping firmly tight screws.
- Smooth edges and corners.
- Avoid extensive modelling of the bone graft. For shaping the graft, the use of the bone cutter is preferred instead of drills.
- Do not dip the graft in saline solution before placing it; it has been observed that the sodium chloride (saline solution) starts the degradation process of the mineral bovine matrix.
- Do not mix different kind of bone substitutes. Do not put the particles under the bone graft. Particles can be used to fill eventual gaps around, or on top of the graft.
- The use of osteosynthesis screws are suggested.
- Besides these recommendations, it is widely suggested preparing the gums in order to have sufficient soft tissue to close the wound and to suture tightly.
- Always put a membrane on top of graft, before suturing.
- To avoid the dehiscence of the soft tissue, it is imperative to suture without tension.




7
smartbone® on demand™

7.1 SmartBone® ON DEMAND™

SmartBone® On Demand™ is a service provided by Industrie Biomediche Insubri SA according to the 93/42/CEE Legislation regarding custom-made medical devices.

7.1.1 HOW TO GET YOUR GRAFT?

Diagnosis prescription

Take a CT Scan in DICOM format of the Patient concentrating on the defect. Please check on our website the guidelines.

Digital planning

Send the CT Scan with a brief clinical description. IBI's trained Engineers will get in contact with you, discuss the plan and share with you the economical offer as well.

Custom made

You will receive a confirmation document that must be sent signed referring your unique case, in order to approve the project and let's start the production. IBI's trained Engineers, in conformity with your indications and suggestions, will design the graft until your approval.

Surgery

3 weeks later you will receive your graft ready for the surgical operation.
No sterilization or extra shaping required.

7.1.2 MODES OF SUPPLY

1 If you choose to send us the patient's DICOM file, together with his clinical prescription, IBI is able to plan the custom-made piece.

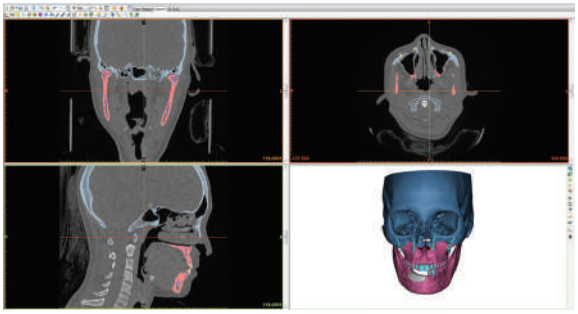


Figure 185: Design Software.

2 You can choose to send us the stereolithographic model , reproducing a plastic model of the missing piece of bone (usually the doctors rely on an external laboratory). IBI can use the stereolithographic model to reconstruct the custom-made piece, by previous HD scan.

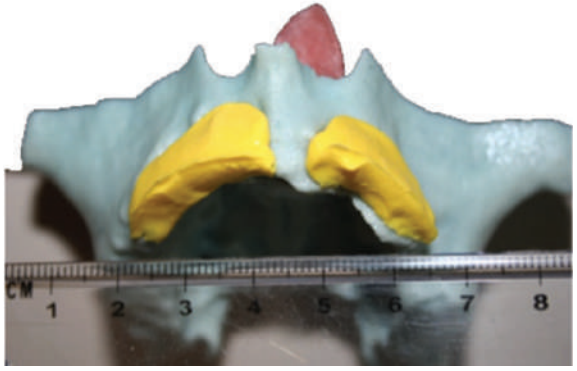


Figure 186: Stereolithographic model.

3 If you send the design file (.STL), IBI can produce directly the piece, without additional costs. After the IBI's feasibility check.

Figure 187: .STL model, output of the design software.

7.2 SMARTBONE® ON DEMAND™ CLINICAL PROCEDURE

It's mandatory to plan each clinical case by using a CBCT technology that provides an increased accuracy, and less morbidity (Figure 166).

It is suggested proceeding with these steps:

- Evaluate the oral epithelium of the gum, which must be well keratinized.
- Perform a surgical incision on the crest.
- Remove muscle fibers, using a dissector, and incise a muco-periodontal flap, only in the area where the bone block is inserted, because apically a partial thickness has to be performed in order to avoid tension on the flaps during the closure.
- Proceed with a blunt dissection of the muco-periodontal flap and elevate it in distal direction to access the bone (Figure 167).
- Perform an intramedullary canalization to let the blood flow towards the surgical area; SmartBone® is highly hydrophilic and absorbs blood quickly.
- The platelet promotes cellular colonization of the biomaterial, in particular by the mesenchymal stem cells that promote the osteogenic process.
- Before placing the custom bone graft, it is always a good practice to hydrate the graft during the fixing process exclusively with patient's blood (Figure 167).

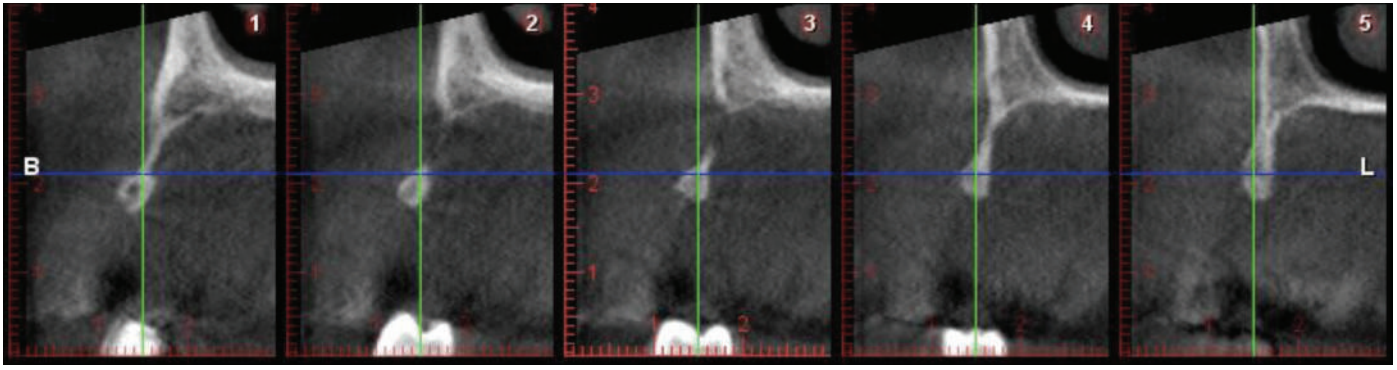


Figure 188: CBCT evaluation in order to formulate the treatment plan.

- Place the block of SmartBone® On Demand™ in the patient's bone defect. Thanks to the polymeric coating, SmartBone® is not reabsorbed during the first healing/osteo-integration period. SmartBone® allows to manage the flaps easily without using a bigger volume compared to the real needed volume: flaps tension, after suturing, will be reduced. If it is preferred to add extra material, 5-10% extra-volume should not be exceeded (Figure 168).
  Fix the block with osteo-synthesis screws in order to ensure perfect primary stability to prevent any future micro

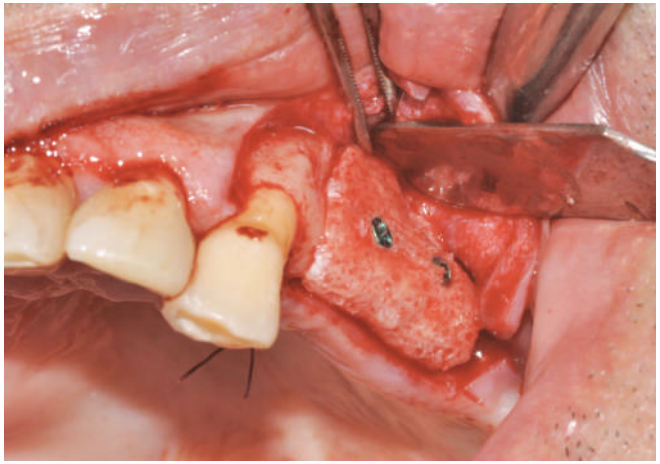


Figure 189: Custom bone graft fixation.

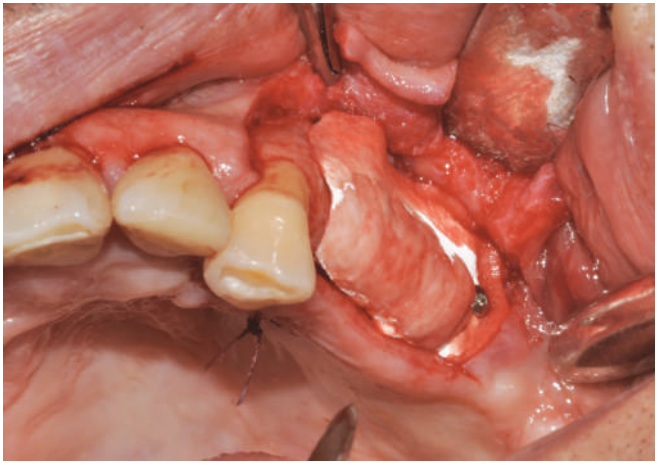


Figure 190: Surgical area covered by reasorbable membrane.

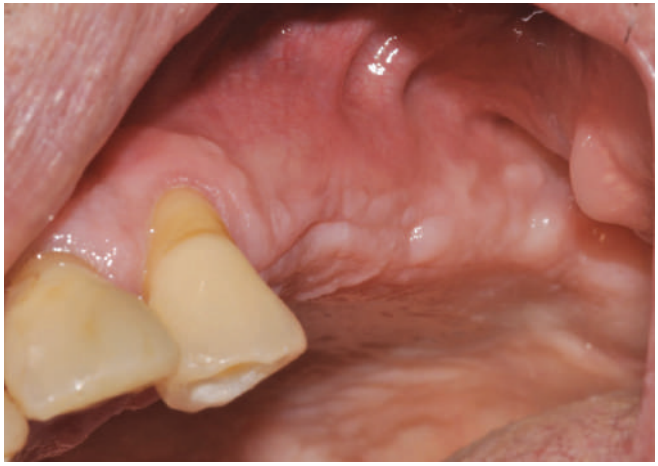


Figure 191: Soft tissue during the healing period.

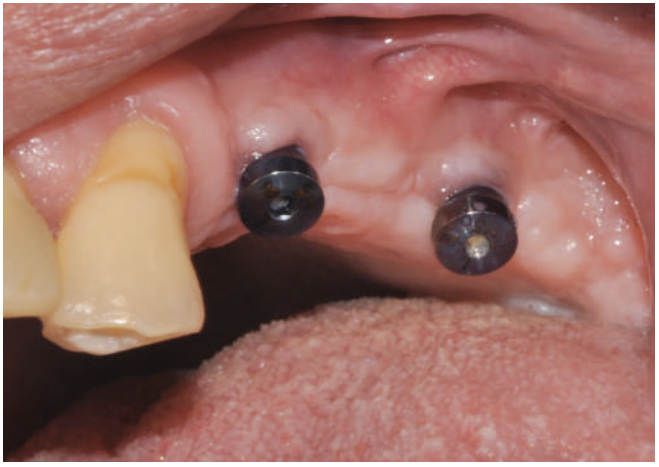


Figure 192: Soft tissue healed after implant placement.

These instructions are for educational purposes only. Surgical techniques may vary depending on the clinical operator.

movements. SmartBone® has a good screw tenacity, so it can be fixed with screws without the risk of breaking the biomaterial; furthermore, this procedure enhances its stability (Figure 169).
Cover the surgical area with a resorbable membrane to stabilize the platelet, bovine pericardium membrane is suggested (Figure 168).

- Suture the flaps. Ensure an adequate release of the flap to obtain a closure without tension and reconnect the flap of the soft tissue; release the periosteum to facilitate the closure. It is preferable to suture using an atraumatic needle, and ensure a continuous closure by primary intention without tension.

- Evaluate the passive mobilization of the flap, already performed previously with the partial apical thickness, and if needed ease/loose the apical part better, to guarantee a passive coverage of the graft and the membrane without any tension. It is preferred to use at least 2 horizontal mattress sutures, to enable the contact between the connective wall of the opening flaps, avoiding eventual epithelial migration, and use single sutures after complete closure of the flaps. The closure must be perfect without leaving any opening space.

- After 6-8 months, it is normally possible to proceed with the implant placement; however, each case needs a specific clinical evaluation by radiography/CT scan (Figure 170).

Use a scan programto discover further information about SmartBone® On Demand™

These instructions are for educational purposes only. Surgical techniques may vary depending on the clinical operator.

7.3 CLINICAL CASES

CASE 1 - SMARTBONE® ON DEMAND™

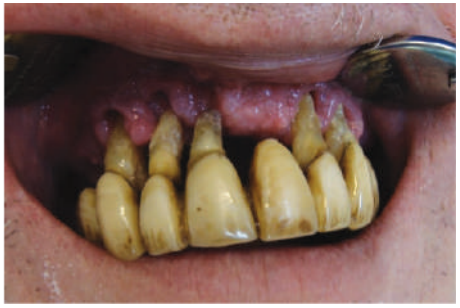


Figure 193: Initial condition.

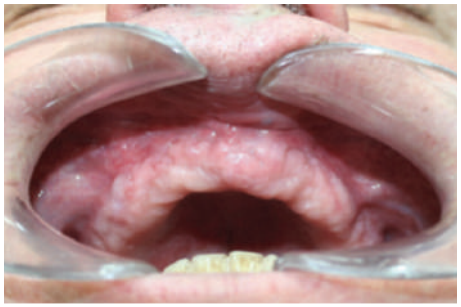


Figure 194: Pre-surgical situation after elements extraction.

Physician:
Dr. E. Messo

Patient:

Male, 60 years old, no smoker, no disorder.

Surgical anatomic site:

Right top arch.

Surgical procedure:

Horizontal and vertical augmentation with SmartBone® On Demand™.

PRE-OPERATION

Horizontal and vertical augmentation with SmartBone® On Demand™.

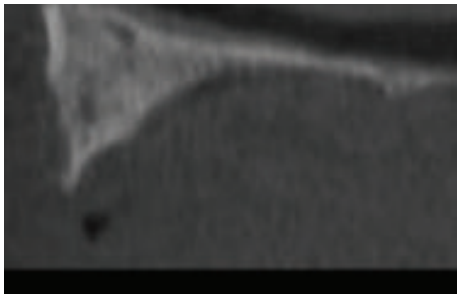


Figure 195: CBCT section of the bone defect.

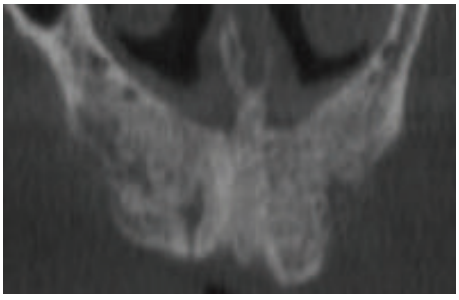


Figure 196: CBCT section of the bone defect.

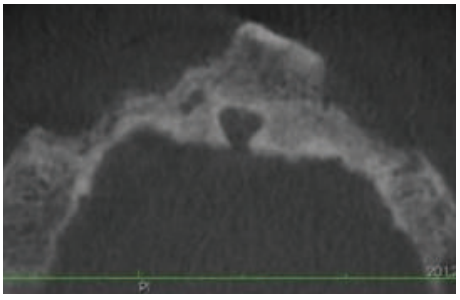


Figure 197: CBCT section of the bone defect.

Courtesy of Dr. E. Messo

PROJECT

3D-reconstruction (obtained starting from the CT-scan) by using software. The pieces were also reconstructed and tested on a stereolithographic model.

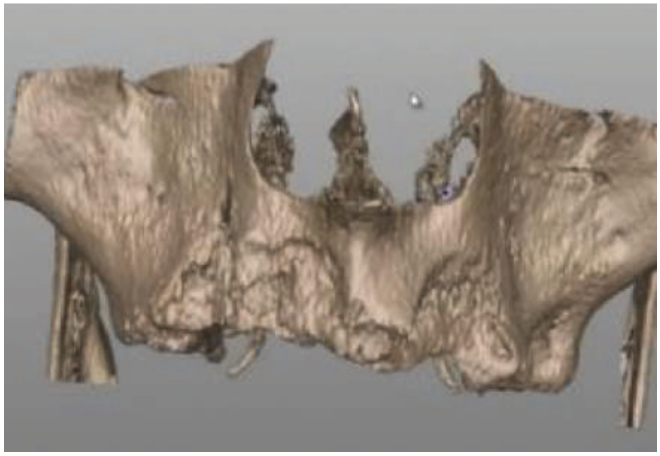


Figure 198: Virtual model.

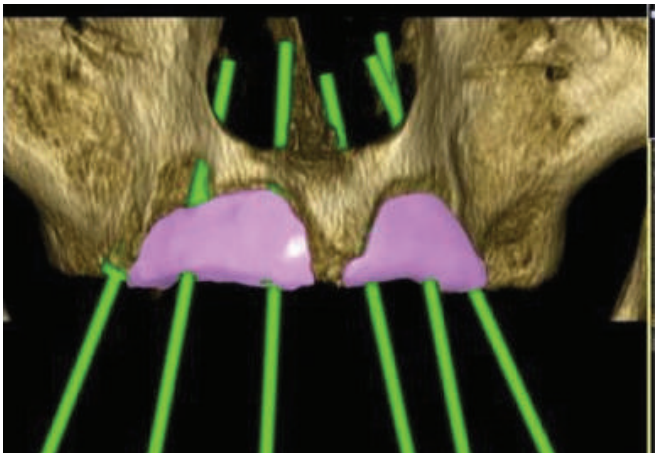


Figure 199: Virtual planning.

SURGERY

The graft has been placed and fixed tight with 2 osteosynthesis screws.

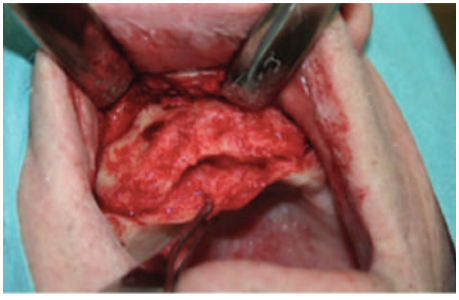


Figure 200: Skeletization of the surgical site.

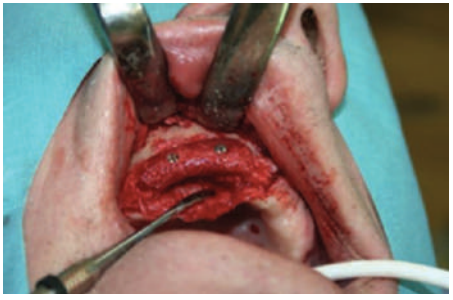


Figure 201: Perfect fit of the custom graft during fixation.

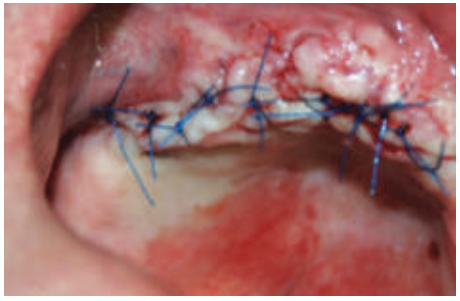


Figure 202: No tension sutures.

Courtesy of Dr. E. Messo

FOLLOW-UP 2 MONTHS

The status of the tissues and the new bone is very good.

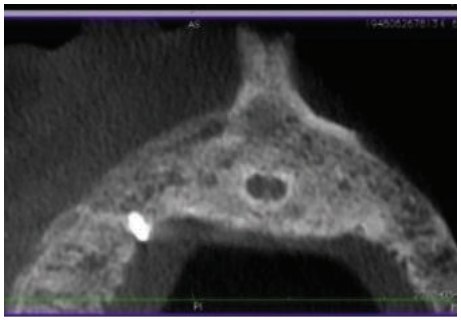


Figure 203: CBCT section of the surgical site.

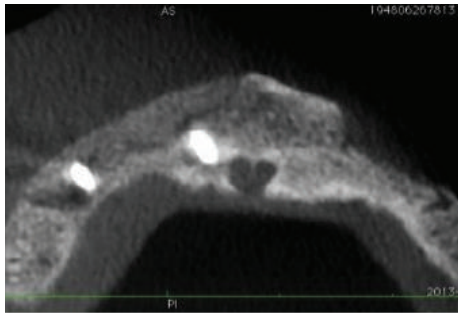


Figure 204: No resorption occurred, the graft volume is preserved and the status of the new bone is good.

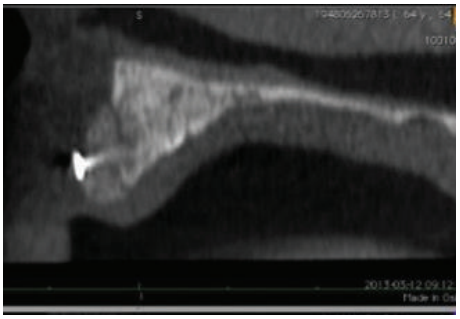


Figure 205: CBCT section of the surgical site.

IMPLANT PLACEMENT 8 MONTHS AFTER BONE AUGMENTATION

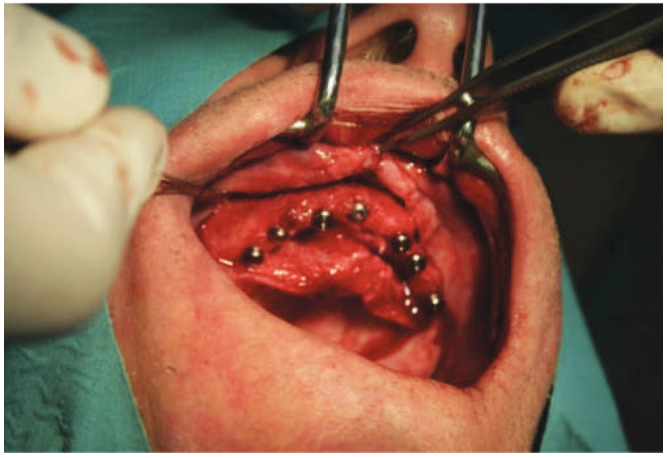


Figure 206: no resorption occurred, the graft volume is preserved and the status of the new bone is good

Courtesy of Dr. E. Messo

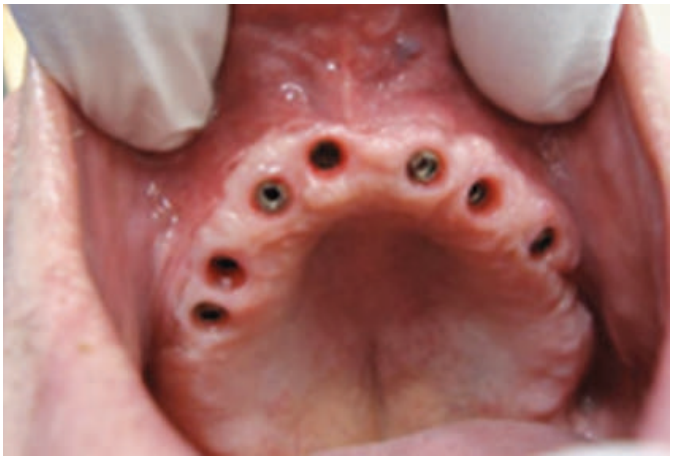


Figure 207: Good healing of the soft tissue.

HISTOLOGICAL ANALYSIS

Histology (highlight SmartBone® VS newly formed tissue; staining method): thin trabecular bone with a mature lamellar structure. No reaction for foreign body.

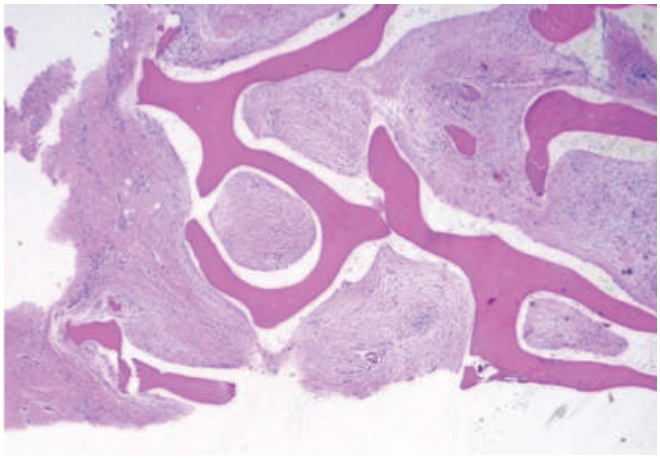


Figure 208: Histological analysis 8 months.

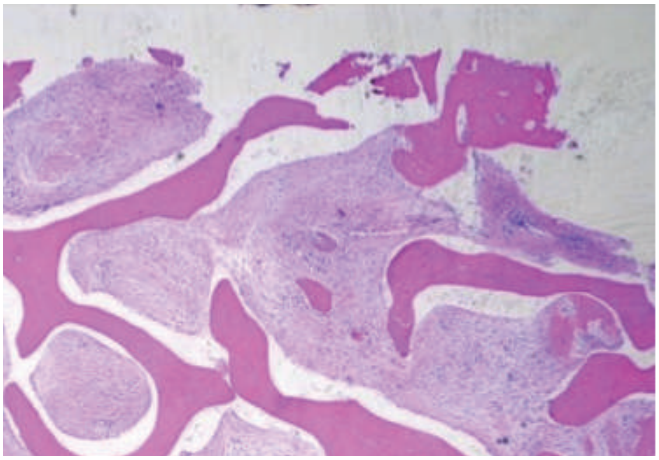


Figure 209: Histological analysis 8 months.

FOLLOW-UP 1 YEAR

Valuation: Final prosthesis placement.

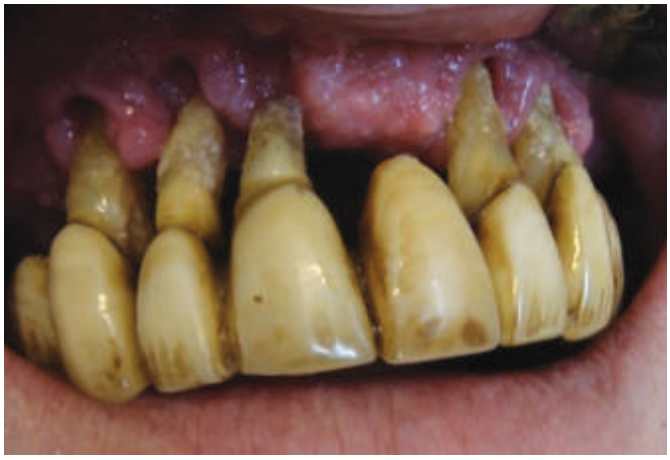


Figure 210: Initial condition.

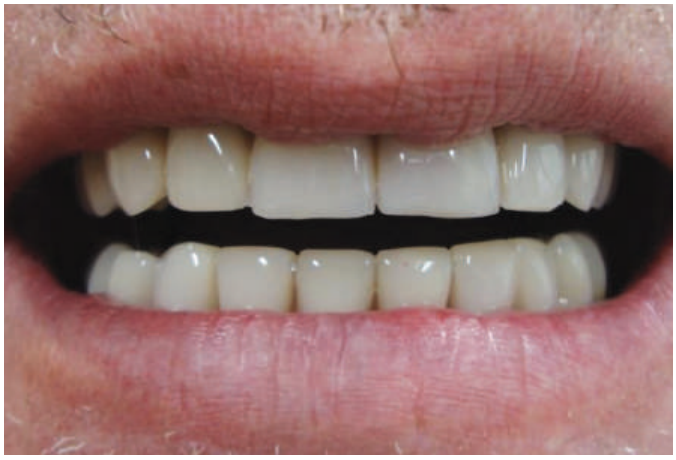


Figure 211: Final prosthesis placement; satisfactory aesthetic result.

Courtesy of Dr. E. Messo

FOLLOW-UP 7 YEARS

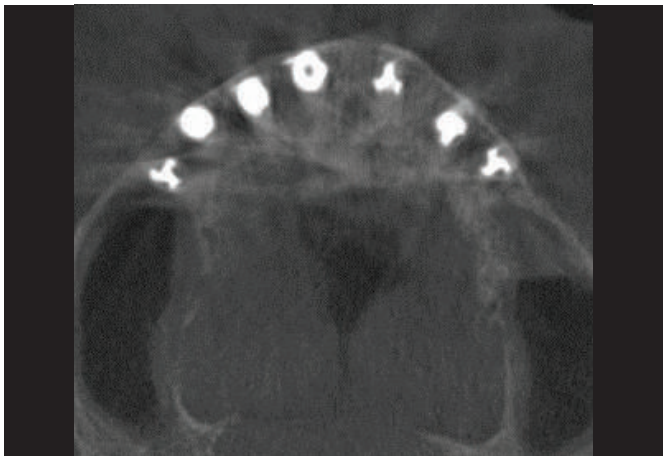


Figure 212: CBCT Axial view section 1.

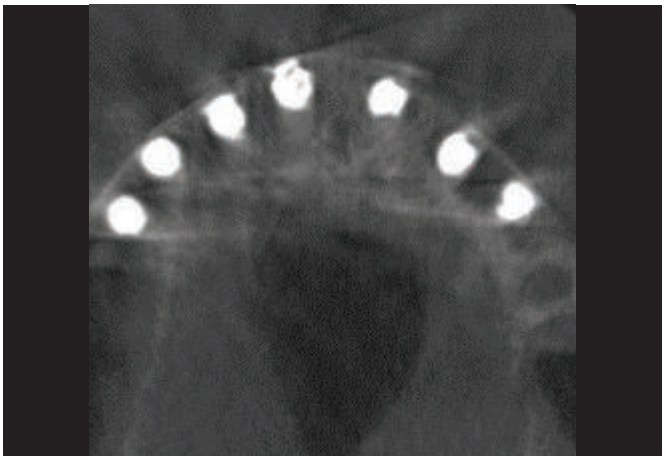


Figure 213: CBCT Axial view section 2.

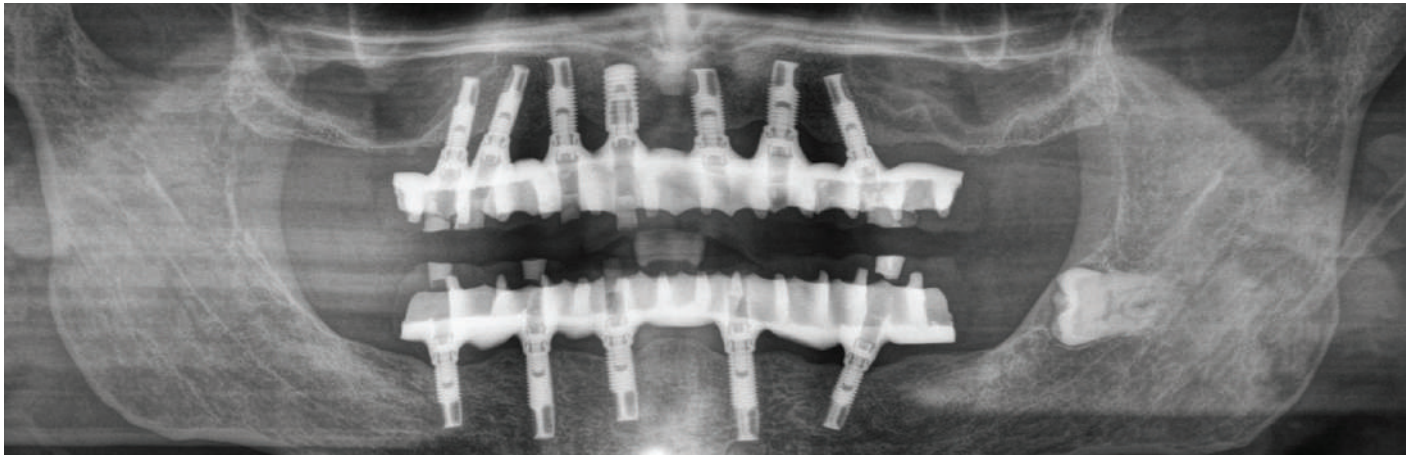


Figure 214: Rx panoramic view.

applied sciences

MDPI

Case Report

Custom-Made Horizontal and Vertical Maxillary Augmentation with Smartbone® On Demand™: A Seven-Year Follow-Up Case

Elias Messo [1,2], Carlo F. Grottoli [3,*], Giuseppe Perale [3,4,5] and Jan-Michaél Hirsch [2,6]

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2 Department of Surgical Sciences, Oral and Maxillofacial Surgery, Medical Faculty, Uppsala University, 75185 Uppsala, Sweden; Jan.Hirsch@surgsci.uu.se or jan.hirsch@sll.se
3 Industrie Biomediche Insubri SA, 6805 Mezzovico-Vira, Switzerland; giuseppe@ibi-sa.com
4 Faculty of Biomedical Sciences, University of Southern Switzerland (USI), 6900 Lugano, Switzerland
5 Ludwig Boltzmann Institute for Experimental and Clinical Traumatology, 1200 Vienna, Austria
6 Department of Research & Development Public Dental Services Region Stockholm, 11382 Stockholm, Sweden
* Correspondence: carlo.grottoli@ibi-sa.com

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Abstract: The presence of non-sufficient bone height and width requires an increase in the amount of bone available to insert an implant. Different materials are described in the literature, and the "custom-made bone graft approach" is a modern option which currently requires a preoperative stage of studying the bone defect and designing the implant. SmartBone® (SB®) mimics the characteristics of healthy human bone. Thanks to the strong performance, high workability, resistance and shape retention of SB®, it is possible to obtain SmartBone® on Demand™, a bone graft uniquely shaped exactly to patient specifications, produced by following the data precisely and contoured to the bone defect site. The aim of this study was to determine the success over 7 years following a customized SmartBone® on Demand™, a xeno-hybrid bone graft and installation of implants in a maxillary horizontal and vertical atrophy. This case study presents the diagnosis for a 60-year-old male patient requesting the rehabilitation of his edentulous maxilla with dental implants. Preoperative evaluation included the study of photographs, a radiological examination and 3D reconstruction to assess the missing bone, implant size, positioning of implants and anatomical landmarks. Rehabilitation included the insertion of a custom-made xeno-hybrid bone block into the maxilla in order to restore the anatomy prior to the implants' placement. The newly developed bone substitute SB® is a safe and effective material, and its custom-made variant SmartBone® on Demand™ has been shown to be a valid alternative to traditional autologous bone grafting techniques in terms of accuracy, absence of infection/rejection and overall clinical outcome.

Keywords: bone substitute; SmartBone On Demand; custom implants; bone regeneration; xeno-hybrid bone graft

CASE 2 - SMARTBONE® ON DEMAND™

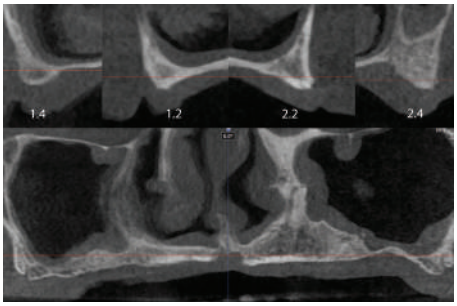


Figure 215: Pre-operation.

Physician:
Dr. R. Ghiretti

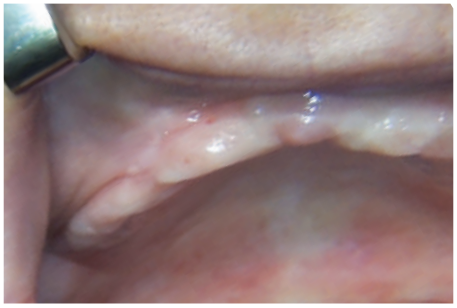


Figure 216: Initial condition of the soft tissue.

Patient:	Female, 64 years old.
Surgical anatomic site:	Pre Maxillary recostruction due to bone atrophy.
Surgical procedure:	Horizontal and vertical augmentation with SmartBone® On Demand™.

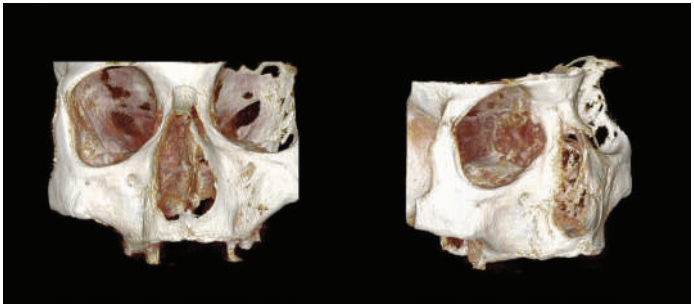
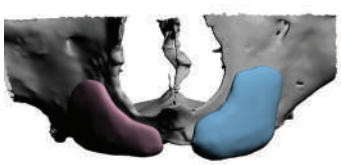


Figure 217: 3D Render pre-operation.



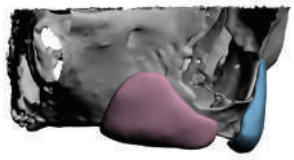


Figure 218: 3D visual reconstruction.

Courtesy of Dr. R. Ghiretti

SURGERY

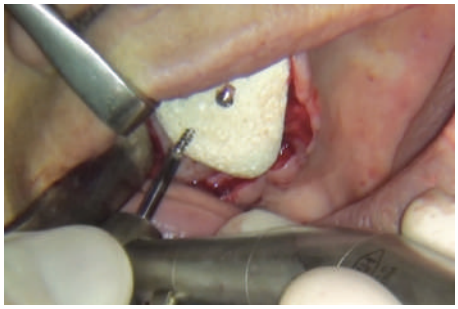


Figure 219: Perfect fit of the custom graft.

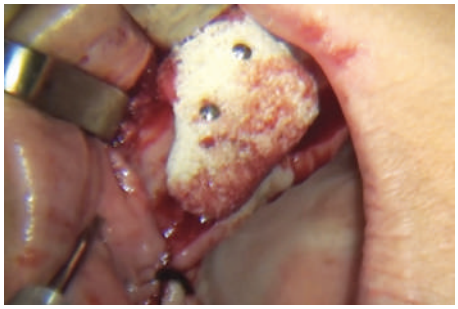


Figure 220: Fixation of the custom graft.

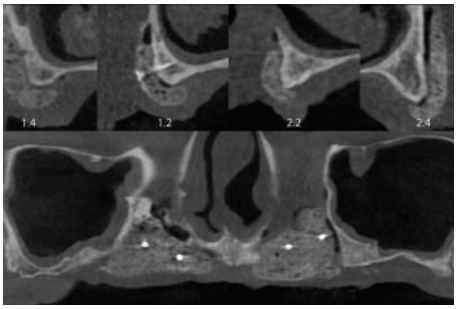


Figure 221: CBCT image after surgery.

IMPLANT PLACEMENT AFTER 8 MONTHS

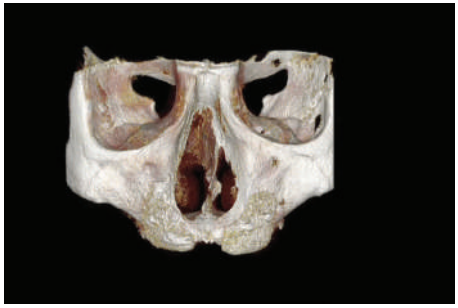


Figure 222: 3D Render of the reconstruction.

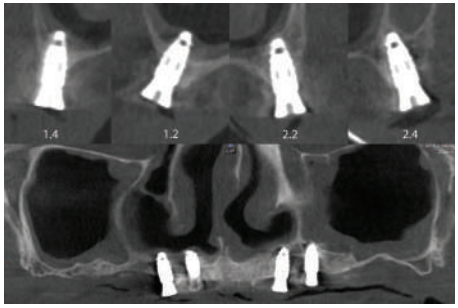


Figure 223: CBCT check after placement.

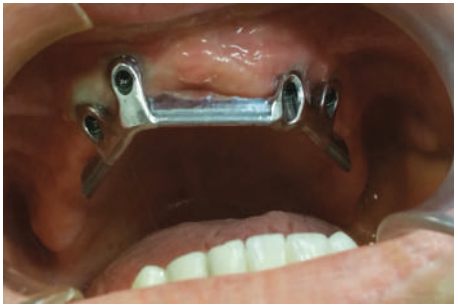


Figure 224: Prosthesis.

FOLLOW-UP

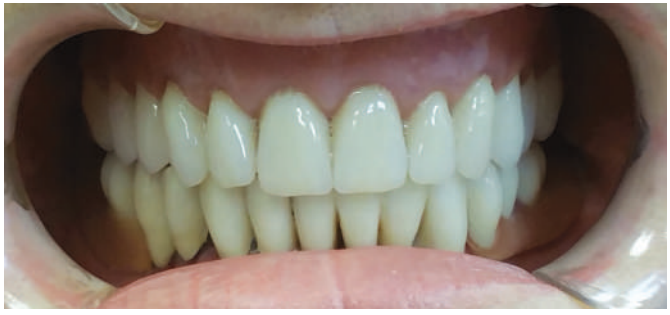


Figure 225: Final restoration.

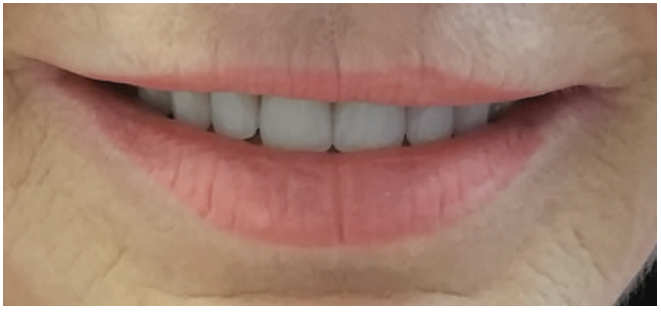


Figure 226: Final prosthesis placement; satisfactory aesthetic result.

Courtesy of Dr. R. Ghiretti

CASE 3 - SMARTBONE® ON DEMAND™

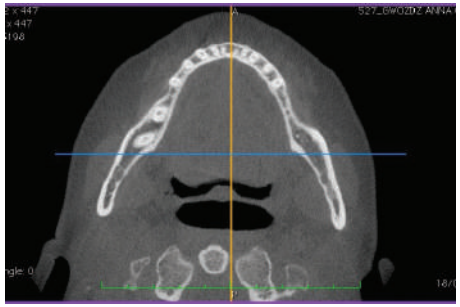


Figure 227: CTCB pre-op.

Physician:
Dr. M. Martini

Patient: Female, 57 years old.

Surgical anatomic site: Bone atrophy 35-36.
Surgical procedure: Horizontal and vertical augmentation with SmartBone® On Demand™.

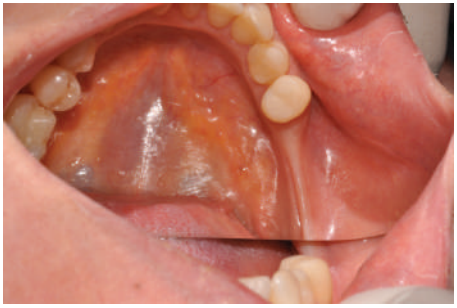


Figure 228: Clinical situation before surgery.

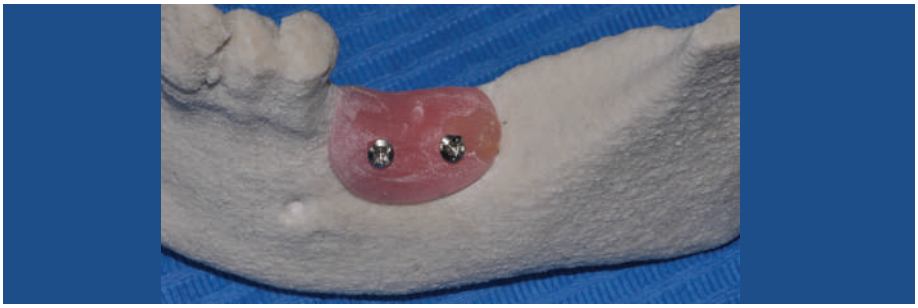


Figure 229: Acrylic resin graft shaped on stereolytographic model.

SURGERY

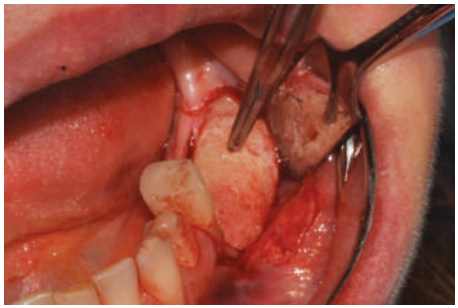


Figure 230: Perfectly matching bone graft placement.

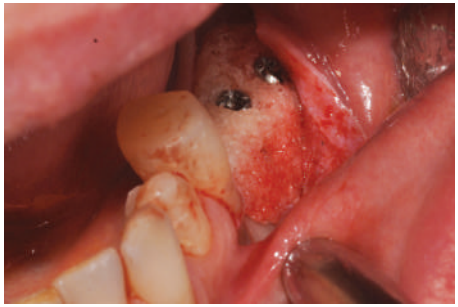


Figure 231: Bone graft screwed to the mandible.

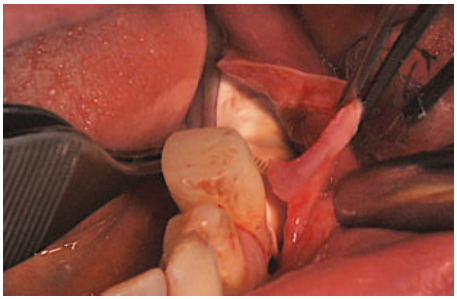


Figure 232: Collagen membrane.

Courtesy of Dr. M. Martini

FOLLOW-UP FROM 1 MONTH TO 6 MONTHS

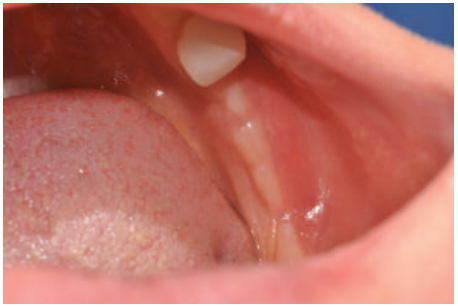


Figure 233: Healing after 1 month.

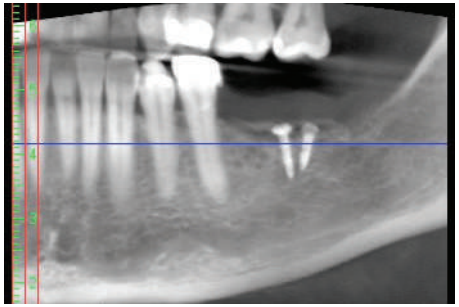


Figure 234: Healing after 6 months.

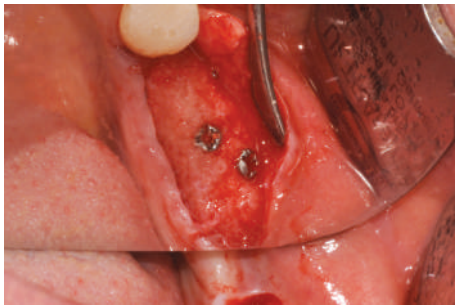


Figure 235: Bone quality after 6 months.

IMPLANT PLACEMENT

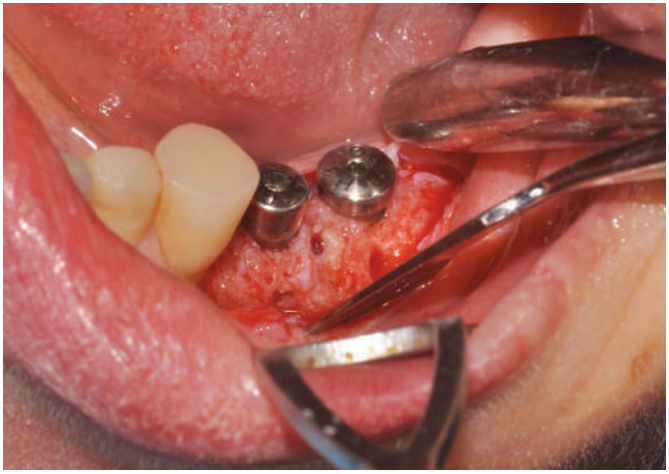


Figure 236: Implant placement after 6 months.

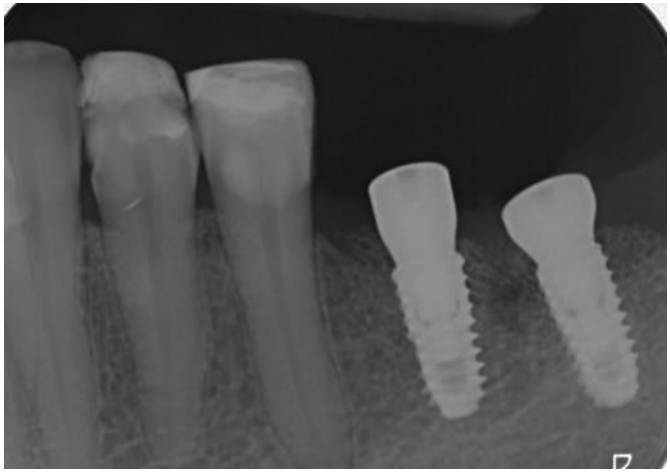


Figure 237: X-Rays post-op.

Courtesy of Dr. M. Martini

CASE 4 - SMARTBONE® ON DEMAND™

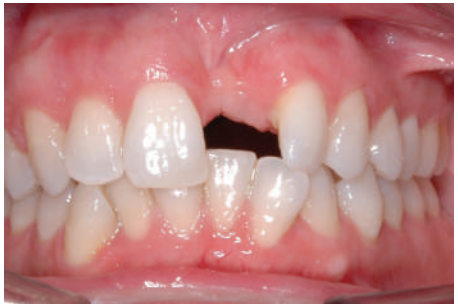


Figure 238: Initial condition.

Physician:
Dr. J. L. Latorre Valenzuela

Patient: Female, 42 years old.

Surgical anatomic site: Pre maxilla, 21.
Pre-surgical clinical situation: Bone atrophy and periodontal recurrent complication.

SURGERY

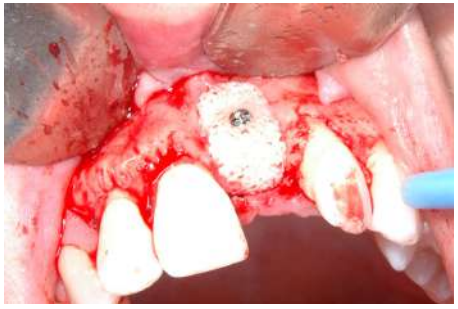


Figure 239: Custom graft fixation.

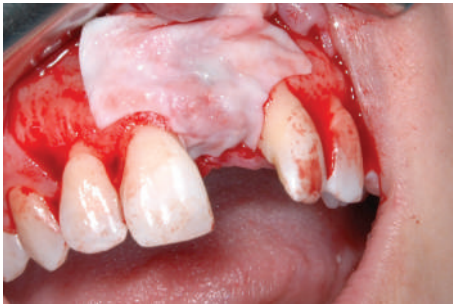


Figure 240: Membrane positioning.

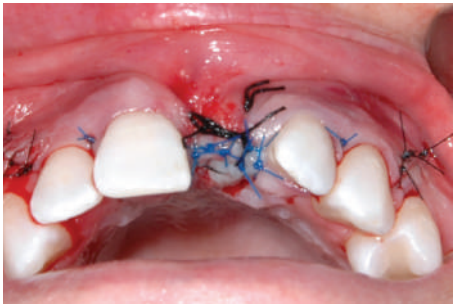


Figure 241: Suture.

FOLLOW-UP FROM 5 MONTHS TO 2,5 YEARS

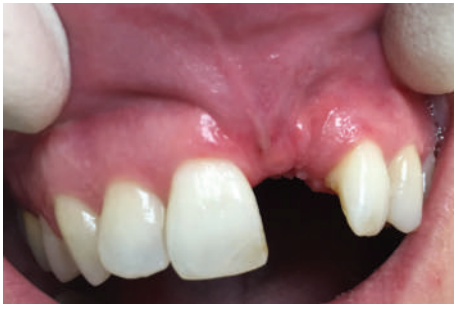


Figure 242: Follow-up 5 Months.

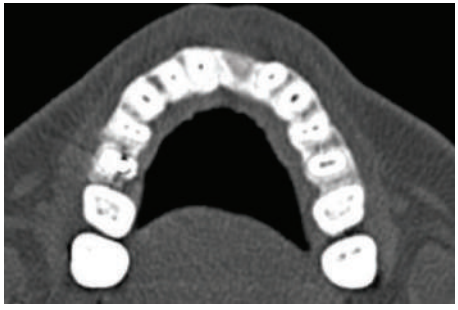


Figure 243: Follow-up 10 Months.

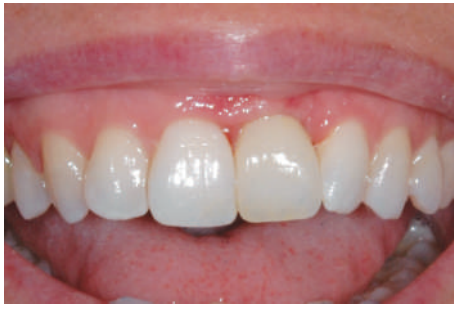


Figure 244: Follow-up 2,5 Years.

Courtesy of Dr. J. L. Latorre Valenzuela

CASE 5 - SMARTBONE® ON DEMAND™ adapted from (La Monaca et al. 2020)

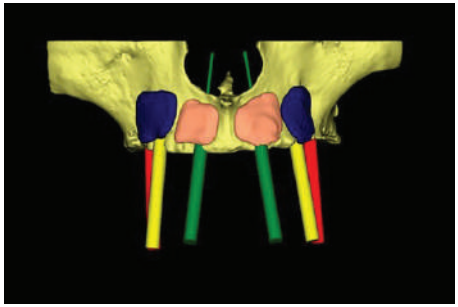


Figure 245: Virtual model of the graft blocks.

Physician:
Dr. G. La Monaca

Patient: Female.

Surgical anatomic site: Entire upper jaw (12,14,21,24)

Pre-surgical clinical situation: Severe horizontal atrophy treated with custom made bone blocks.

SURGERY

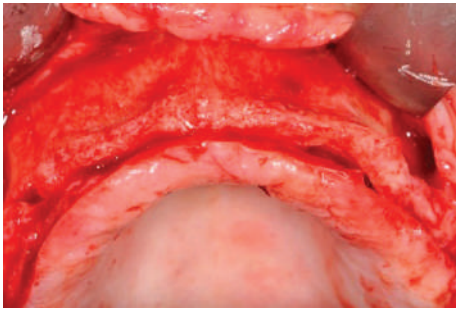


Figure 246: Skeletonization of the maxillary buccal surface by elevating the mucoperiosteal flap.

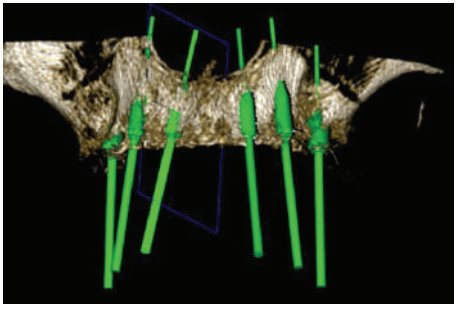


Figure 247: Planning of the imppant insertion.

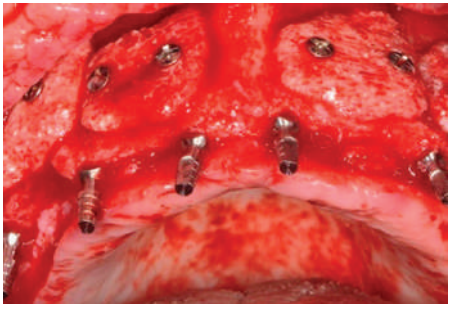


Figure 248: Custom-made blocks fixation and six provisional implants insertion.

REOPENING AT 6 MONTHS

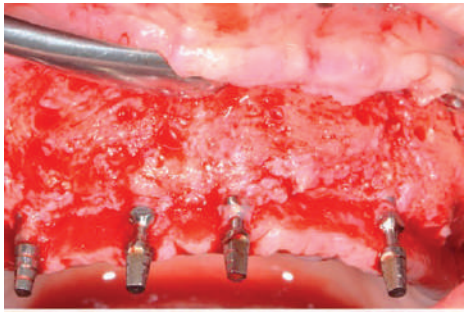


Figure 249: Exposition of the grafted maxillary buccal surface.

Courtesy of Dr. G. La Monaca

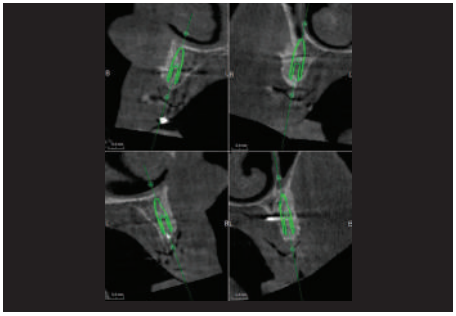


Figure 250: CBCT performed at 6 months after reconstructive surgery, shows the integration of grafted blocks at planned implant sites.

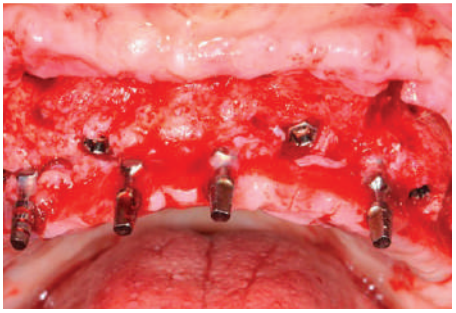


Figure 251: Six implants positioned at planning sites.

HYSTOLOGICAL ANALYSIS 6 MONTHS

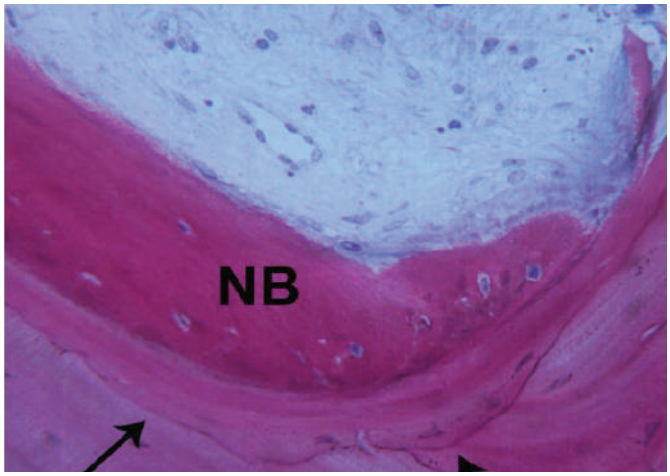


Figure 252: Newly formed bone (NB) and biomaterial interface (black arrows) show a similar affinity for dyes. (Acid fuchsin-Toluidine blue 100 and 200X).

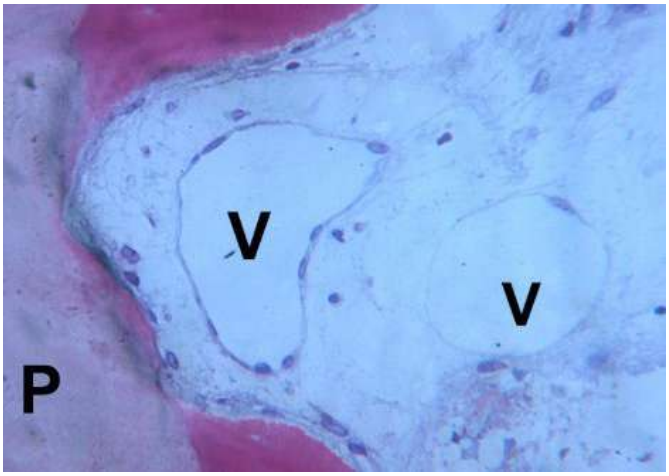


Figure 253: Close to the newly formed bone (NB) and biomaterial block (P), many blood vessels (V) are present. (Acid fuchsin-Toluidine blue 200X).

FOLLOW-UP 8 MONTHS

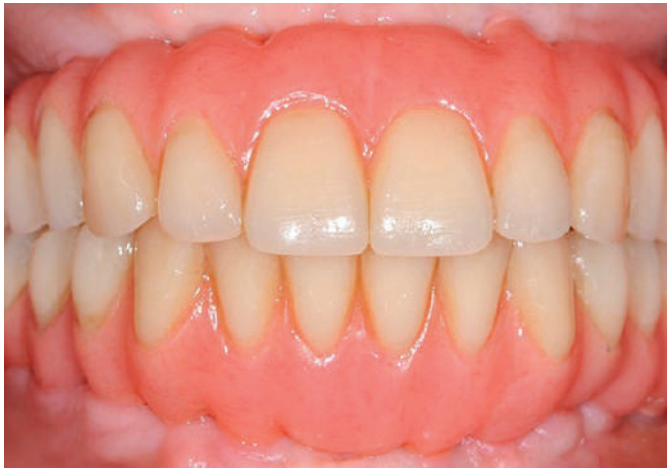


Figure 254: Definitive prosthetic rehabilitation at 8 months.

FOLLOW-UP 2 YEARS

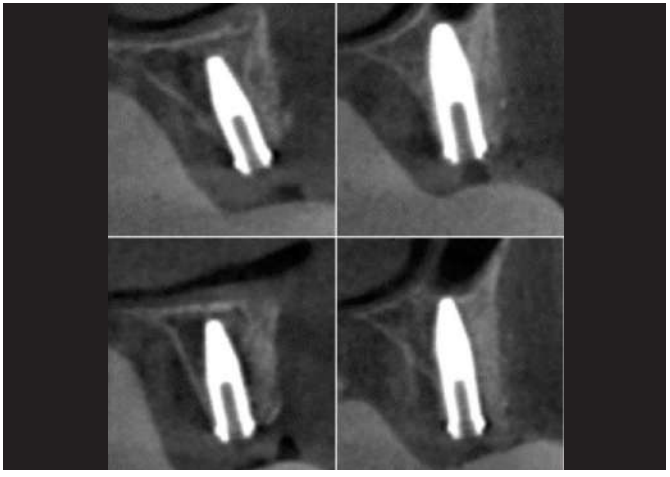


Figure 255: CBCT, performed at a 2-year follow-up, shows no signs of inflammation and bone resorption at the grafted sites and around implants.

applied sciences

MDPI

Technical Note

Xeno-Hybrid Composite Scaffold Manufactured with CAD/CAM Technology for Horizontal Bone-Augmentation in Edentulous Atrophic Maxilla: A Short Communication

Maria Paola Cristalli [1], Gerardo La Monaca [2], Nicola Pranno [2,*], Susanna Annibali [2], Giovanna Iezzi [3] and Iole Vozza [2]

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[2] Department of Oral and Maxillo-Facial Sciences, Sapienza, University of Rome, 00161 Rome, Italy; gerardo.lamonaca@uniroma1.it (G.L.M.); susanna.annibali@uniroma1.it (S.A.); iole.vozza@uniroma1.it (I.V.)
[3] Department of Medical, Oral and Biotechnological Sciences, University of Chieti-Pescara, 66100 Chieti, Italy; giovanna.iezzi@unich.it
* Correspondence: nicola.pranno@uniroma1.it; Tel.: +39-06-49976651; Fax: +39-06-44230811

Received: 9 March 2020; Accepted: 10 April 2020; Published: 12 April 2020

check for updates

Abstract: The present short communication described a new procedure for the reconstruction of the horizontal severely resorbed edentulous maxilla with custom-made deproteinized bovine bone block, fabricated using three-dimensional imaging of the patient and computer-aided design/computer-aided manufacturing (CAD/CAM) technology. The protocol consisted of three phases. In the diagnosis and treatment planning, cone-beam computed tomographic scans of the patient were saved in DICOM (digital imaging and communication in medicine) format, anatomic and prosthetic data were imported into a dedicated diagnostic and medical imaging software, the prosthetic-driven position of the implants, and the graft blocks perfectly adapted to the residual bone structure were virtually planned. In the manufacturing of customized graft blocks, the CAD-CAM technology and the bovine-derived xenohybrid composite bone (SmartBone® on Demand - IBI SA - Industrie Biomediche Insubri SA Switzerland) were used to fabricate the grafts in the exact shape of the 3D planning virtual model. In the surgical and prosthetic procedure, the maxillary ridge augmentation with custom-made blocks and implant-supported full-arch screw-retained rehabilitation were performed. The described protocol offered some advantages when compared to conventional augmentation techniques. The use of deproteinized bovine bone did not require additional surgery for bone harvesting, avoided the risk of donor site morbidity, and provided unlimited biomaterial availability. The customization of the graft blocks reduced the surgical invasiveness, shorting operating times because the manual shaping of the blocks and its adaptation at recipient sites are not necessary and less dependent on the clinician's skill and experience.

Keywords: bone tissue regeneration; xenografts; bone substitutes; computer-aided design /computer-aided manufacturing; deproteinized bovine bone

1. Introduction

Fixed implant-supported prostheses are considered a successful and predictable treatment for the rehabilitation of edentulous patients in the presence of an adequate volume of available bone. In edentulous atrophic jaws, bone deficiencies can prevent implants placement in the ideal prosthetic position with impairment offunction and aesthetics. To overcome these limitations,

Original Article

Evaluation of custom made xenogenic bone grafts in mandibular alveolar ridge augmentation versus particulate bone graft with titanium mesh

Mohammed S. Abuelnaga, Nader N. Elbokle, Mohammed M. Khashaba

Department of Oral and Maxillofacial Surgery, Faculty of Oral and Dental Medicine, Cairo University, Cairo, Egypt.

ABSTRACT

Aim: This study was to evaluate clinically and radiographically the volume ch
customized xenogenic bone graft.
Materials and Methods: A total of 12 patients with mandibular horizontal and v
were selected. They were divided into 2 groups: Group I (Test Group) included 6
ridges were reconstructed with customized Xenogenic bone graft Smartbone (IBI
Group) included 6 patients in which mandibular alveolar ridges were reconstruc
(Smart bone, IBI S.A., Switzerland) grafting to posterior mandibular ridge with ti
analysis of the changes in alveolar ridge in both Groups were obtained before and
CBCT. Densitometric analysis of the Postoperative bone formed and compared wit
Results: Four months postoperatively. Measurements made on cone-beam con
postoperative showed significance increase in bone volume by 40 % in the are
(Customized bone) compared with 23% in Control Group. Statistical significant
newly formed bone four months post-operatively in both Groups, however there
density postoperatively between Group I (customized Bone) and Group II (Control
Conclusion: According to the results, the treatment of defective alveolar ridge augn
customized xenogenic bone graft Smartbone (IBI S.A., Switzerland) is successful
the control Group.

Key **Words:** Alveolar ridge defect, bone substitute, CAD/CAM, cone beam computed

Received: 28 June 2018, **Accepted:** 16 August 2018

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and Dental Medicine, Cairo University, Egypt, **Tel.:** 0503758753, **E-mail:** abuelnag

ISSN: 2090-097X, May 2018, Vol. 9, No.2

ORIGINAL ARTICLE

Three-Dimensional Craniofacial Bone Reconstruction With SmartBone on Demand

Enzo Facciuto, MD,* Carlo Francesco Grottoli, MSE, † Maurizio Mattarocci, MD,* Fausto Illiano, MD,* Mara Compagno, PhD,‡ Riccardo Ferracini, MD, PhD, § and Giuseppe Perale, MSE, PhD†‖

Abstract: This is a report of a 34-year-old male lacking of bone development in the frontal and orbital part of the skull due to a surgical removal of a right orbital-front osteoma at the age of five. The integrity of the craniofacial district was important for the young patient also for social acceptance and self-esteem.
Based on computed tomography patient images, a skull model was reconstructed, both digitally and on 3D real model, to best design the needed bone graft. Defect wide extension and surface curvature called for the use of the puzzle technique, where the whole graft is composed by several elements, mechanically slotting into each other. The realization was made possible thanks to the use of a composite xenohybrid bone substitute specifically developed for reconstructive surgery (SmartBone@, by Industrie Biomediche Insubri SA). SmartBone® technology allowed the realization of custom-made grafts which perfectly joined each other and fitted the bone defect thanks to mechanical strength, also at low thicknesses and wide extensions.
The postoperative course was uneventful and computed tomography scans showed new bone formation and complete calvaria continuity already ten months after surgery, with no signs of inflammation over the entire follow up.
This case study represents a proof of concept that SmartBone® On Demand ™ custom-made bone grafts, together with puzzle technique, are effective, easy to handle and provide final excellent functional and aesthetic results.

Key Words: Bone substitute, osteoma, reconstructive surgery, xenograft

(J Craniofac Surg 2019;30: 739–741)

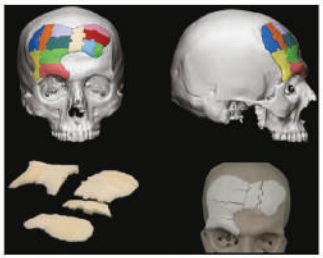
From the *AORN Antonio Caldarelli Napoli UOSC of Maxillo-Facial Surgery; †Industrie Biomediche Insubri SA, Mazzovico-Vira, Switzerland; ‡Center for Research and Medical Studies, AOU Citta della Salute e della Scienza, Turin; §Department of Surgical Sciences (DISC), Orthopaedic Clinic, IRCCS AOU San Martino, Genoa, Italy; and ‖University of Applied Sciences and Arts of Southern Switzerland (SUPSI), Manno, Switzerland.

Received June 15, 2018.
Accepted for publication November 8, 2018.

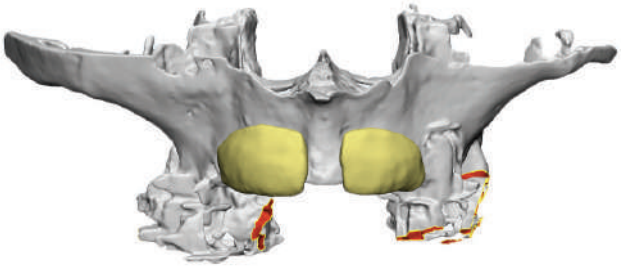
Address correspondence and reprint requests to Carlo Francesco Grottoli, MSE, Via Cantonale 67, CH-6805 Mezzovico-Vira, Switzerland; E-mail: carlo.grottoli@ibi-sa.com

GP is among shareholders of Industrie Biomediche Insubri SA, the Swiss Company owning intellectual property rights on SmartBone, manufacturing and commercializing it, including its custom-made line SmartBone on Demand, that was investigated in this study. CG works for the same company. RF is external clinical advisor to the same company. The other authors report no conflicts ofinterest

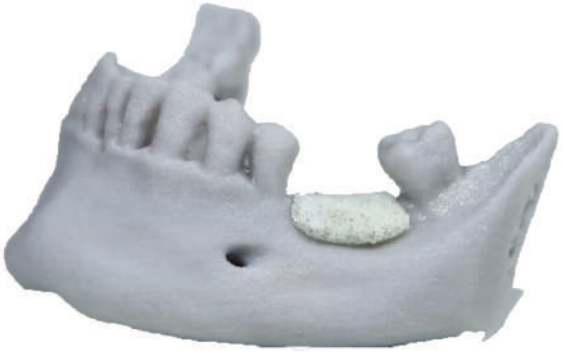
ISSN: 1049-2275
DOI: 10.1097/SCS.0000000000005277



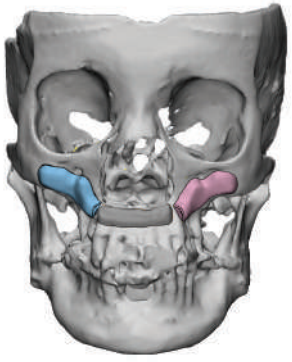
7.4 CLINICAL CASES DESIGN



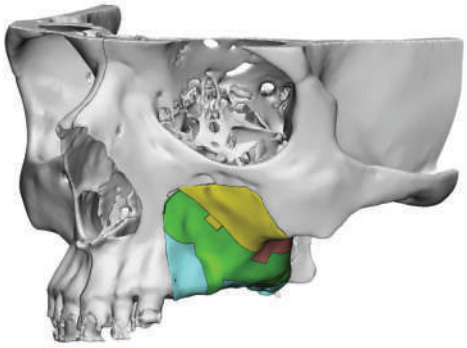
Vertical and horizontal maxillary augmentation
Courtesy of Dr. R. Ghiretti,
Private Dentistry Practice, Mantova



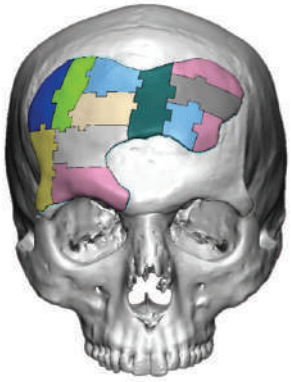
J-shape reconstruction for vertical and horizontal mandibular augmentation



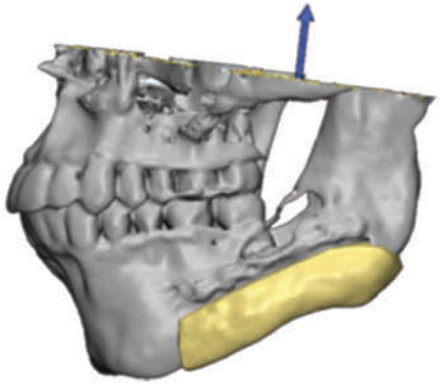
Zygomatzic reconstruction with 3 grafts
Courtesy of Prof. Dr. P. Cascone / Dr. V. Ramieri, Policlinico Umberto I, Roma



Zygomatic, crestal and hemipalatin reconstruction with 4 grafts
Courtesy of Prof. Dr. M. Innocenti / Dr. M. Squadrelli, Azienda Ospedaliera Universitaria, Firenze

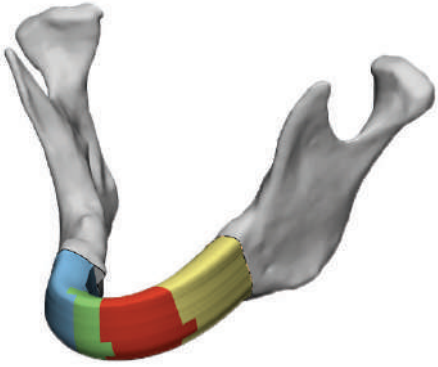


Aesthetic cranial reconstruction with 12 grafts
Courtesy of Dr. E. Facciuto,
Azienda Ospedaliera "A. CARDARELLI", Napoli

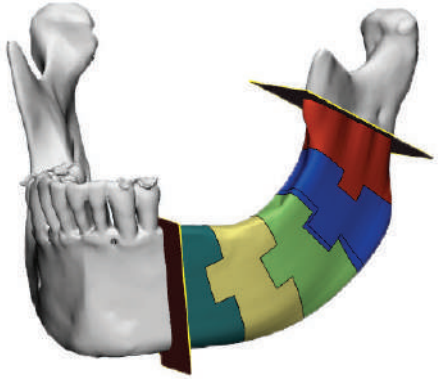


Mandibular reconstruction
Courtesy of Prof. Dr. P. Cascone / Dott. V. Ramieri,
Policlinico Umberto I, Roma

DESIGN SAMPLES



Total mandibular reconstruction



Hemimandibular reconstruction

8

Relevant papers from some of our customers

materials

MDPI

Article

The Influence of Residual Alveolar Bone Height on Graft Composition after Maxillary Sinus Augmentation Using Two Different Xenografts: A Histomorphometric Comparative Study

Silvio Taschieri [1,2,3], Moses Ofer [4], Stefano Corbella [1,2,3], Tiziano Testori [1,2,5], Claudia Dellavia [1], Carlos Nemcovsky [4], Elena Canciani [1], Luca Francetti [1,2], Massimo Del Fabbro [1,2,*,†] and Gianluca Tartaglia [1,†]

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3 Department of Oral Surgery, Institute of Dentistry, I. M. Sechenov First Moscow State Medical University, 119146 Moscow, Russia
4 Department of Periodontology & Dental Implantology, School of Dental Medicine, University of Tel Aviv, 6997801 Tel Aviv-Yafo, Israel; mosesofer@gmail.com (M.O.); carlos@tauex.tau.ac.il (C.N.)
5 Department of Periodontics and Oral Medicine, The University of Michigan, School of Dentistry, Ann Arbor, MI 48109, USA
* Correspondence: massimo.delfabbro@unimi.it; Tel.: +39-02-50319950; Fax: +39-02-50319960
† The authors share the last position.

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Abstract: Aim: To evaluate the hypothesis of a correlation between the preoperative residual alveolar bone height (RBH) and graft maturation after maxillary sinus floor augmentation procedures using two di fferent bone substitutes. Methods: A total of 20 patients who underwent unilateral maxillary sinus floor augmentation with either mineralized deproteinized bovine bone (DBBM) or a xenograft enriched with polymer and gelatin (NBS) were included in this prospective study. Six months after sinus surgery, bone biopsies were harvested with a 3.2 mm diameter trephine bur, prior to dental implant placement. Histomorphometric analysis was performed, and the results were correlated with the individual RBH. Implants were loaded after 5 months ofinsertion, and 1-year implant success and marginal bone level change were assessed. Results: RBH was 2.17± 1.11 mm (range 0.5–3.5 mm) and 2.14 ± 0.72 mm (range 0.5–3.0 mm) in the NBS and DBBM group, respectively. The biopsy analyses for the DBBM group showed woven bone increases by 5.08% per 1-mm increment of RBH; medullary spaces decreased by 9.02%, osteoid decreased by 4.4%, residual biomaterial decreased by 0.34%, and lamellar bone increased by 5.68% per 1-mm increase of RBH. In the NBS group, samples showed woven bone increases by 8.08% per 1-mm increase of RBH; medullary spaces decreased by 0.38%; osteoid increased by 1.34%, residual biomaterial decreased by 0.58%, and lamellar bone decreased by 5.50% per 1-mm increase of RBH. There was no statistically significant difference in the correlation between RBH and lamellar bone, woven bone, and osteoid, independently of the material used. Implant success was 100% in both groups, and marginal bone loss was 1.02 ± 0.42 mm in DBBM and 0.95 ± 0.31 mm in the NBS group after the 1-year follow-up. Conclusion: In spite of the absence of significance, the observed trend for woven bone to increase and medullary spaces to decrease when RBH increases deserves attention. Residual bone dimension might be a determinant in the bone graft maturation after maxillary sinus augmentation.

Accepted: 19 February 2018
DOI: 10.1111/clr.13144

ORIGINAL RESEARCH

WILEY CLINICAL ORAL IMPLANTS RESEARCH

New bone formation after transcrestal sinus floor elevation was influenced by sinus cavity dimensions: A prospective histologic and histomorphometric study

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[2]Private Practice, Cassano allo Ionio, Italy
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[4]Department of Medical, Oral and Biotechnological Sciences, University of Chieti-Pescara, Chieti, Italy

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Claudio Stacchi, Department of Medical, Surgical and Health Sciences, University of Trieste, Trieste, Italy.
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Abstract

Objective: The aim of this multicenter prospective study was to analyze clinically and histologically the influence of sinus cavity dimensions on new bone formation after transcrestal sinus floor elevation (tSFE).

Material and Methods: Patients needing maxillary sinus augmentation (residual crest height <5 mm) were treated with tSFE using xenogeneic granules. Six months later, bone-core biopsies were retrieved for histological analysis in implant insertion sites. Bucco-palatal sinus width (SW) and contact between graft and bone walls (WGC) were evaluated on cone beam computed tomography, and correlations between histomorphometric and anatomical parameters were quantified by means of forward multiple linear regression analysis.

Results: Fifty consecutive patients were enrolled and underwent tSFE procedures, and forty-four were included in the final analysis. Mean percentage of newly formed bone (NFB) at 6 months was 21.2 ± 16.9%. Multivariate analysis showed a strong negative correlation between SW and NFB (R^2 = .793) and a strong positive correlation between WGC and NFB (R^2 = .781). Furthermore, when SW was stratified into three groups (<12 mm, 12 to 15 mm, and >15 mm), NFB percentages (36%, 13% and 3%, respectively) resulted significantly different.

Conclusions: This study represented the first confirmation based on histomorphometric data that NFB after tSFE was strongly influenced by sinus width and occurred consistently only in narrow sinus cavities (SW <12 mm, measured between buccal and palatal walls at 10-mm level, comprising the residual alveolar crest).

KEYWORDS
histomorphometry, osteotomes, sinus floor elevation, sinus width, transcrestal


smartbone®
Bone regeneration technologies
swiss made
smartbone®
INTERNATIONAL PATENTS

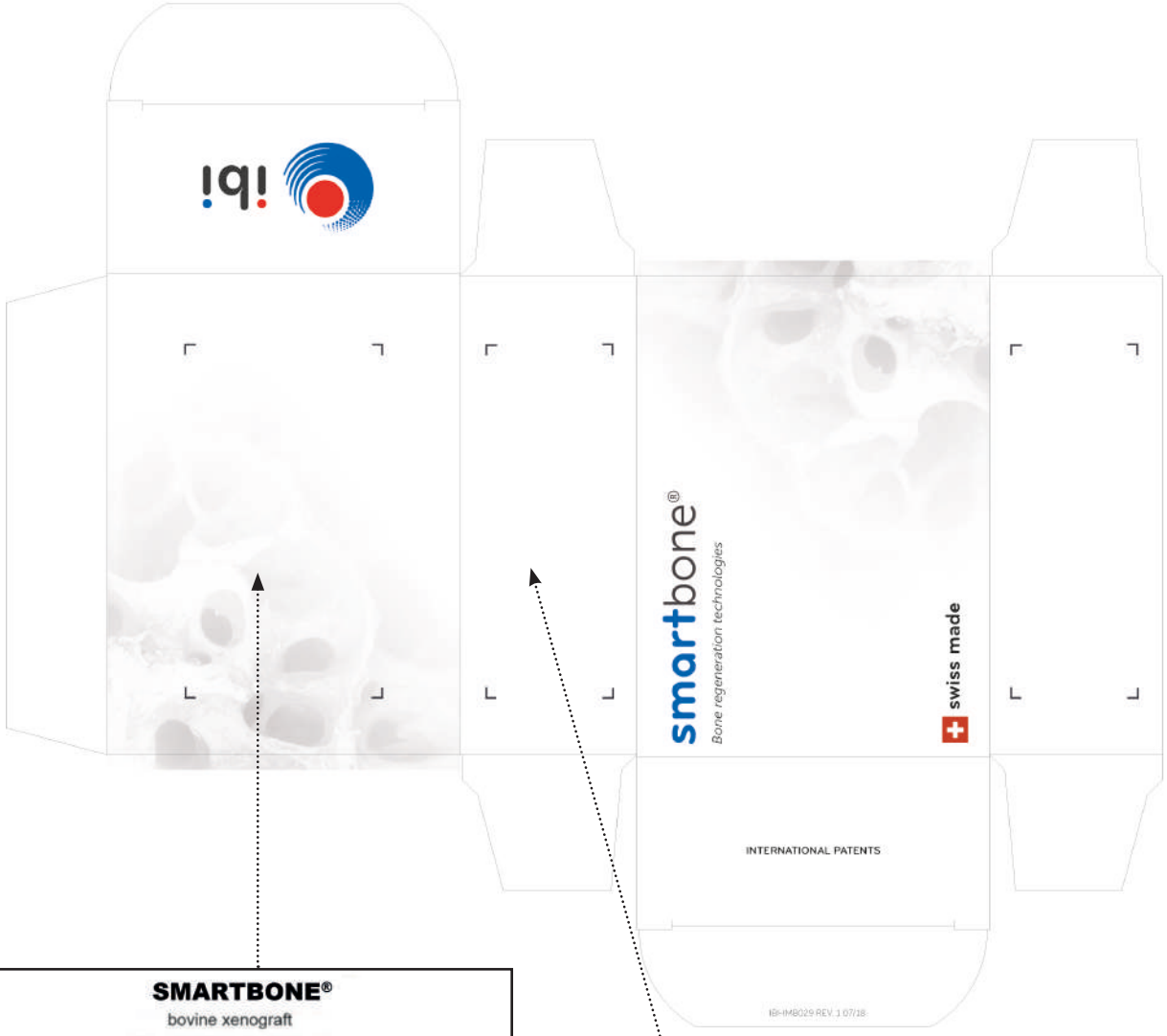
9

Technical information

INTERNAL PACKAGING

Hereunder you can find an example of a SmartBone® 's labes, packagings and the description of the symbols used.

LABELS


smartbone®
Bone regeneration technologies
swiss made
INTERNATIONAL PATENTS
SMARTBONE®
bovine xenograft
Product Description
REF XXXXXXXXX
LOT YYYY-NNN
YYYY-MM
CE
2797
STERILE
SMARTBONE®
Product Description
REF XXXXXXXXX
LOT YYYY-NNN
YYYY-MM
(01)07640178680111
(10)YYYY-NNN
(17)YY-MM-DD

SYMBOLS

Conformity Mark

Legal Manufacturer

Use-by date

Do not resterilize

Do not use if package is damaged

Keep away from sunlight

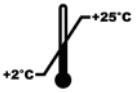
Keep dry

Catalogue number

Sterilized using ethylene oxide

Sterilized using irradiation

Batch code



Temperature range

Do not re-use

Consult instructions for use

Caution

10

FAQs

IBI SA

- **What is IBI's "nationality"?**
  IBI is a Swiss company, headquartered in Canton Ticino, in the south-eastern corner of Switzerland.

- **Where are IBI products manufactured?**
  All IBI production is Swiss made, a guarantee of extreme excellence in terms of both quality and safety.

- **What are IBI's system certifications?**
  IBI is ISO13485:2016 certified.

TECHNICAL INFORMATION

- **What is SmartBone® made of?**
  It's a composite material, made of a bovine derived mineral matrix, reinforced with biopolymers and collagen fragments of porcine origin.

- **What's the biological mechanism of osteointegration of a bone graft?**
  Bone generally has the ability to regenerate completely, but it requires a very small fracture space or some sort of scaffold to do so. Indeed, bone grafting is possible because bone tissue has the ability to regenerate completely if provided the space into which to grow, a bone graft.

  As native bone grows, it will generally replace the graft material completely, resulting in a fully integrated region of new bone. The biologic mechanisms that provide a rationale for bone grafting with composite grafts and xenografts are osteoconduction (guiding the reparative growth of the natural bone) and osteoinduction (encouraging undifferentiated cells to become active osteoblasts). Only few bone grafts ensure a complete remodeling, SmartBone® is among these, together with autografts.

- **What are the top mechanical performances of SmartBone®?**
  Breaking Stress of about 26MPa (av.)
  Elastic Modulus of about 1,2GPa (av.)
  Breaking torque under screw fixation (screw tenacity) >55Ncm (av.)

- **Is SmartBone® an open-porous material?**
  Yes! SmartBone® has an open interconnected porous structure.

- **How is SmartBone®'s microstructure?**
  SmartBone® microstructure was specifically designed to mimic natural healthy human bone, in terms of composition and porosity.

- **Which is the expected (average) time of resorption of the biopolymers present within SmartBone®?**
  They are degraded and resorbed in about 4-6 months: meanwhile they degrade and get resorbed, new born bone is formed.

- **Is SmartBone® hydrophilic?**
  Yes! Due to its composition SmartBone® is extremely hydrophilic and can sustain a 38% w/w (av.) swelling in physiologic fluids. This feature allows the graft to quickly and massively absorb blood once *in situ*, hence sparkling a better and faster integration with the host tissue.

- **Which biopolymers are used?**
  We use biodegradable polymers, the same used in resorbable sutures.

- **Where does the bovine derived mineral matrix of SmartBone® come from?**
  We supply our production with bovine derived tissues directly from fully certified companies in New Zealand, a "BSE negligible risk Country" (formerly known as "BSE free Country").

  We control all our supply chain, according to the most strict norms and highest quality standards, including those of ISO 22442.

- **How is SmartBone® produced?**
  IBI applies a proprietary process to produce SmartBone®.

- **Can the biomaterial be mixed with a saline solution?**
  ABSOLUTELY NOT, the saline solution extracts the proteins from the polymeric reinforcement surface, compromising performances of the graft and thus the final success!

- **Can the biomaterial be added with PRGF?**
  Clinical experience shows that PRGF has no negative effects on the graft. However, it should be noted that this type of protocol tends to favour soft tissue healing more than true bone regeneration.

- **Can the biomaterial be added with CGF?**
  Clinical experience shows that CGF has no negative effects on grafting. However, it should be noted that this type of protocol tends to favour soft tissue healing more than true bone regeneration.

- **Can the biomaterial be added with autologous bone?**
  Clinical experience shows that in particular cases, such as large bone augmentations, the use of patient bone improves the integration process, and it is hence recommended.

- **Can the biomaterial be added with cadaveric/donor bone?**
  The starting material has all the characteristics to achieve an excellent integration and a complete bone remodeling, the insertion of a cadaveric bone unnecessarily increases risk factors.

- **Can the biomaterial be added with synthetic bone (bioglasses, phosphate tricalcium, hydroxyapatite, polymers, collagen sponges, etc.)?**
  The starting material has all the characteristics to achieve by itself an excellent integration and a complete bone remodeling, the insertion of a synthetic bone unnecessarily increases risk factors.

- **Can the biomaterial be inserted into a syringe to increase perfusion and wettability?**
  The material has a very high wettability and hydrophilicity, does not require any kind of treatment. In case of use of larger blocks, or when looking for improved granulates handling, it is recommended to mix SmartBone®
  with patient's blood.

- **Do I need to use a membrane?**
  The use of the membrane is recommended in oral surgery, *e.g.* in cases of horizontal augmentations, in order to protect the graft from any dehiscence.

- **Once the vial or envelope has been opened, can I close it again, re-sterilise it and, if necessary, within what period of time should I use it?**
  Once the primary packaging has been opened (in sterile surgerical environment), the material must be used immediately on a single patient. The surplus material must be disposed of according to IFU. SmartBone® IS SINGLE USE.

- **Why is SmartBone® single use?**
  SmartBone® is provided, in its intact packaging, as a sterile medical device; once opened, it must be used immediately. Storage after opening does NOT ensure safety! SmartBone® is, hence, single use.

- **Can I keep the material in the fridge?**
  The material must be stored according to the instructions on the labels, therefore away from light or heat sources, in a dry place and between +2 and +25 °C.

- **The packaging arrived damaged. What should I do?**
  DO NOT USE THE PRODUCT! Contact your dealer immediately.

- **There were no IFU and/or adhesive label inside the box, what should I do?**
  DO NOT USE THE PRODUCT! Contact your dealer immediately.

SmartBone® MECHANISM OF ACTION

- **When does osteoconduction occur in bone grafting?**
  Osteoconduction occurs when the bone graft material serves as a scaffold for new bone growth that is perpetuated by the native bone. Osteoblasts from the margin of the defect, that is being grafted, utilize the bone graft material as a framework upon which to spread and generate new bone. In the very least, a bone graft material should be osteoconductive.

- **Is SmartBone® osteoconductive?**
  YES! Histological analyses performed during *in vivo* and clinical studies confirmed that SmartBone® supports the ingrowth of stromal stem cells and osteoblasts, which then spread and colonize it, hence generating new bone.

- **How does osteoinduction occur?**
  Osteoinduction involves the stimulation of osteoprogenitor cells to differentiate into osteoblasts that then begin new bone formation.

- **Is SmartBone® osteoinductive?**
  YES! SmartBone is a bone graft material that is both osteoconductive and osteoinductive: histological analyses performed during *in vitro* and *in vivo* and clinical studies confirmed that does not only serve as a scaffold for currently existing osteoblasts but will also triggers the formation of new osteoblasts, theoretically promoting faster integration of the graft.

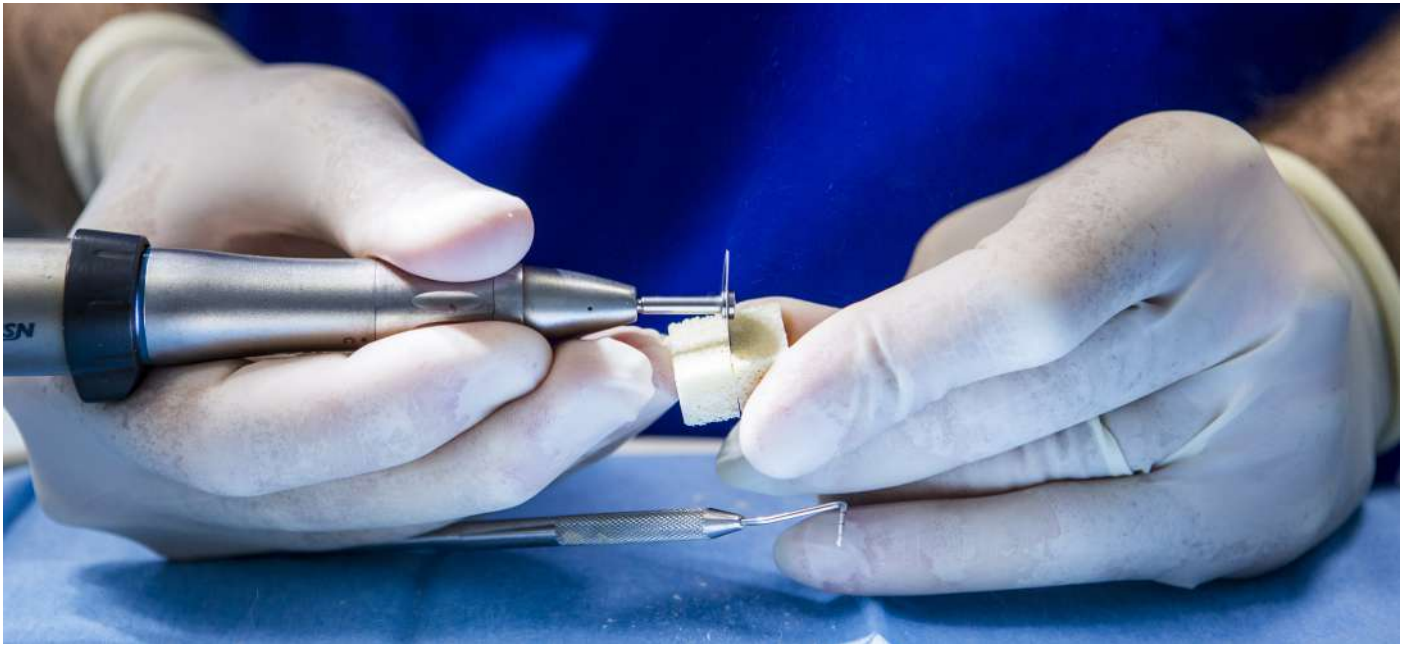
- **What is SmartBone®'s osteointegration dynamic?**
  The cellular response to SmartBone® graft can be described as a progressive neoformation of healthy bone, which occurs alongside the resorption of the graft: both osteoconductive and osteoinductive processes are involved.

- **Which is the timeframe for complete osteointegration of SmartBone®?**
  SmartBone® graft integration can be described as a progressive neoformation of healthy bone, which occurs alongside the reabsorbtion of the graft, involving both osteoconductive and osteoinductive processes on a 16-18 months time window (depending on grafted volume, anatomical position, patient age, sex, health conditions, *etc*).

- **Which type of bone is being formed after grafting with SmartBone®?**
  The osteointegration of SmartBone leads to the formation of type II and type III bone.

- **What type of bone graft exists?**
  Bone grafts may be autologous (bone harvested from the patient's own body, often from the iliac crest), allograft (cadaveric bone usually obtained from a bone bank), or synthetic (often made of hydroxyapatite or other naturally occurring and biocompatible substances) with similar mechanical properties to bone

- **Which type of bone graft is SmartBone®?**
  SmartBone® is a composite bone graft made of a bovine derived mineral matrix, reinforced with biopolymers and collagen fragments: it can hence be categorized as a composite xeno-synthetic graft.



11

Literature References

Papers and books cited in the text are hereby listed, in alphabetical order of first author' surname.
Bold citations are those related to SmartBone® directly.

Abuelnaga, M. S. ; Elbokle, N. N. ; Khashaba M. M. Evaluation of custom made xenogenic bone grafts in mandibular alveolar ridge augmentation versus particulate bone graft with titanium mesh. *OMX.* **2018**, Volume 9 Issue 2 Pages 62-73.

Annals of Oral & Maxillofacial Surgery **2014** Feb 14;2(1):4.

Bornstein, M.M.; Chappuis, V.; von Arx, T.; Buser, D. Performance of dental implants after staged sinus floor elevation procedures: 5-year results of a prospective study in partially edentulous patient. *Clin. Oral Implants Res*. **2008**, 19, 1034-1043.

Carusi, G.; Salin, M.; Scilla, M. *Tecnica MISE – procedure chirurgiche*; EDRA Ed., 2016.

Cingolani (1), A.; Grottoli, C. F.; Esposito, R.; Villa, T.; Rossi, F.; Perale, G. Improving Bovine Bone Mechanical Characteristics for the Development of Xenohybrid Bone Grafts. *Curr. Pharm. Biotechnol.* 2018, *19*, 1005–1013.

Cingolani (2), A.; Casalini, T.; Caimi, S.; Klaue, A.; Sponchioni, M.; Rossi, F.; Perale, G. A Methodologic Approach for the Selection of Bio-Resorbable Polymers in the Development of Medical Devices: The Case of Poly(l-lactide-co-ε-caprolactone). *Polymers (Basel)*. 2018, 10, 851, doi:*10*.3390/polym10080851.

Choukroun J.; Khoury, G.; Khoury F.; Russe, P.; Testori, T.; Komiyama Y.; Sammartino, G.; Palacci, P.; Tunali, M.; Choukroun, E. Two Neglected Biologic Risk Factors in Bone Grafting and Implantology: High Low-Density Lipoprotein Cholesterol and Low Serum Vitamin D, *Journal of Oral Implantology*. **2014**, *40(1)*, 110-114.

Cristalli, M. P.; La Monaca, G; Pranno, N.; Annibali, S.; Iezzi, G.; and Vozza, I. Xeno-Hybrid Composite Scaffold Manufactured with CAD/CAM Technology for Horizontal Bone-Augmentation in Edentulous Atrophic Maxilla: A Short Communication. *Appl. Sci.* **2020**, 10, 2659; doi:10.3390/app10082659

D'Alessandro, D.; Perale, G.; Milazzo, M.; Moscato, S.; Stefanini, C.; Pertici, G.; Danti, S. Bovine bone matrix/poly(L-lactic-co-ε-caprolactone)/gelatin hybrid scaffold (SmartBone®) for maxillary sinus augmentation: A histologic study on bone regeneration. *Int. J. Pharm*. 2017, 523, 534–544, doi:10.1016/j.ijpharm.2016.10.036.

Datta, A.; Gheduzzi, S.; Miles, A.W. A Comparison of the Viscoelastic Properties of Bone Grafts. *Clinic. Biomech.* **2006**, *21(7)*, 761.

Deshpande S. ;Deshmukh J.; Deshpande S. Kahtri R., Deshpande S. Vertical and horizontal ridge augmentation in anterior maxilla using autograft, xenograft and titanium mesh with simultaneous placement of endosseous implants. *J Indian Soc Periodontol*. **2014** Sep-Oct; 18(5): 661–665.

Diss, A.; Dohan, D.M.; Mouhy, J.; Mahler, P. Osteotome Sinus Floor Elevation using Choukroun's Platelet-rich Fibrina as a Grafting Material: a 1year Prospective Pilot Study with Microthreaded Implants. *Oral Surg. Oral Med. Oral Pathol. Oral Radiol. Endod*. **2008**, *105*, 572-579

Duong L.T.; Rodan G. A. Integrin-mediated Signaling in the Regulation of Osteoclast Adhesion and Activation, *Frontiers in Bioscience*. **1998**, *3*, d757-768.

Facciuto, E.; Grottoli, C.F.; Mattarocci, M.; Illiano, F.; Compagno, M.; Ferracini, R.; Perale, G. 3D craniofacial bone reconstruction with SmartBone® on demand™. *The Journal of Craniofacial Surgery*. 2019, *in press*, doi: 10.1097/SCS.0000000000005277.

Fawad, J.; Hameeda, B. A.; Crespi, R.; Romanos, G. E. Role of primary stability for successful osseointegration of dental implants: Factors of influen¬ce and evaluation. *Intern. Med. Appl. Sci.* **2013**, *5(4)*, 162–167.

Fernandez de Grado, G.; Keller, L.; Idoux-Gillet, Y.; Wagner, Q.; Musset, A.-M.; Benkirane-Jessel, N.; Bornert, F.; Offner, D. Bone substitutes: a review of their characteristics, clinical use, and perspectives for large bone defects management. *J. Tissue Eng.* **2018**, *9*, 204173141877681, doi:10.1177/2041731418776819.

Ferracini, R.; Martínez Herreros, I.; Russo, A.; Casalini, T.; Rossi, F.; Perale, G. Scaffolds as Structural Tools for Bone-Targeted Drug Delivery. *Pharmaceutics* 2018, *10*, 122, doi:10.3390/pharmaceutics10030122.

Ferrigno, N.; Laureti, M.; Fanali, S. Dental implants placed in conjunction with osteotome sinus floor elevation: a 12-year life-table analysis from a prospective study on 588 ITI implants. *Clin. Oral Implants Res*. **2006**; *17*, 194-205

Ganz, S. D. CT/CBCT diagnosis and treatment planning concepts for bone grafting applications in Toffler, M. *Implant Site Development*. First edition. Edited by Michael Sonick, Debby Hwang. **2012.**

Ghiretti, R.; Grottoli C., Cingolani, A.; and Perale, G. Clinical Case Employing Two Different Biomaterials in Bone Regeneration. *Appl. Sci*. 2020, 10, 4516; doi:10.3390/app10134516.

Gitelis, S.; Saiz, P. What's new in orthopaedic surgery. *J. Am. Coll. Surg.* **2002**, *194*, 788-91.

Grecchi, F.; Perale, G.; Candotto, V.; Busato, A.; Pascali, M.; Carinci, F. Reconstruction of the Zygomatic Bone with SmartBone®: Case Report. *Journal of Biological Regulators and Homeostatic Agents*. 2014, *29*, 42-47.

Grottoli, C.F., Ferracini, R.; Compagno, M.; Tombolesi, A.; Rampado, O.; Pilone, L.; Bistolfi, A.; Borrè, A.; Cingolani, A.; Perale, G. (2019) A Radiological Approach to Evaluate Bone Graft Integration in Reconstructive Surgeries. *Applied Sciences*, 9, 1469.

Haugen, H.J.; Lyngstadaas, S.P.; Rossi, F.; Perale, G. Bone Grafts: Which is the Ideal Biomaterial? *Journal of Clinical Periodontology*. 2019, *1*, 1–11.

Hierholzer, C.; Sama, D.; Toro, J.B.; Peterson, M.; Helfet, D.L. Plate fixation of ununited humeral shaft fractures: effect of type of bone graft on healing. *J. Bone Joint Surg. Am.* **2006**, *88,* 1442.

Helmy, M.A.; Maxillary Sinus Lifting: Review of the Two Main Approaches. *Global Journal of Otolaryngology*. **2017**, *8 (4)*, 555745

Kuhn L.T.; Grynpas M.D.; Rey C.C.; Wu Y.; Ackerman J.L.; Glimcher M.J. A comparison of the physical and chemical differences between cancellous and cortical bovine bone mineral at two ages. *Calcif. Tissue Int.* **2008**, *83,* 146-154.

Lanka M.; Poonia N.; Morales H. Management of a Failed Implant Site with Guided Bone Regeneration, Reimplantation, and Root Submergence Technique. *International Journal of Oral Implantology and Clinical Research*. 2016; 7(2):1-3.

Lanka, M.; Devich, A.S.; Sagrika, S.Socket Preservation Using a Small Particulate Xenograft: A Case Report. *The Journal of Implant & Advanced Clinical Dentistry*. 2017, 9 (*4*), 12-17.

Mandelli, F.; Perale, G.; Danti, S.; D'Alessandro, D.; Ghensi, P. Clinical and Histological Evaluation of Socket Preservation using SmartBone®, a Novel Heterologous Bone Substitute: A Case Series Study. *Oral & Implantology*. 2018, 2, 87-94.

Messo, E. ; Grottoli, Grottoli, C. F. ; Perale, G. ; and Hirsch, J. Custom-Made Horizontal and Vertical MaxillaryAugmentation with SmartBone® On Demand.:A Seven-Year Follow-Up Case. *Appl. Sci.* 2020, 10, 8039; doi:10.3390/app10228039

Mistry, A.S.; Mikos, A. G. Tissue Engineering Strategies for Bone Regeneration. *Adv. Biochem. Engin.* **2005**, *94*, 1.

Pertici, G.; Müller, M; Perale, G. Bioresorbable Bioactive Matrix for Bone Regeneration. *Tissue Engineering Part A*. 2010, 16(*8*), A-10.

Pertici, G.; Rossi, F.; Casalini, T.; Perale, G. Composite Polymer-Coated Mineral Grafts for Bone Regeneration: Material Characterisation and Model Study. *Ann. oral Maxilofac. Surg.* 2014, 2, 1–7, doi:10.1016/S0142-9612(00)00330-6.

Pertici, G.; Carinci, F.; Carusi, G.; Epistatus, D.; Villa, T.; Crivelli, F.; Rossi, F.; Perale, G. Composite Polymer-Coated Mineral Scaffolds for Bone Regeneration: From Material Characterization To Human Studies. *J. Biol. Regul. Homeost. Agents* 2015, *29*, 136–148.

Piattelli, M.; Favero, G. A.; Scarano, A.; Orsini, G.; Piattelli, A. Bone Reactions to Anorganic Bovine Bone (Bio-Oss) used in Sinus Augmentation Procedures: A Histologic Long-term Report of 20 Cases in Humans. *International Journal of Oral and Maxillofacial Implants*, **1999**, *14(6)*, 835-840.

Planell, J. A. *Bone Repair Biomaterials*; Woodhead Publishing Limited, 2009; ISBN 9781845693763.

Poonia N.; Morales H.; Mahesh. L. Management of a failed implant site with guided bone regeneration, reimplantation, and root submergence technique. International Journal of Oral Implantology and Clinical Research. 2016, May-August 7 (2) 1-3.

Ramesh, N.; Moratti, S.C.; Dias, G.J. Hydroxyapatite–polymer Biocomposites for Bone regeneration: A Review of Current Trends. *J Biomed. Mater. Res. Part. B.* **2018**, *Jul;106(5)*, 2046-2057.

Roato (1), I.; Belisario, D. C.; Compagno, M.; Verderio, L.; Sighinolfi, A.; Mussano, F.; Genova, T.; Veneziano, F.; Pertici, G.; Perale, G.; Ferracini, R. Adipose-Derived Stromal Vascular Fraction/Xenohybrid Bone Scaffold: An Alternative Source for Bone Regeneration. *Stem Cells Int*. 2018, *2018*, 1–11, doi:10.1155/2018/4126379.

Roato (2), I.; Belisario, D. C.; Compagno, M.; Lena, A.; Bistolfi, A.; Maccari, L.; Mussano, F.; Genova, T.; Godio, L.; Perale, G.; Formica, M.; Cambieri, I.; Castagnoli, C.; Robba, T.; Felli, L.; Ferracini, R. Concentrated adipose tissue infusion for the treatment of knee osteoarthritis: clinical and histological observations. *Int. Orthop*. 2018, doi:10.1007/s00264-018-4192-4.

Rossi, F.; Santoro, M.; Perale, G. Polymeric Scaffolds as Stem Cell Carriers in Bone Repair. J. *Tissue Engineering and Regenerative Medicine*. 2015, *9*, 1093-1119.

Ruoslahti, E. RGD and Other Recognition Sequences for Integrins. *Ann. Rev. Cell Dev. Biol.* **1996**, *12*, 697-715.

Sarkar, S. K.; Lee, B. T. Hard Tissue Regeneration using Bone Substitutes: an Update on Innovations in Materials. *Korean J. Intern. Med.* **2015**, *30*, 279–293, doi:10.3904/kjim.2015.30.3.279.

Sartori, S.; Silvestri, M.; Forni, F.; Icaro Cornaglia, A.; Tesei, P.; Cattaneo, V. Ten-year Follow-up in a Maxillary Sinus Augmentation using Anorganic Bovine Bone (Bio-Oss). A Case Report with Histomorphometric Evaluation. *Clinical Oral Implants Research*. **2003**, *14(3)*, 369-372.

Secondo, F.; Grottoli, C. F.; Zollino, I.; Perale, G.; Lauritano, D. Positioning of a Contextual Implant along with a Sinus Lift Anchored with a Block of Heterologous Bone. *Oral Implantol. (Rome)*. 2017, *4*, 457–467

Senn, N. Senn on the Healing of Aseptic Bone Cavities by Implantation of Antiseptic Decalcified Bone. *Ann Surg.* ***1889 Nov****; 10(5):352-68.*

Stacchi, C.; Lombardi, T.; Ottonelli, R.; Berton, F.; Perinetti, G.; Traini, T. New bone formation after transcrestal sinus floor elevation was influenced by sinus cavity dimensions: A prospective histologic and histomorphometric study. *Clin. Oral Implants Res*. 2018, 465–479, doi:10.1111/clr.13144.

Taschieri, S.; Ofer, M.; Corbella, S. ; Testori, T.; Dellavia, C.; Nemcovsky, C.; Canciani, E.; Francetti, L.; Del Fabbro, M.; and Tartaglia, G. The Influence of Residual Alveolar Bone Height on Graft Composition after Maxillary Sinus Augmentation Using Two Different Xenografts: A Histomorphometric Comparative Study. *Materials.* 2020, 13, 5093; doi:10.3390/ma13225093.

Toffler, M. *Implant Site Development*. First edition. Edited by Michael Sonick, Debby Hwang. **2012**.

Winkler, T.; Sass, F. A.; Duda, G. N.; Schmidt-Bleek, K. A review of biomaterials in bone defect healing, remaining shortcomings and future opportunities for bone tissue engineering. *Bone Joint Res.* **2018**, *7*, 232–243, doi:10.1302/2046-3758.73.BJR-2017-0270.R1.

Yamamoto, M.; Yamato, M.; Aoyagi, M.; Yamamoto, K. Identification of Integrins Involved in Cell Adhesion to Native and Denatured Type I Collagens and the Phenotypic Transition of Rabbit Arterial Smooth Muscle Cells. *Experimental Cell Research*. **1995**, *219 (1),* 249–256.

Younger, E.M.; Chapman, M.W. Morbidity at Bone Graft Donor Sites. *J. Orthop. Trauma.* **1989**, *3*, 192-5.

Zollino, I.; Carusi, G.; Carinci, F.; Perale, G. Positioning of a Contextual Implant Along with a Sinus Lift with SmartBone® Microchips of Composite Heterologous-Synthetic Bone. *Indian J. Stomatol*. 2015, 6(*2*), 59-62.

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