

MICROSPHERES-BASED TISSUE ENGINEERING PRODUCT FOR CRANIOFACIAL BONE RECONSTRUCTION

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ABSTRACT

MICROSPHERES-BASED TISSUE ENGINEERING PRODUCT FOR CRANIOFACIAL BONE RECONSTRUCTION

Craniofacial reconstruction is difficult in patients with large bone defects and insufficient bone volume. In this cases for assistance and promotion of natural healing processes the preferred treatment is autologous iliac bone graft. However, its resorption is unpredictable, and surgical expertise decreases but never eliminated the morbidity at the donor site. Bone graft alternatives and autogenic drugs are the only remaining option. The presence of a network of peptidic nerve fibres in the skeleton, expressing several neuropeptides, and substantial emerging evidence indicate that the nerve growth factor (NGF), either alone or synergistically with other biological endogenous molecules, plays a crucial role in cartilaginous and bone tissue genesis. During the implant placement or sinus lifting some small quantities of bone autografts are available in limiting quantities. Therefore we need for synthetic alternatives as a scaffolds for new bone ingrowth.

Our approach was to combine synthetic pre-fabricated scaffolds (combined composite-based growth factor loaded substitutes using microspheres technology) with own bone autograft. In this way will be used good properties of natural and synthetic tissue and also augment bone volume available for reconstruction. Autograft were prepared using new type of surgical drill (Patent Pend) for bone explants which allowed collection of high quality viable bone. The microsphere matrix were designed using poly(lactide-co-glycolide) (PLLA), β -tricalcium phosphate (β -TCP), chitosan and NGF/FG neurotensinogenic factor by solvent evaporation method. Autograft and microspheres were mix on site (50:50) and used for alveolar bone reconstruction. This formulation, used also for sustaining drug release, was evaluated by different methodologies: XRD, FTIR, SEM, NGF-elution and ELISA study. In vitro culturing (24h) were done to support remaining osteoblast and to stimulate its proliferation. With a simple, on site surgical procedures for alveolar bone reconstruction, this new tissue engineered (TE) product gave good clinical results as expected. This new, ready for market, tissue engineering (TE) product will present viable scaffolds for new alveolar bone ingrowth.

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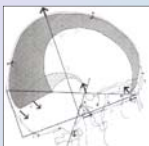
- Business Strategic Planning (Europe)
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- Government Affairs (Italy)
- Manufacturing Consulting
- Market Research and Media Relations (Europe)
- Medical Affairs Quality
- Systems Services **ICNO**
- Regulatory Affairs

INTRODUCTION

Aim: CRANIOFACIAL BONE RECONSTRUCTION WITH TE PRODUCT based on polymer composite, growth factor and autologous alveolar bone

- FUNCTIONAL & AESTHETIC RECONSTRUCTION**
- CONGENITAL DEFORMITIES
 - DEVELOPMENTAL DEFORMITIES
 - PLASTIC RECONSTRUCTIVE SURGERY
 - TUMOR & TRAUMA

Alveolar bone is a specialized part of the maxillofacial and maxillary bones that forms the primary support structure for teeth. Although fundamentally comparable to other bone tissues in the body, alveolar bone is subjected to continual and rapid remodeling associated with tooth eruption and subsequently the functional demands of mastication. The ability of alveolar bone to undergo rapid remodeling is also important for positional adaptation of the teeth but may be detrimental to the progression of periodontal disease.



MATERIAL & METHODS

SYNTHETIC PRE-FABRICATED SCAFFOLD

- Functional polymer microspheres: PLLA/TCP β /NGF β composites** features:
- Small size and volume
 - Large specific surface area
 - High diffusibility and mobility
 - Stable dispersions
 - Uniformity
 - Variety and multi-functionality
 - Injectable, irregular defects

Surgical drill for autologous bone explant

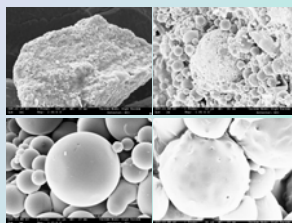


Human trials

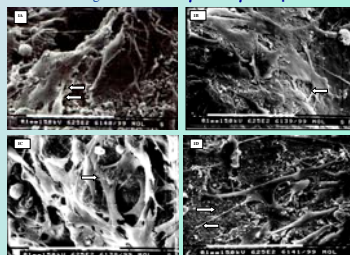
Therapeutic indication	Aim location	Formulation to be implanted/ No. of patients per group/ Volume of implant	Controls	Clinical follow-up	Clinical monitoring
1. Oral/maxillo-facial congenital malformations	Inching and		The control group consists of age and health matched persons in whom surgery is not indicated at the various standard surgical procedures have been obtained.	Clinical assessment at the various 1, 3, 6 and 12 months after the treatment	1. Anatomical data (post-surgery via CT-scans)
2. Oral/maxillo-facial post-traumatic malformations of New Bone	Adolescents and New Bone	(n=7)			2. Esthetic-photic
3. Oral/maxillo-facial congenital malformations	Inching and New Bone				3. Conventional X-rays
4. Orthognathic surgery/TMJ disorders		1.3 cm ³			4. Qualitative and quantitative computer tomography (CT)
5. Teeth extraction bone reduction/maxillofacial surgery					5. DentalScan
6. Reconstructive pre-prosthetic surgery	Alveolar ridge reconstruction				
7. Cosmetic facial surgery	Implantology				

RESULTS

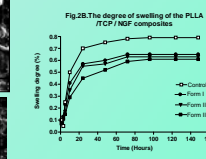
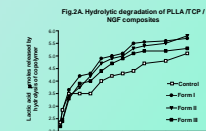
In vitro: Bio-Composite (SEM Micrograph): Microspheres of PLLA/TCP β /NGF β composites



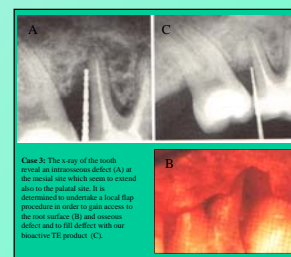
Osteoblast culturing on PLLA/TCP β /NGF β composites



Dynamic in vitro test of sustaining drug release



In vivo:



CONCLUSION

- Optimisation of a new 3D multi-functional bioactive TE product composed of a) resorbable polymer composite enriched with B) NGF β factor and c) autologous alveolar bone;
- Set up of chemical and physical scaffold conditions for a) microspheres polymeric drug delivery device for sustainable release of growth factor and b) autologous osteoblasts from bone explants;
- Clinical application in Periodontal diseases for reconstruction of intrabony defects (cases 1, 2 and 3). Clinical management were with the method of guided tissue regeneration (GTR), using our TE product;
- Finally, proposed TE product could:
- a) be used as filling elements of irregular defects for maxillo-facial reconstructive surgery;
- b) reduce bone healing period after operation;
- c) develop new surgical techniques.