LETTER TO THE EDITOR

SEGMENTAL MANDIBULAR BONE RECONSTRUCTION THROUGH THE USE OF A SPECIAL OSTEOSYNTHESIS PLATE WITH IMPLANTS COVERED WITH A MODULAR ENDOPROTETIC SCAFFOLD OF POLY (ε-CAPROLACTONE) COATED WITH HYDROXYAPATITE

P. DI EMIDIO, D. CARDINELLI, A. FABRIZI and A. CAMA

Department of Maxillo-Facial Surgery and Odontostomatology, "G. Mazzini" Hospital, Piazza Italia, Teramo, Italy

Received December 6, 2019 – Accepted January 10, 2020

To the Editor,

The mandibular bone provides the skeletal support for the dental elements, assuming a fundamental role regarding function (chewing and phonation) and aesthetic (facial profile). Reconstruction of mandibular defects due to traumas, cancer resections, malformations and osteonecrosis, represents an interesting challenge for clinicians (1, 2). At present, the gold standard for mandibular reconstruction is the use of osseus free flaps, such as fibular free flap or iliac crest free flap. Nevertheless, this type of reconstruction has some tridimensional limits, not being able to replace exactly the architectonic form of the original mandible. Moreover, this technique requires a long operating time, demanding post-operative care, an increase of hospitalization and an important morbility of the donor site. For these reasons, many authors have discussed different types or methods of mandibular reconstruction, such as the use of reconstructive plate, bone grafts, or biological bone (1-5). To improve and facilitate mandibular replacement, different researchers have tried to find alternative methods for bone reconstruction, such as heterotopic bone induction, modular titan endoprosthesis through engineered models, and ε-polycaprolactone scaffold (6-8).

The aim of the present study is to find an alternative method for mandibular reconstruction, using an innovative system composed of an ergonomic titanium plate, with dental implants connected, covered in ε-polycaprolactone scaffold, while ensuring a good osteointegration, replacing the exact morphology of mandible, improving the degree of mastication, and satisfying the aesthetic outcome. The use of the ε-polycaprolactone scaffold could allow for a lower operative burden compared with conventional techniques by avoiding creation of a secondary bone defect.

MATERIALS AND METHODS

The proposed project for mandibular reconstruction was designed by the Authors to improve the field of mandibular reconstruction options. A biodegradable endoprosthesis modular scaffold was designed. This scaffold constituted poly ε-caprolattone (PCL) which is a bio-absorbable polymer, resistant, durable, stable and bio-available (9, 10). The realization of the PCL scaffold

Key words: poly (ε-caprolactone); hydroxiapatite; mandible reconstruction; tissutal engineer; bone morphogenetic protein -2; osteosynthesis; plate dental implants

Corresponding Author:
Dr Antonia Cama,
Department of Maxillo-Facial Surgery
and Odontostomatology, Hospital "G. Mazzini",
Piazza Italia, Teramo, 64100, Italy
Tel.: +39 3465440993
e-mail: taniacama.tc@gmail.com

0393-974X (2020)

was obtained using prototype additive manufacturing and Selective Laser Sintering technology (SLS). A dedicated software monitored the porosity, the structure, and the mechanical resistance of the scaffold. The osteoinductive property of the scaffold was stimulated by the addition of simulated body fluids (mSBF), similar to human plasma, but enriched with calcium and phosphate. mSBF induces the release of growth factors (VEGF e rhBMP-2), moreover, the scaffold is activated by the introduction of stromal multipotent mesenchymal cells from bone marrow (BMSC) produced with cell cultures, or isolated from bone marrow or adipose tissue.

The design phase of the ε-PCL scaffold is made up of different stages. Firstly, we defined the correct mandibular resection, then we projected and realized the ε-PCL scaffold and the surgical time.

Phase 1

Three-dimensional computed tomography (3D-CT) scanning was performed, and computer-aided design techniques were used to produce an ideal virtual replacement for the mandibular defect. ε-PCL scaffold was created using SLS technology (EOS P110), after the creation of a 3D TC model (slice <1mm) in STL file. The printer employs a powdered mix of polycaprolactone and hydroxyapatite 4%.

Using a custom-made technique, an exact stereolithografic model reproducing the mandible was obtained. This led to identifying the mandibular segment for resection and what would have to be reconstructed.

Phase 2

During this phase we projected and created the entire system of reconstruction, formed by a surgical plate (Patent U.S.A-Europa-United States Patent No.: US 6,613,055 B2 Di Emidio (45) Date of Patent: September 2, 2003) upholstered in ε PCL scaffold.

The plate has two lateral ports with five holes predisposed for positioning the screws to fix the entire scaffold. Between those two portions, the middle part of the plate is characterized by a tridimensional conformation and pliability; this central portion is composed of a series of spheres interconnected by cylindrical segments. The smooth shape of these components avoids the traumatic action of the plates, enabling the best fitting of the plate system.

The spheres have microholes (0.02 mm Ø) on their surface, obtained with the *auxilium* of a laser. On the top of each sphere we connect a modified dental implant, which could be of different lengths (Fig. 2). These implants have different features: a threaded shank with a microhole at the extremity; inside the implant there is a tubular channel that creates a connection with the internal part (Fig. 3A). When the modified implant is connected with the sphere, an internal via of communication is created between the implant and the plate. This system permits to insert, using a syringe, therapeutic substances, such as Recombinant human bone morphogenetic protein (PMR), in the superior extremity of the dental implant, after removal of the screw top, that go through the implant and arrive at the spheric part of the plate, leading to the diffusion of these substances in the entire PLC scaffold (Fig. 3B-C). After the complete osteointegration of the entire system, it is possible to perform the prosthetic rehabilitation.

Phase 3

The reconstructive system, composed by titanium plate and ε-PCL scaffold, was sterilized. Afterwards, the resection was inserted and fixed on human cadaver (Fig. 4). The scaffold was activated using injection of plasma and mSBF; this injection could be repeated during the post-operative weeks by just removing the screw cup from the top of the implants.

RESULTS

The entire reconstructive system, composed of an osteosynthesis plate with implants, a modular endoprotetic scaffold of poly (ε-caprolactone) coated with hydroxyapatite, guarantees a precise reconstruction of the bone defects. The system has optimal mechanical properties, porosity of the scaffold is in a range between 37% and 55%, the mechanical compression module is in the range between 52-68-MPa, the maximum resistance is in a range between 2.0- 3.2-Mpa. The fusion degrees for processing PCL is 60°C. The PCL has a molecular weight of 50.000 kDa and a particle size distribution in a range between 10–100 lm. Mechanical analysis confirm a fracture point with a strength equal to 60 N. These characteristic are similar to the biomechanic of human bone, having a good bearing capacity.

Micro-CT analysis shows a homogenous structure and an interconnection of all pores. The print time is 180 min.

The poly (ε-caprolactone) scaffold added with growth substance (rhBMP-2 and BMSC) has a capacity of osteoinduction, which demonstrated that the bone regeneration was obtained in 6 months.

DISCUSSION

PCL scaffolds are largely used for bone and cartilage reconstruction . The possibility to print and shape

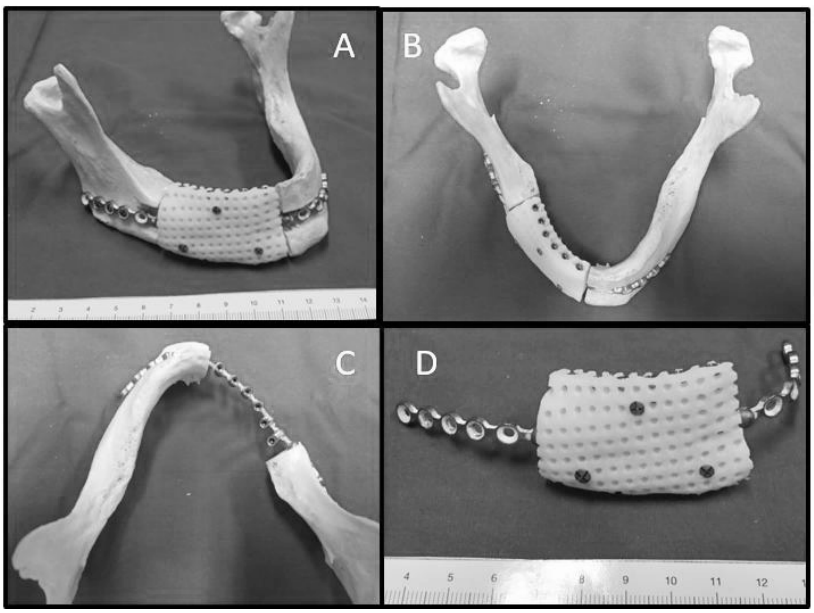

Fig. 1. *Custom-made model of mandibular reconstruction segment (**A,B,C**), with the ε-PCL scaffold and relative plate (**D**).*

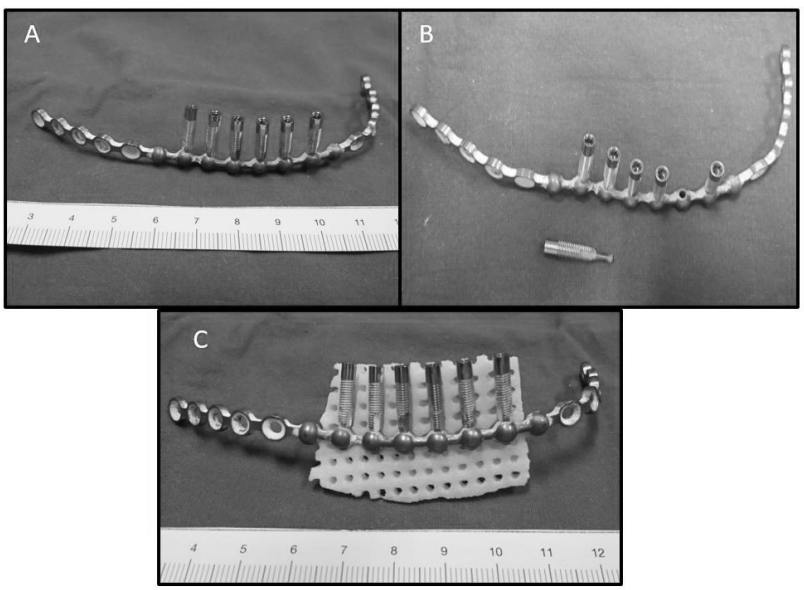

Fig. 2. *Surgical plate with tridimensional components and modified dental implants (**A**, **B**) upholstered in ε-PCL (**C**).*

this biomaterial through rapid prototypization and additive manufacturing, as well as its bio compatibility, could guarantee a diffuse use of this material. The ostheoinductive properties and the possibility to add growth factors and BMSC improve the possibility to use this reconstructive system (11, 12).

In 2014, some Authors described the possibility to reconstruct a segmental defect of mandibular body using an ε-PCL scaffold combined with bone marrow homolog cells (ε-PCL-BMP) in a primate model similar to human. They wanted to valid the use ε-PCL-BMP and its efficacy compared to a control PCL group. The mechanic results show a major bearing capacity in the first group. Those researchers, after a six-month period, valued, in their sample, the appearance of complications (infections, inadequate mechanic resistance of the plate) (9).

Warncke at all. describes the use of bone without antigens; they created a titanium mesh cage filled with bone mineral blocks and infiltrated with recombinant human bone morphogenetic protein and 20 mL of the patient's bone marrow, obtaining an etherotopic osteoinduction, but a low mechanical resistance and a rapid resorption (6).

The innovation of our reconstructive system is represented by a complex system, in which we overcame the problem of mechanical resistance using a tridimensional ergonomic plate. We tried to reduce the risk of the plate's exposure by coating the entire plate with ε-PCL scaffold and hydroxiapatite, which guaranteed osteoinduction. Moreover, another advantage is to have the possibility to change the length of implants and to have a prosthetic rehabilitation. The insertion of growth factors and BMSC through the implant is another good characteristic of the system as, after the operation, it activates the ε-PCL scaffold.

Our proposal would be to start an animal

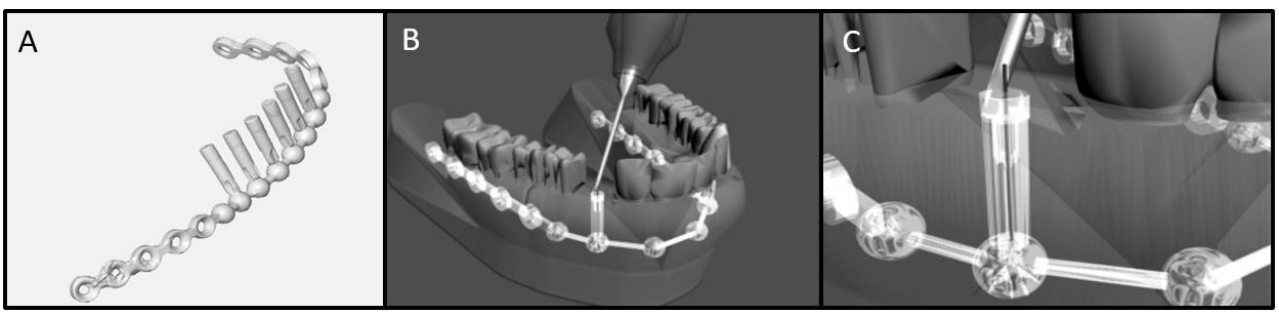

Fig. 3. *3D computer-model of surgical plate (**A**) and relative modified implants (**B**, **C**).*

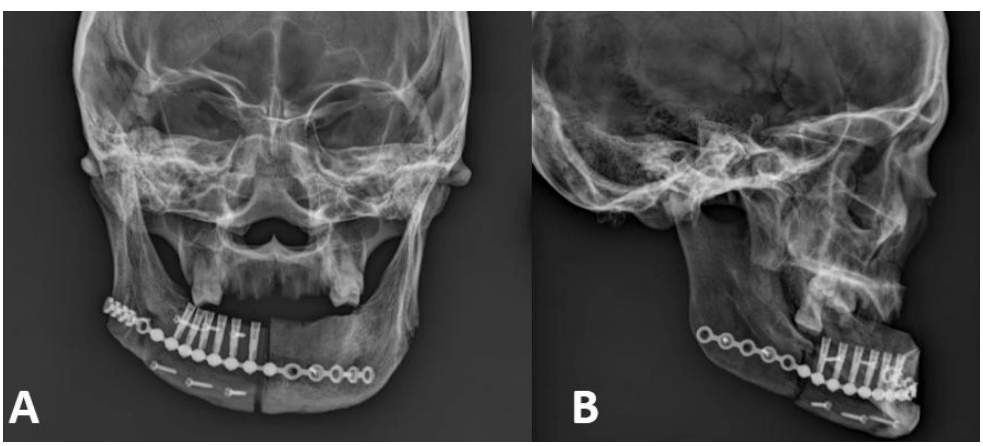

Fig. 4. *Cranial X-ray in antero-posterior (**A**) and latero-lateral view (B) in human cadaver.*

experimentation to verify the entire reconstructive system, creating a collaboration with biomedical engineering laboratories. This project could represent in the future a good alternative method for mandibular reconstruction in selected cases, even if at present this system is not valid in humans.

REFERENCES

1. Ardary WC. Reconstruction of mandibular discontinuity defects using autogenous grafting and a mandibular reconstruction plate. J Oral Maxillofac Surg 1993; 51(2):125-30.
2. Divi V, Schoppy DW, Williams RA, Sirjani DB. Contemporary Mandibular Curr Opin Otolaryngol Head Neck Surg 2016; 24(5):433-39.
3. Stopa Z, Siewert-Gutowska M, Abed K, Szubińska-Lelonkiewicz D, Kamiński A, Fiedor P. Evaluation of the Safety and Clinical Efficacy of Allogeneic Bone Grafts in the Reconstruction of the Maxilla and Mandible. Transplant Proc 2018; 50(7):2199-201.
4. Hellem S, Olofsson J. Titanium-coated hollow screw and reconstruction plate system (THORP) in mandibular J Craniomaxillofac Surg 1988; 16(4):173-83.
5. Chim H, Salgado CJ, Mardini S, Chen HC. Reconstruction of mandibular defects. Semin Plast Surg 2010; 24:188-97.
6. Warnke PH, Springer IN, Wiltfang J, et al. Growth and transplantation of a custom vascularised bone graft in a man. Lancet 2004; 364(9436):766-70.
7. Lee S, Goh BT, Tideman H, Stoelinga PJ, Jansen JA. Modular endoprosthesis for mandibular body reconstruction: A clinical, micro-CT and histologic evaluation in eight Macaca fascicularis. Int J Oral Maxillofac Surg 2009; 38(1):40-47.
8. Suarez-Gonzalez D, Barnhart K, Migneco F, Flanagan C, Hollister SJ, Murphy WL. Controllable mineral coatings on PCL scaffolds as carriers for growth factor release. Biomaterials 2012; 33:713-21.
9. Chanchareonsook N, Tideman H, Feinberg SE, et al. Segmental mandibular bone reconstruction with a carbonate-substituted hydroxyapatite-coated modular endoprosthetic poly (ε-caprolactone) scaffold in Macaca fascicularis. J Biomed Mater Res B Appl Biomater 2014; 102(5):962-76.
10. Herford AS, Cicciu M. Recombinant human bone morphogenetic protein type 2 jaw reconstruction in patients affected by giant cell tumor. J Craniofac Surg 2010;21:1970-75.
11. Augello A, De Bari C. The regulation of differentiation in mesenchymal stem cells. Hum Gene Ther 2010; 21:1226-38.
12. Di Emidio P. Proposal of an innovative technique for mandibular reconstruction: preliminary study. J Orth 2019; 11:1.