Clinical Experience with a Macroporous Synthetic Bone Substitute (Eurocer®) in the Treatment of the Patients with Bone Defects

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Abstract— **The treatment of bone defects was a major challenge and may still be a problem today. Due to the disadvantages with biologically bone grafts there is a high clinical demand for synthetic bone substitution materials. The aim of this prospective study is to reveal biocompatibility integration and extension of osseous healing for a biphasic synthetic ceramic bone substitute (Eurocer), when used in the treatment of 31patients with 33 bone defects (fractures, nonunions, osteoarthritis). Eurocer® (FH Orthopaedics France) is an osteoconductive ceramic material representing a mixture of 55% hydroxyapatite and 45% tricalcium-phosphate and is available in granular form and in various geometric shapes. The authors used GESTO (Greffes et Substitutes Tissulaires en Orthopedie) protocol for preoperative selection and postoperative follow-up. The mean defect volume for all defects treated with Eurocer was 12cc. According to the size and type of defects the authors used Eurocer® as a single component or mixed with autologous bone graft. Stabilization was achieved by internal fixation in all operation except one (a fracture of humeral head). We have used for osteosynthesis classic plates or plates with angular stability, especially in compression fractures associated with osteoporosis. All patients have been followed-up clinically and radiologic for 2, 3, 4, 6, 9, 12 and 18 months post-operative. The mean time to clinically healing was 3.2 months while the mean time to radiographic healing was 4.5 months. We observed no implant fragmentation and no local inflammation or sepsis. Due to minimally invasive surgery and fast rehabilitation, no joint stiffness or limited joint motion was recorded. This prospective study demonstrates that the biphasic synthetic ceramic material Eurocer® is an effective bone graft substitute for usage in patients with bone defects. To insure a consistent result it is mandatory to strictly follow the three requirements for osteoconduction: proximity, viability and stability**.

Keywords— **macroporous, synthetic bone substitute, osteoconduction, biocompatibility, bone defects.**

I. Introduction

Bone defects of various etiologies - trauma, osteoporosis, tumors or metabolic diseases - represent an important medical issue with socio-economical implications, due mainly to the lack of spontaneous healing or to the treatment problems and long lasting healing [1]. Approximately 10% of the bone surgery requires bone grafts or bone substitute use [2]. Bone is the most frequently transplanted tissue. Usage of the patient own bone from ilium or other site (autografts) has traditionally been the "gold standard" in treatment of the bone defects [1,3,4]. This is because autogenous bone is osteogenic (viable transplant which contain living cells capable of new bone formation), osteoconductive (it serves as a scaffold in which new bone can deposit) and osteoinductive (it provide growth factors that sustain new bone formation) [1,3,5]. The advantages of autologous bone grafts include long experience in use, availability in most patients, minimal costs and maximal biocompatibility. The disadvantages are represented by the morbidity of the donor site (21% minor complications and 9% major complications - pain, longer than 6 months, infections, dysesthesia, wound drainage, reoperation), limited availability, poor mechanical properties in osteoporotic patients [3,6]. The allografts have osteoconductive and osteoinductive properties (depending on the processing techniques) but their usage involves the infection risk (viral or bacterial) and high costs while it requires a bone bank with all facilities. The disadvantages of the auto- and allografts facilitated the development of bone substitutes and especially the synthetic bone substitution materials that can - theoretically - be prepared in unlimited amounts and with no risk for potential infections [1,4,6]. According to Bauer and Muschler [7] bone substitutes may fall into two categories: osteoinductive and osteoconductive materials [1]. In the first category we distinguish the mineralized bone matrix (DBM) [8] that induces the bone formation when implanted in soft extraskeletal tissues, (compared with conventionally prepared allografts, with a minimal osteoinductive activity). The bone morphogenic protein (BMP) represents a protein (extracted from DBM) that acts as osteoinductive growth factor [1]. The osteoconductive materials are represented by coral hydroxyapatite [9], the calcium sulphate (the oldest osteoconductive bone graft but with very high absorption rate), biovitroceramics [10], ceramic materials or calcium phosphate materials [11] and calcium-phosphate cements [1,11].

II. Purpose

The aim of this of this prospective study is to evaluate a biphasic synthetic ceramic bone substitute (Eurocer®)

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regarding intraoperative maneuverability, biocompatibility, integration and extension of osseous healing when used in the treatment of 31 patients with bone defects.

III. Material and methods

Eurocer® (FH Orthopaedics, France) is a macroporous synthetic bone substitute representing a mixture of 55% hydroxyapatite and 45% tricalcium-phosphate. Eurocer400® is produced in granular form with a granule diameter of 2-3 mm (with a porous structure with 300-500 µm pores) and is recommended for usage in areas not subjected to stress. Eurocer200PLUS® is available in various geometric shapes (cylindrical, disk-shaped, rods, cube and truncated corners) with a porous structure (60% total porosity, partially interconnected by 300-500 µm pores) and must not be used in areas subjected to compression stress greater than 10MPa. These structural properties allow fast osseointegration followed by gradual resorption.

Between June 2006 - October 2009, 31 patients with 33 bone defects (2 patients with bilateral lesions) were included in a prospective study realized in the Orthopaedic Departments of Emergency Hospital and Rehabilitation Hospital in Iasi, Romania. The mean age for these patients was 57 years, with males averaging of 51 years and females averaging of 65 years. Eurocer was used in various clinical circumstances: Bone defects in proximal tibia fractures - 14 cases with 16 lesions (Fig. 1-4); femur fractures - 2 cases; supracondylar femoral nonunions - 3 cases; delayed union in supracondylar femoral fractures (Fig. 5) - 2 cases; humeral head fractures; - 1 case humeral nonunuions - 2 cases (Fig. 6); malunion of distal radius fractures - 2 cases (Fig. 7); ankle arthrodesis - 2 cases (Fig. 8); subtalar arthrodesis - 3 cases.

The authors used GESTO (Greffes et Substitutes Tissulaires en Orthopedie) protocol for preoperative selection and postoperative follow-up and GESTO classification of loss TOD (type, os, dimensions) for intraoperative quantification of missing bone. In fact, the mean defect volume for all defects treated with Eurocer was 12 cc. Only for metaphyseal defects, the mean defect volume was 8.4 cc. Stabilization was achieved by internal fixation in all operation except one (a fracture of the humeral head). In most cases (24 patients – 77.4%), we have used Eurocer as a single component for bone replacement, mainly for small sized metaphyseal and epiphyseal defects. In limited defects that are conserving bone continuity we have used Eurocer400 (granules) while in defects lacking bone continuity, we have used either Eurocer200 (truncated corners) either Eurocer400 mixed with autologous bone graft harvested from iliac bone. During reconstructive surgery, the surgeons respected the three requirements of the osteoconduction, called the "triad of osteoconduction" [3]: (a) the implant must be in direct contact with the surrounding bone; (b) the surrounding bone must be viable; some factors that decrease this viability are devascularisation, infections and some metabolic bone disease; (c) the interface between the surrounding bone and implant must be stabilized (in most cases, this purpose is reached by internal fixation). The aim of the surgical team was to fill as completely as possible the whole defect area with Eurocer. In some cases (arthrodesis), bone defect was tailored according to the implant contour.

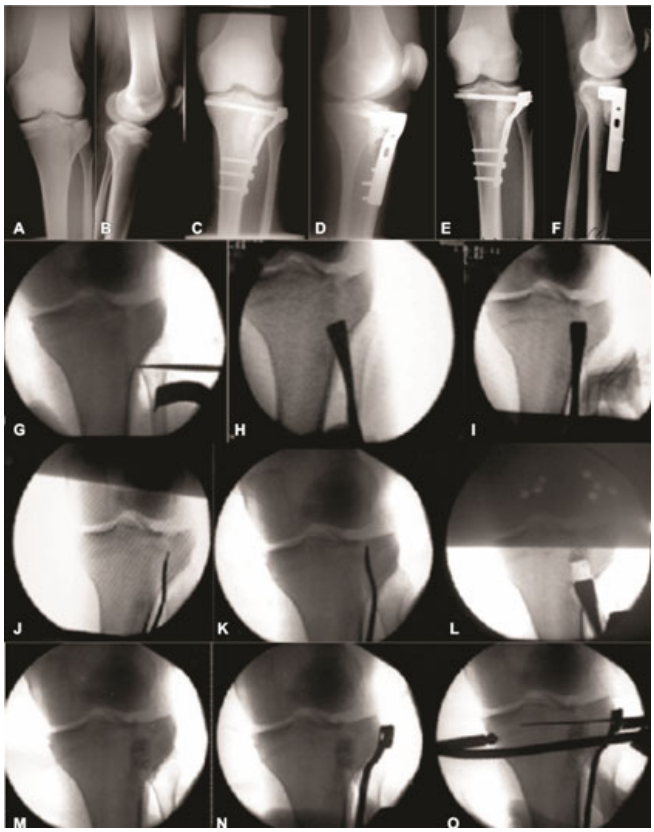

Fig. 1 (A-O) Mixed fracture of the external tibial plateau (type B3/AO). Plate and bone substitute (A,B) preoperative X-rays; (C,D) postoperative; (E,F) X-ray control at 3 months (radiologic evidence of decreasing granular aspect of bone substitute); G - cortical window; (H-K) elevation of the articular surface; (L,M) Eurocer filled bone defect; (N,O) osteosynthesis with L-plate and screws

Thus, 48.4% of the treated defects were located into the proximal tibia, the fracture types being a combination between comminution and compression associated with osteoporosis in many cases.

Our surgical protocol in these circumstances included the following steps: reduction of the lateral articular surface, using a limited cortical window (Fig. 1G) with elevation of

the articular surface using a curved instrument (Fig. 1 H-K), filling the epiphyseal-metaphyseal defect with Eurocer, (Fig. 1 L, M) fixation with a lateral plate (Fig. 1 N, O). In some fractures that included both condyles of the tibia we have to reduce first the fracture of the internal plateau followed by fixation with a butress plate placed medially (Fig 2, A–F).

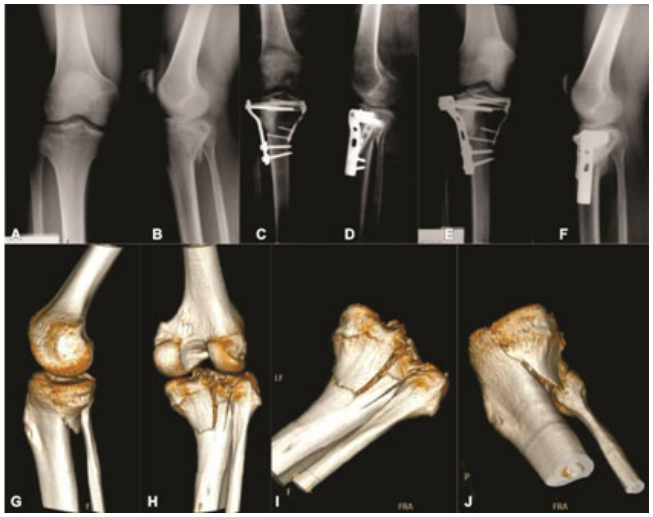

Fig. 2 (A-J) Complex fracture of the proximal tibia (type C3/AO). (A,B) Preoperative radiologic aspect (C,D) postoperative radiologic aspect, medial limited approach, reduction and fixation with small T plate, lateral closed reduction filling the bone defect with Eurocer, L plate and screws (E,F) radiologic aspect at 2 months (vanishing of the radiologic gap at bone-biomaterial interface and homogenisation of the bone substitute structure (G-J) preoperative CT with 3D reconstruction

A CT exam with 3-D reconstruction (Fig. 2, G-J) emphasized the real aspect of the fractures and compressions.

In 2 cases, the complexity of the displacement and compression made us check the articular reduction by arthroscopic surgery (Fig. 3, E-H).

In patients with complex fractures in both tibial condyles, associated with osteoporosis we have used laterally placed plates with angular stability in order to limit the secondary displacement and to allow faster knee rehabilitation.

We have used either plates with monoaxial angular stability type Less Invasive Stabilization System - Proximal Lateral Tibia (LISS-PLT), Locked Compression Plate (LCP-PLT) or plates with polyaxial stability that has the advantages of screw pathway adjustment (their position being adapted to a specific fracture) [12,13].

All patients have been followed-up clinically and radiologic for 2, 3, 4, 6, 9, 12 and 18 months following surgery.

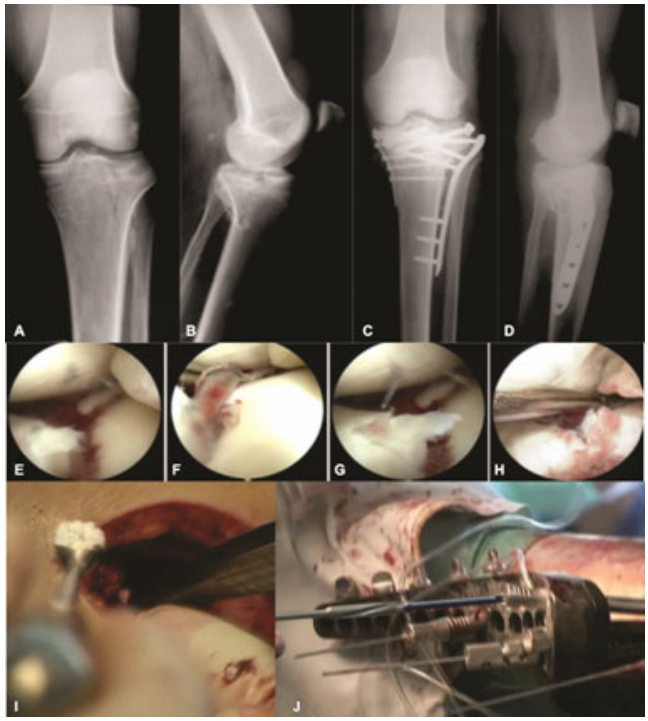

Fig. 3 (A-J) Proximal tibia fracture (type C3/AO) (A,B) preoperative aspect (C,D) medial approach, reduction of the articular surface, small T-plate, lateral approach, close reduction, LCP-PLT, bilateral filling with Eurocer - postoperative aspects (E,H) arthroscopic reduction control; (I) defect filled with Eurocer granules; (J) internal fixation with LCP-PLT on the lateral side.

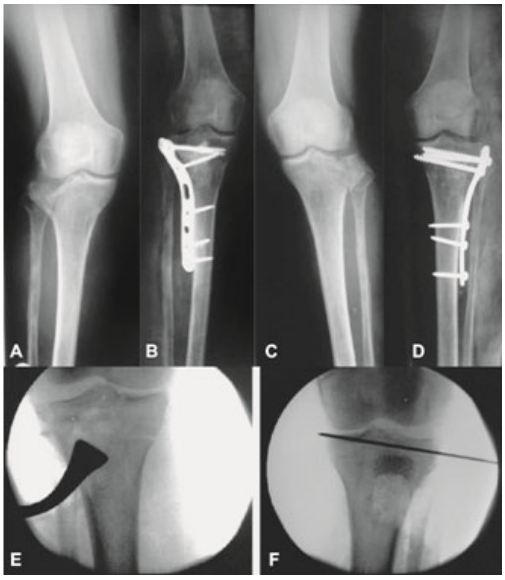

Fig. 4 (A-F) Bilateral complex proximal tibia fractures. (A-D) close reduction, bone defect filled with Eurocer, fixation with plates (polyaxial stability on the right side) (E,F) intraoperative fluoroscopic aspects

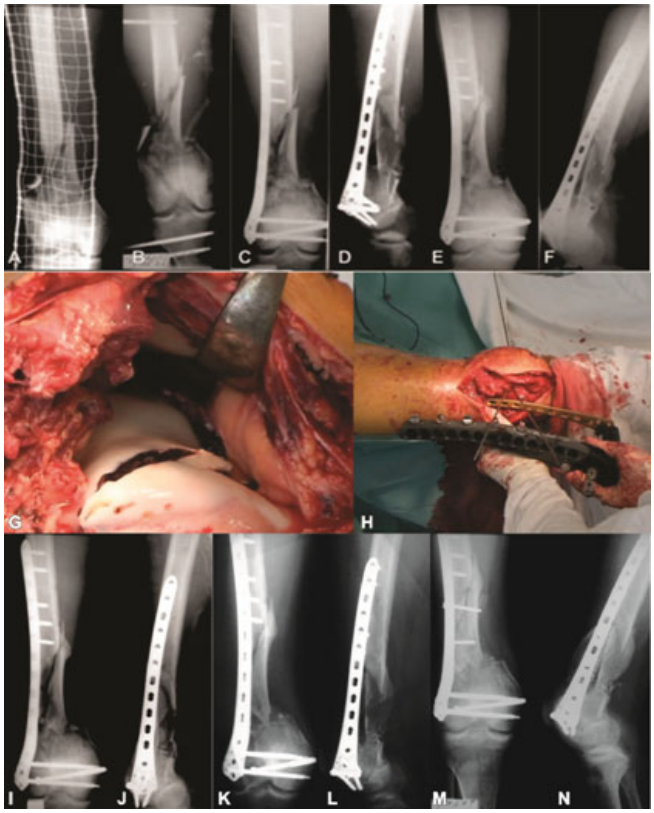

Fig. 5 (A-N) Distal femoral fracture (type C3/AO) with bone loss and open type II Gustilo. (A) preoperative aspect (B) external temporary fixation in damage control period (C,D) Internal fixation with LCP-distal femur, postoperative control (E,F) Radiographic aspect at 1 month postoperatively (G,H) intraoperative aspects (I,J) 3 months postoperative (K,L) 5 months postoperative, delayed union (M,N) defect filled with Eurocer granules mixed with bone graft from iliac crest

IV. Results

Bone substitute osseointegration for all 33 bone defects in 31 patients, treated with Eurocer® was evaluated according to clinical and radiological criteria. In order to determine the effectiveness of clinical healing, all 31 patients were evaluated for the degree of pain at rest, degree of pain during weight bearing or movement and for the degree of movement impairment. The mean time to clinically healing was 3.2 months. None of the patients undergone local inflammation or sepsis. No articular stiffness or limited joint motion was recorded. Due to the fact that performed knee surgery was minimally invasive (mainly in proximal tibia fractures) with indirect reduction using a plate with angular stability, the patients started an immediate rehabilitation and the functional results were excellent.

The radiologic results were interpreted according to three radiographic parameters [5]: interface between biomaterial and the receiving tissue; radiological biomaterial density, eventuality radiological biomaterial fragmentation. The postoperative radiological gap at the bone-material interface was filled at 3-4 months in all bone defects (Fig. 2E-F, 6F, 8G). At 3-6 months, the biomaterial granularity disappeared and became homogenous in 31 bone defects (Fig. 1 E-F), while in two cases with femoral nonunion, this phenomena appeared later, at 9-12 months (due to the large bone defect). The mean time to radiographic healing in all patients was 4.5 months with no implant fragmentation.

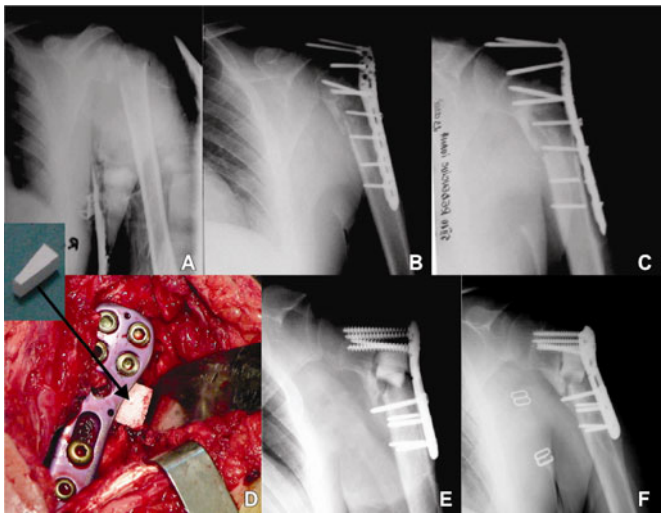

Fig. 6 (A-F) Nonunion of the proximal humerus (A) fracture of the proximal humerus, preoperative aspect (B) internal fixation with plate with monoaxial stability type Phylos (C) construct secondary displacement with broken screws at 3 months (D) reoperation with Phylos plate removal, fixation with plate with polyaxial stability, filling the defect with Eurocer 200 - trapezoidal shape (E) postoperative aspect (F) 2 months postoperative, radiological gap fading with early consolidation

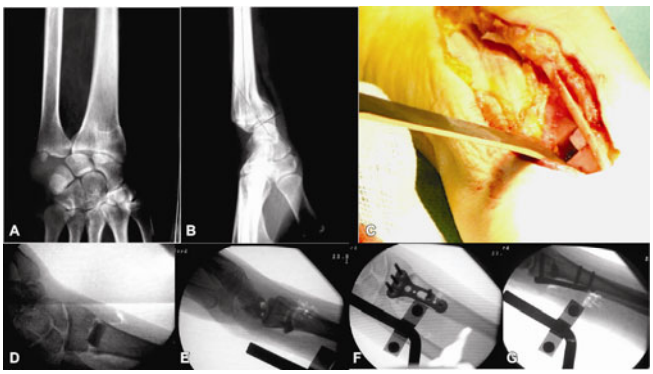

Fig. 7 (A-G) Malunion following a distal radius fracture (A,B) preoperative aspects (C) osteotomy, defect filled with Eurocer 200, intraoperative aspect (D,E) fluoroscopic aspect of the Eurocer block filling the defect (F,G) internal fixation with titanium plate with polyaxial stability

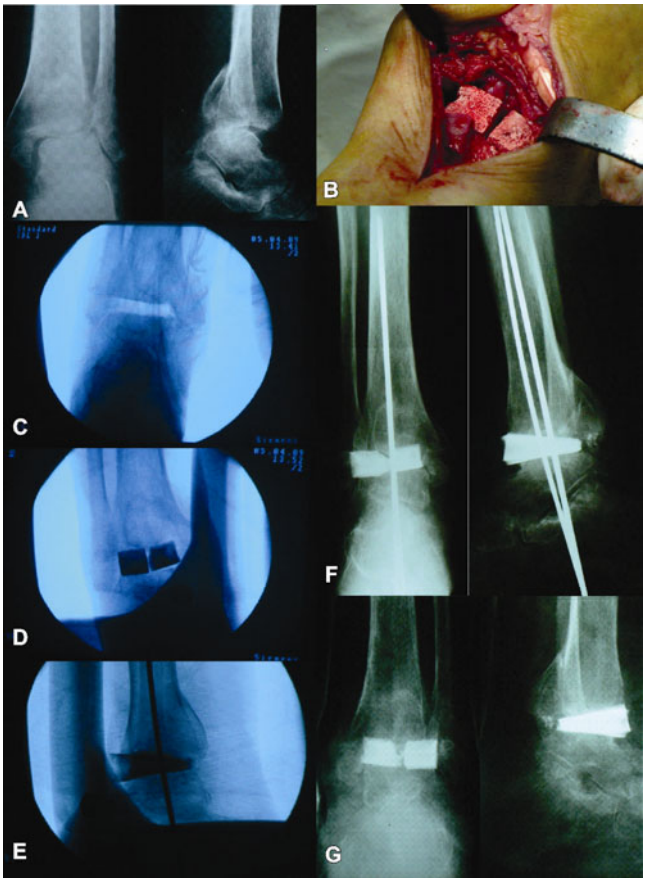

Fig. 8 (A-G) Ankle arthrodesis (A) malunion following a bimaleolar fracture (B) intraoperative aspect of bone defect filling after osteotomy with two blocks of Eurocer 200 (C,D,E) intraoperative fluoroscopic aspects of bone defect following osteotomy, filling with Eurocer 200 and fixation with two Steinmann pins (F) postoperative aspect (G) radiological aspect at 3 months, radiologic gap fading with early consolidation of the arthrodesis site

V. Discussions

Bone defects treatment remains a difficult problem and a challenge for the orthopaedic surgeon. There are various ways to solve these problems but they are usually difficult. The therapeutic means extend from the classical autologous graft to expensive allografts that require a bone bank. The disadvantages of auto and allografts facilitate the development of synthetic bone substitutes. They consist of calcium-based ceramic materials, collagen, non-collagenous proteins, inductive molecules, bioglass and biological degradable polymers. [6]. The ideal bone substitute should be biocompatible, bioresorbable, osteoconductive, osteoinductive, with a structure similar to the bone, with a good intraoperative maneuverability and cost-effective [6]. None of the known bone substitutes fulfill these requirements. Recently, the osteoconductive materials as bi- or triphasic phospho-calcic ceramics played the main roles as bone substitutes. These substances have a composition similar to bone mineral matrix and are biocompatible [1]. The good results obtained by using these materials is due mainly to the physical properties and especially to their macroporosity [5]. The Eurocer was used in experimental study performed on rabbits [12] and we have observed a good radiological osseointegration. Histological findings confirmed that the material is visible and surrounded by lamellar bone (newly formed bone) and the bone sequestration is absent.

Actual research is directed toward the production of macroporous phosphocalcic cements in order to increase the osteoconductivity and biodegradability without altering the biomechanical properties.

VI. Conclusions

This prospective study demonstrated that the biphasic synthetic ceramic material Eurocer® is an effective bone graft substitute for usage in patients with bone defects. The authors appreciated the intraoperative versatility of this product. In all cases, bone consolidation was fast and of good quality, with lack of inflammatory processes. To insure a consistent result it is mandatory to strictly follow the three requirements for osteoconduction: proximity, viability and stability.

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