Biphasic synthetic bone substitute use in orthopaedic and trauma surgery: clinical, radiological and histological results

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Searching for an alternative to bone grafts in orthopedic and trauma surgery, two biphasic synthetic calcium phosphate ceramics BCP are made: the first, Eurocer 400®, in granule form with a high interconnected porosity for void-filling, and the second, Eurocer 200®, available in different shapes, with a good mechanical resistance in compression. Two hundred cases are reported with more than a six-month follow-up. The first 72 cases relating to hip arthroplasty revision surgery (29 involving acetabular and 43 femoral stem loosening) are exposed with some technical details. The next 71 cases concerning trauma and sequels are displayed with technical particulars. The remaining 57 other cold orthopedic indications are then enumerated. The very good biocompatibility of these ceramics is confirmed. Radiological incorporation is quickly seen in all the cases, faster with the filling substitute than with the second one, which, however, presents no mechanical failures when classical technical principles are respected. Finally, some histological studies are presented; the ceramics are progressively resorbed and bone reconstruction in and close to the substitutes is noticed. Therefore, the use of biophasic ceramics in almost all orthopedic and trauma surgery is recommended.

1. Introduction

Dealing with bony defects is a daily challenge for the orthopaedic and trauma surgeon. Easily performed in case of a small defect without impairment of the mechanical properties of the bone, this repair can be difficult for larger losses of substance. Autografts, while bringing potentially osseoinductive living cells, are still valued as a good technique. Nevertheless, due to restricted stock and possible morbidity during the harvesting procedure, indications of autografts are limited to some atrophic pseudarthroses. Xeno- and allografts share an immunological risk, leading to potential sequestration, as proven histologically for xenografts and explaining middle and long-term failure rates by progressive resorption for allografts. Both techniques are suspected of viral and bovine spongiform encephalopathy (BSE) transmission, even with increased security measures. Meanwhile, calcium phosphate ceramics have gained from these problems and enlarged their indications.

2. Material and methods

A high degree of biocompatibility of synthetic calcium phosphates has been shown by many authors after multiple animal experiments and proven by a 10-year-old clinical application [1–12]. Bacterial and viral innocuity, thanks to the manufacturing technique of sintering, impose a full respect of manufacture and packing safety rules. Their bioactivity is proven by many authors [13–22]. Until now the only limiting factors in calcium phosphates ceramic utilization are their poor mechanical properties when made porous. Bioactivity relies on physical and chemical properties of biphasic calcium phosphate ceramics (BCP), likewise their mechanical strength has been shown to be a function of their porosity, the pore diameters and the respective composition of their two mineral phases [4, 19, 20, 23–29]. Furthermore, Trecant *et al.* [30] showed a fast and significant increase of these properties during the first weeks after implantation into the human body. As a conclusion of the previous experiments, we studied the possibility of synthetizing two new different ceramics: one for defect filling, another more mechanically orientated. Eurocer 400* is a biphasic ceramic with 400 μm wide pores. It is composed of 55% hydroxyapatite and 45% tricalcic phosphates, leading to a totally interconnected porosity of 60%. It is presented in

2–3 mm large, roughly square granules. Eurocer 200* is also a biphasic ceramic, composed of 65% hydroxyapatite and 35% tricalcic phosphates. Its pores are 150–200 μm wide, the occupied volume representing 40%, only partially interconnected and mainly on the surface. The presentation forms are multiple (cubes, sticks, discs, wedges). Eurocer 200*'s most original feature is its compressive resistance, designed to be comparable to human bone; σ_M value oscillates between 21 and 30 Mpa. These ceramics are prepared in a classic way: the chemically synthetized basic products are transformed from a powder to a compact structure, and then sintered. These products have been available since October 1996, after having gained all safety and administration approvals, including European Community tracing.

Two hundred patients (97 females, 103 males; 5 to 90 years old, average age 55) treated by the authors with these two products, have now 6 to 36 months follow-up. This is a prospective study with paper as well as computer data, allowing accurate and quick evaluation. A general principle, never to be transgressed, for the use of these ceramics is the need of a living recipient site: calcium phosphates, while not or indeed for some authors weak osseoinductors, increase only speed and quality of bone production. According to these rules, the milestone is a thorough debridement with complete bone necrosectomy before insertion of the substitute. For Eurocer 200*, the contact surface between bone and substitute needs to be as large and intimate as possible, as well as in compression, and weight bearing will be encouraged. Of course, any flexion or shearing stresses must be avoided.

In 72 cases, hip revision surgery was addressed. Twenty-nine cases involved an acetabular cup loosening, and 43 others a femoral stem loosening, mainly on cemented arthroplasties. The loosenings were staged according to Paprosky's classification. The femoral anatomical status often imposed a transfemoral approach. Moreover, it makes easier the necessary thorough curettage and debridement; completely removing any loosening granuloma, fibrosis, cells, and wear and tear particles, is mandatory. In the technique we have proposed, the acetabulum is reconstructed with a ring leaning on the substitute which fills up any gap and cavity. We used the compression mechanically strong Eurocer 200* as cubes and/or discs filled in in the remaining acetabulum. This paving is completed by small chisel-cut BCP chips, wherever larger cubes or discs were inadequate, or better with the second BCP, Eurocer 400*, to fill up the gaps in this support frame. The support ring is then applied and positioned in such a way that its hook anchors in the obturator foramen and is then strongly fixed in the iliac wing, achieving good stability and allowing immediate weight bearing. The last stage of the procedure is the application of a polyethylene cup onto the ring, cemented with the thinnest layer possible so as to be strong enough, but not to spread out between the substitute layout (Fig. 1).

Nevertheless when a good peripheral mechanical continuity remains, we use large cementless press-fitted cups, after actabulum cavities and perforations into the pelvis have been filled with Eurocer* and good hemispherical regularity is achieved. On the femoral side also, BCP will be used to fill up any loosening cavity. Quite a huge quantity of substitute can be compressed between the cementless prosthesis stem and the somewhat thin cortices of the remaining femur. A transfemoral approach enables a better filling of geodic cavities along the loosened femur in grade III or IV, and allows for disposing Eurocer 400* along vertical or horizontal osteotomy notches, which leads to a faster and better consolidation. The rarer use of Eurocer 200* in the femur can be regarded as useful for wedging the femoral stem against weak metaphyseal cortices, by impacting chisel-fragmented BCP chips, or for closing a femoral window with a piece of substitute which will be embedded in it and fixed by a cerclage (Fig. 2).

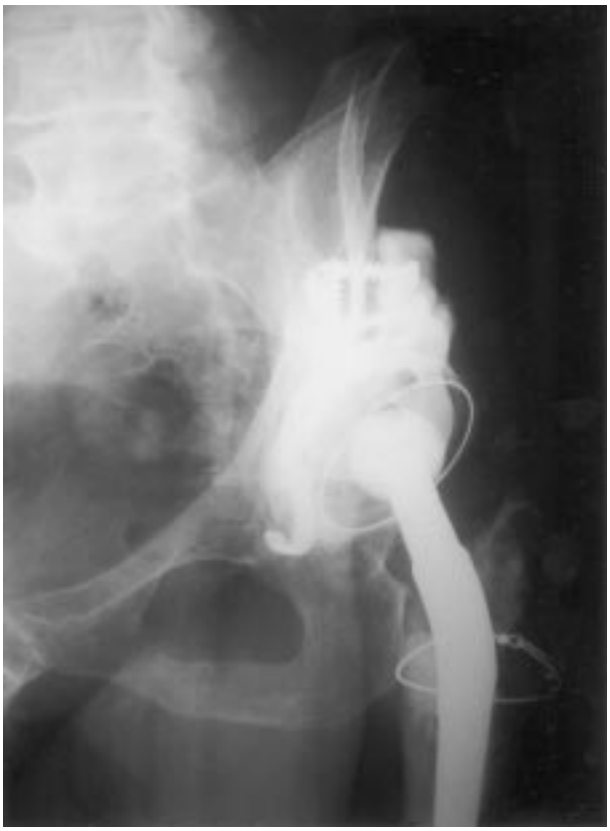

Figure 1 Paprosky's type III acetabular loosening, reconstructed with a screwed ring and Eurocer 200* after 2 years.

In any case the remaining surrounding soft tissues (capsule, fat) are used to avoid any possible contact between joint cavity and substitute particle, so minimizing any risk of third body.

Seventy-one cases concerned recent trauma cases (49 recent fractures) or sequelae (22 pseudarthrosis) (Table I). In traumatic impaction or comminutive losses of substance, the use of ceramics is advantageous, instead of autograft. Once again, all technical standards should be respected: no extensive periosteum stripping, removal of any devitalized cortical fragment, as strong an osteosynthesis as possible, covering of the fracture site by surrounding soft tissues. Impaction of different forms of Eurocer 200* in compact cancellous bone acts as a buttress, as in tibial plateau fractures, and allows non-constrained mobilization and partial weight bearing Fig. 3).

The same results are obtained for cancellous impaction fracture previously treated by an osteosynthesis and

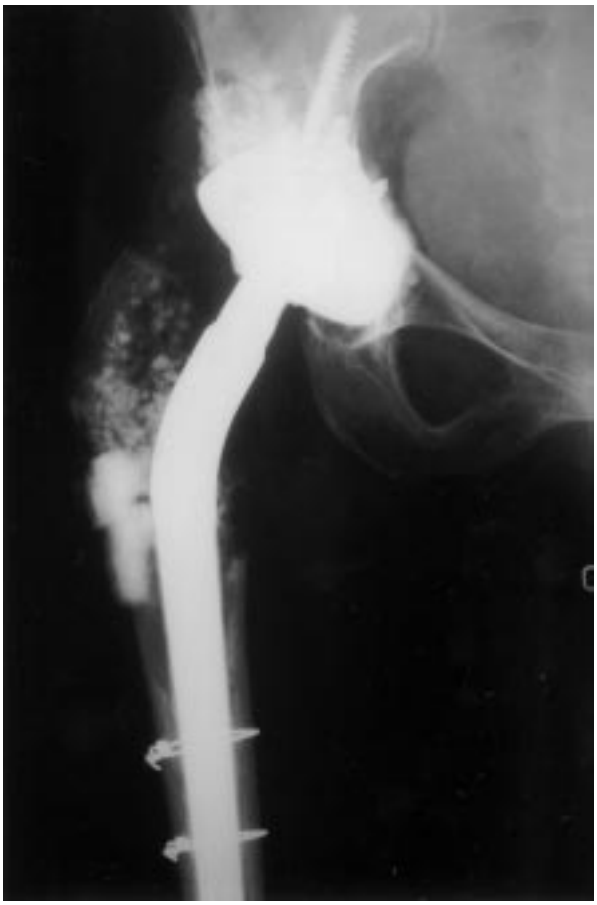

Figure 2 Paprosky's type II acetabular loosening, reconstructed with Eurocer 400* and femoral loosening type III reconstructed with Eurocer 200* and Eurocer 400*: after 1 year.

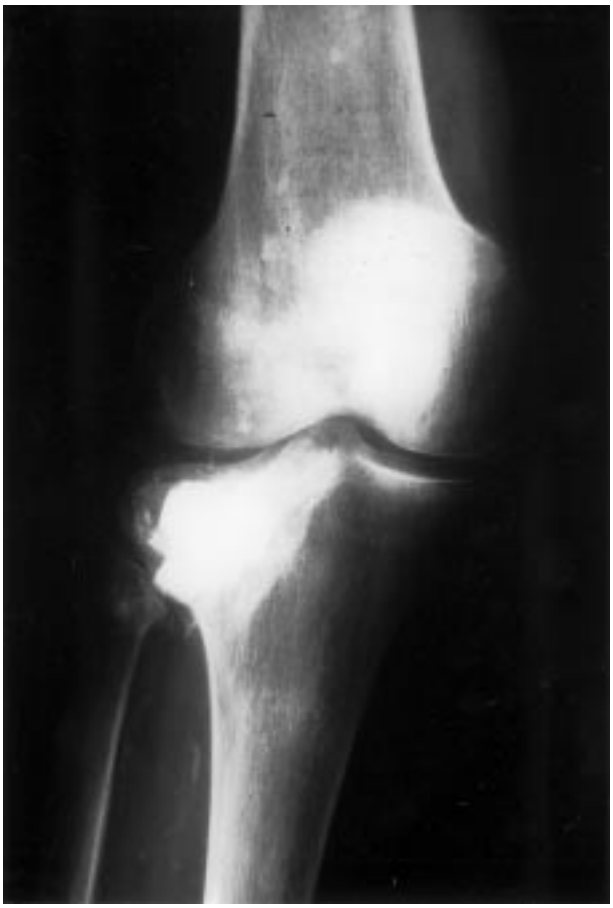

Figure 3 Tibial plateau fracture repaired with Eurocer 200*: result after 6 months.

cancellous autograft (tibial *pilon,* femoral supracondylar fracture, etc. Fig. 3). The same respect of technical standards are expected in treatment of pseudarthrosis: decortication, perforation of the medullary canal and a strong fixation, are of course mandatory. Eurocer 400* is then applied around the fracture site over a few centimeters in the bone defect and in the medullary canal. Nevertheless, complement with classic autograft will be necessary for wide atrophic pseudarthrosis where poor local biological conditions will not allow the use of substitutes alone; these products lacking osseoinductive factors for the moment. Neither should they be used in infected pseudarthrosis, for even after careful debridement and wash-out, any inert body can cause a high risk of failure in case of remaining infection. Antibiotic added substitutes with delayed release remain experimental in our country. The more frequently observed prosthesis fractures, especially on senile bone with beginning or confirmed loosening, have benefited from the use of Eurocer 400* in addition to fixation. At last, owing to the good results of these indications, we now use BCP granules in addition to osteosynthesis when dealing with very porotic fractured bones in elderly patients.

In the 57 cases involving *cold* orthopedic surgery, we used both substitutes, with a small preference for Eurocer 200* because of its mechanical advantages. This point is especially valuable in addition osteotomies (Table III) where a stable fixation is mandatory to achieve immediate partial weight bearing, and thus quick healing. Eurocer 400* and Eurocer 200* were used to fill the opening after osteotomy in coxarthrosis or

TABLE I Division of trauma lesions and sequelae

	Clavicle	Humerus	Radiusulna	Femur	Tibia	Spine	Hand
Fractures	5	3	2	17	15	6	1
Pseudarthrosis	3	2	4	10	3	0	0

TABLE II Division of osteotomies

	Distal radius	Proximal femur	Distal femur	Proximal tibia	Anterior tibial tuberosity
Osteotomies	1	6	2	12	13

gonarthrosis. It was, on the other hand, used in six benign tumors (chondromas, Grade I & II giant cell tumors, fibromas, etc.) after thorough curettage, then filling up the defect with BCP granules, in some cases as large as 4–5 cm, sometimes supplemented with Eurocer* 200 when mechanical support is needed (Fig. 4). The same technique was used in 11 other different voids and gaps, after device removal for example. These were used for four posterolateral grafts in lumbar spine arthrodesis, as in a knee and an ankle arthrodesis, with regular consolidation without delay and with bone, blood and time and money saving.

3. Results

No biological problems were noted, as already guessed with other ceramics by numerous published clinical applications [31-43]. The only mechanical failures needing revision, in three cases, were due to technical mistakes, that is to say insufficient osteosynthesis. Radiological controls showed very quick integration of Eurocer 400* with homogeneous aspect of cloudy new bone in intimate contact with the recipient site. Callus densification increases quickly with time, together with recipient bone trophicity. We think this is of course due to better mechanical activity, especially in prosthesis loosening, as well as good supply of reconstruction material by BCP. The radiological follow-up of our revised femurs, operated through transfemoral approach, leads us to this hypothesis. Local bone reconstruction quality and speed are enhanced by these substitutes. A paper by Le Huec and Clement [10], studied the evolution of ^{45}Ca labeled tricalcic phosphate in rabbits and showed its important local utilization; it can explain partially our observation. Radiological evolution of the more mechanically Eurocer 200* is different. Fast integration, enhanced by compression, is easily seen as superficial rehabitation. But it seems difficult to quantify this phenomenon in depth. Its unchanged central radiological density after two and a half years follow-up makes any idea of deep biological rehabitation rather doubtful. The follow-up is too short for the time being, remembering the slow pace of haversian remodeling, even in good biological conditions. This question will need 15 to 20 years follow-up time to be discussed again. Nine biopsies have been performed 4–15 months after removal of material in various sites. Histological studies show several stages leading to complete BCP integration to human bone, but different from animal experiments: at first, ceramics are surrounded by a coarse conjunctive tissue, host to many fibroblastio-type cells with tartrate resistant acid phosphatase (TRAP) + nucleus; then appears a thicker conjunctive tissue around BCP with collagen condensation on the implant surface and much membrane alkaline phosphatase active fibroblastic cells; the last stage shows bony tissue in ceramic pores, in the contact areas. Osteoid tissue is present in relatively great quantity, with ceramic fragments included in newly formed bony trabecules, as well as osteoclastic TRAP + cells located in Howship's lacunae on the bone surface; in very poor bone, enhanced bone formation around and in BCP can be observed (Fig. 5).

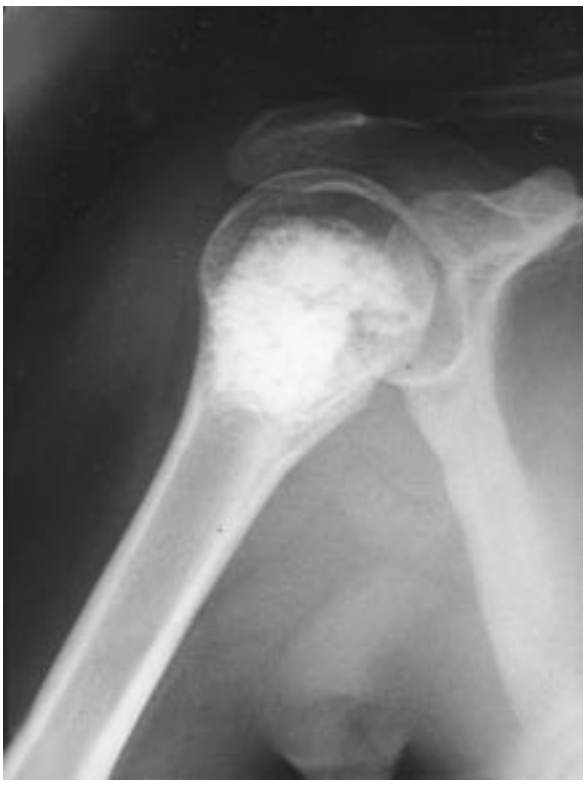

Figure 4 Giant cell tumor grade 2 filled with Eurocer 400* and Eurocer 200*: radiograph after 9 months.

4. Discussion

Even with a relatively short follow-up period, clinical, radiological and histological results of biphasic calcium phosphate utilization in trauma and orthopaedic surgery is very encouraging. No real complications were observed in two and a half years. The synthetic bone substitutes appear to be as safe and as effective as autograft when used in trauma situations. Safety and less morbidity makes it effective compared with other bone

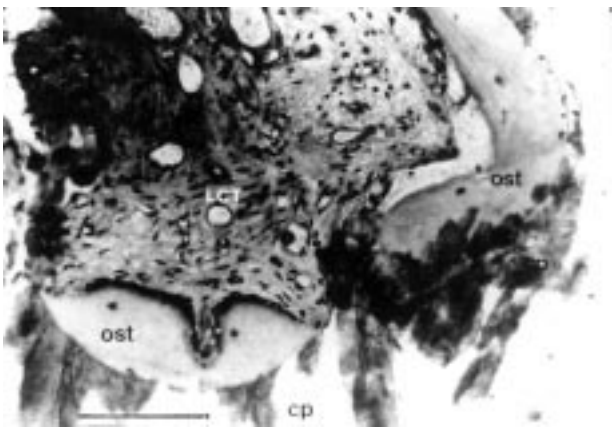

Figure 5 Micrograph of a section of Eurocer 400* in a human femur in close proximity to a hip prosthesis. The ceramic (cp) is in contact with osteoid (ost) which is layered by osteoblasts. A loose connective tissue (LCT) is present in the pores coated by osteoid. This loose connective tissue supplies the osteogenic stem cells. Giemsa stain. Bar = 200 μm.

grafts; last, results will next be improved by osteoinductive factors or cell adjunction. Therefore we use them more and increase their indications.

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