Open trial in 289 patients

Augmentation and Defect Reconstruction with a New Synthetic Pure-Phase Beta-Tricalcium Phosphate

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In a mono-center open trial, 325 patients were treated with beta-tricalcium phosphate granules for bone grafting. In 289 of them, Cerasorb M was used alone, in all others the bone grafting material was combined with autogenous bone. Filling bone voids left after wisdom tooth extraction, extraction sockets and apicectomy cavities were the most common indications. A membrane was used in 84 cases. The patients were followed up at 1 week, 3 and 6 months, some of them also at 9 months. Most of the defects repaired were up to 1.5 ccm in size, some of them up to 7 ccm. Handling of the synthetic granules proved to be easy. Depending on its amount and the site treated, the grafting material was resorbed after 3 to 9 months. Eight patients (2.8%) presented with signs of inflammation. In three of them, postoperative wound healing was impaired.

Introduction

Dental implants have become a generally accepted treatment modality in the prosthodontic management of edentulous and partially dentate patients. An adequate bone volume for accommodating root form implants and adequate primary implant stability ensuring implant osseointegration are key for a successful outcome.

Neukam and Buser [12] showed that a certain minimum bone volume both vertically and transversally is required for implant placement in the upper and lower jaw. But as most of the bone defects secondary to extractions continue to be left alone, the alveolar process is often severely resorbed particularly in the distal maxilla. In the upper jaw sinus descent may complicate vertical and/or horizontal bone loss and require sinus lifting.

Prosthodontists have come to insist on "backward planning" for implant placement based on ideal prosthodontic baseline conditions. Surgery-driven implant placement in what bone is available is no longer acceptable in the referral setting so that there is an increasing need for bone grafting and reconstruction.

Autografts and xenografts, which have widely been used for this purpose, no longer meet what is expected of a safe bone grafting material – not only because of the potential residual risks inherent in biologic materials [5, 6]. While bone autografts continue to be the "golden standard" for many users and for most clinicians, their functionality as a bone grafting material as well as the associated donor site morbidity and the risk of persistent damage to the patients are increasingly given critical attention [9], all the more so as a number of suitable synthetic grafting materials has been around for some time now. Whether or not autogenous bone still fulfills what is currently expected of a suitable bone grafting material should also be considered from an economic point of view.

All of this prompted the present study to evaluate the applicability and clinical usefulness of a new beta-tricalcium phosphate (TCP) with a polygonal granule structure, Cerasorb M, for bone regeneration.

Material and methods

Between September 2004 and December 2005, void filling or bone grafting was performed in all candidate patients with a synthetic bone regenerating material alone or in combination with autogenous bone.

For bone regeneration a new synthetic pure-phase beta-tricalcium phosphate, Cerasorb M, was used. The material comes in two granule sizes, i.e. 500 to 1,000 µm and 1,000 to 2,000 µm. Its distinguishing features are its interconnecting open multiporosity and its polygonal granule structure. The special micro-, meso- and macroporosity of the granules enormously expands the surface area of the material available for wetting by plasma and tissue fluids and for the adhesion of autogenous proteins thus promoting its resorption. The porous structure of Cerasorb M has been optimized with a view to preventing what has often been criticized about pore systems, i.e. their potential colonization by microorganisms, which thus escape the cellular host defense mechanisms [15, 19]. The multipore system of surface expansion also promotes the entry of growth factors subservient to osteogenesis/osteoinduction into the matrix and the ingrowth of bone-forming cells and connective tissue fibers to provide multicentric sources of osteoneogenesis in the matrix. The macropores, in their turn, permit the ingrowth of blood vessels for the nutritive supply of the ingrown cellular and fibrillary elements and the newly formed bone [4, 11].

The beta-tricalcium phosphate Cerasorb M is characterized by an extremely high phase purity of >99%. Even the most sensitive tests fail to detect impurities like hydroxyapatite or alpha-TCP [18].

The biomaterial is composed of large primary particles embedded in a strong sintered scaffold. This structure prevents its early breakdown into small particles, which could cause aseptic inflammation of the surrounding soft tissue with failed bone regeneration, a phenomenon known to occur in the past with unstable bone substitutes of inadequate particle size [2, 3].

Before applying the Cerasorb M granules the surrounding viable bone was invariably freshened vigorously, at times using a burr, and the granules were soaked in the fresh blood oozing from the wound. If the amount of blood was inadequate, venous blood withdrawn intra-operatively was added. Occasionally, PRP (platelet-rich plasma) was also applied.

Depending on the conditions encountered, the grafting material was covered with a resorbable (Epiguide) or non-resorbable (TefGen) membrane for GBR (guided bone regeneration). Epiguide is a fully resorbable synthetic polylactide membrane with a patent-protected multilayer structure. It acts as a barrier for about 2 to 3 months and is resorbed within 6 to 12 months. The hydrophilic membrane (manufactured by Kensey Nash, USA, and distributed by Curasan AG, Germany) is immunologically inactive, broken down to CO_2 and H_2O and very well tolerated. It can easily be trimmed to the desired size, safely handled and readily applied. In most cases it need not be secured, but it should be covered.

The TefGen membrane consists of synthetic polytetrafluoroethylene (PTFE/Teflon) and is highly inert biochemically. Though not resorbable, it is extremely biocompatible. Two variants of appropriate elasticity and surface texture are available. Both variants may be left exposed. Bacterial colonization is rare. The membrane can be removed atraumatically after 4 to 6 weeks in a minimal invasive procedure. This means that no more than a small incision is required in most cases to retrieve it.

After adequate reconstruction or augmentation the patients enrolled in this study received one-stage or two-stage cylindrical or root form titanium implants (3i Implant Innovations Inc., USA).

Ultracain/articain was routinely used for local anesthesia. For pain relief patients were, as a rule, given ibuprofen, 600 mg. Pre-operatively, antibiotics were only administered if dictated by intra-oral conditions. Postoperatively, patients with signs of intra-oral inflammation were prescribed clindamycin HCL, 600 mg t.i.d., for 5 to 8 days.

All patients were followed up clinically and radiologically (digital OPG with software for imaging hard tissue thickness and for linear measurements) at the following time points: Clinical follow-up with removal of sutures at one week; digital OPG at 3 and 6 months. The longest follow-up time was about 12 months.

In keeping with the study design no statistical data analyses was performed. Rather, the radiographs and the clinical course were evaluated descriptively.

Results

Between September 2004 and December 2005, 325 patients were treated with Cerasorb M and documented in an in- and outpatient setting. In the course of this prospective, mono-center open study 289 of them received Cerasorb M alone for bone regeneration. The remaining 36 patients underwent reconstructive and peri-implant treatment or major alveolar reconstruction with Cerasorb M combined with autogenous bone grafts.

As the data of the latter patient group defied comparison with those of patients treated with Cerasorb M alone without autogenous bone or PRP, they were not included in the evaluation.

The Cerasorb M-only group consisted of 108 females and 181 males aged between 14 and 84 years (mean age, 38.5 years). They underwent surgery for grafting, i.e. vertical ridge augmentation/onlay grafting (n = 52), sinus lifting (n = 17), alveolar cyst repair (n = 59), void filling after orthograde or retrograde apicectomy (n = 82), reconstruction of extraction sockets (n = 107) and extraction of wisdom teeth (n = 329 teeth).

In the group of defect reconstructions after wisdom tooth extraction 1 to 4 defects/patient were in need of filling. In the apicectomy group each tooth treated contributed 1 to 3 roots, because no distinction was made between single-, double- or triple-root teeth. In the augmentation/onlay grafting group the area treated in each case corresponded in size to the width of 1 to 6 premolars.

Membranes for GBR were used in 84 patients. Twenty-three of them were non-resorbable (TefGen), some of them exposed, while 61 were resorbable (Epiguide), all of them covered or at best minimally exposed.

In all indications listed above the ß-TCP granules were easily applied to the defects without any problems. Of the 289 patients enrolled in this study, 281 showed no evidence of local or general intra-oral inflammation. None of these developed post-procedural infection or showed poor wound healing. With the wounds bland, the sutures were drawn after 10 days at the latest in all cases. In 13 patients excess bone grafting material escaped through the mucosa in the later postoperative period. Revision was, however, not necessary.

The remaining 8 patients presented with signs of inflammation. Three of them showed poor wound healing, in another 2 membrane loss occurred. Two of the patients with poor wound healing and both of those with membrane loss were nicotine abusers. In none of these patients was there any need to remove the bone grafting material. All of them healed uneventfully on antibiotics.

Three groups of bone defects were distinguished by size: up to 1.5 ccm, 1.5 to 2.5 ccm and more than 2.5 ccm. Defects of more than 5.0 ccm were considered to be “critical size”. Management extended to defects up to 7.0 ccm.

123 patients presented with defects of 1.5 ccm. In 92 of them the bone grafting material was completely replaced by bone at 3 months, in the remaining 31 at 6 months.

106 patients showed defects of 1.5 to 2.5 ccm. In 71 of them the material was completely resorbed at 6 months, in the remaining 35 at 6 to 9 months.

60 patients had defects of more than 2.5 ccm, some of them of more than critical size up to about 7 ccm. In all of them homogenous consolidation was seen radiologically at 6 to 12 months.

Late follow-ups were invariably radiologic. Bone biopsies were obtained from 23 patients, who had undergone vertical ridge augmentation, sinus lifting and reconstruction of extraction sockets, during implant surgery after 3, 6 and 9 months. Some of these biopsies were evaluated histologically. These did not show any histomorphologic evidence of bone loss by phagocytosis or foreign body reactions.

The membranes applied in 84 patients enhanced graft healing and contributed to graft surface consolidation in 82 cases.

Two representative cases

Patient 1 (see Figs. 1 to 6) – SB, age 47 years. Diagnosis: Teeth 46 and 47 lost to restorative procedures. Management: 46 and 47 were extracted, the sockets were filled with 1.0 ccm Cerasorb M, granule size 1,000 to 2,000 µm, covered with Epiguide membrane.

Follow-up: Digital OPG postoperatively. Sutures drawn after 1 week. Digital OPG after 3 and 6 months. Bone biopsy and placement of 2 implants (3i NT 5x15 mm) after 6 months.

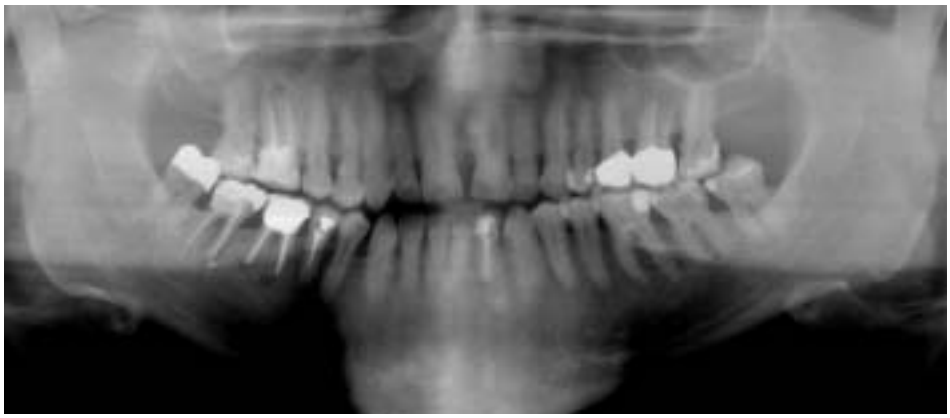

Fig. 1
Baseline OPG

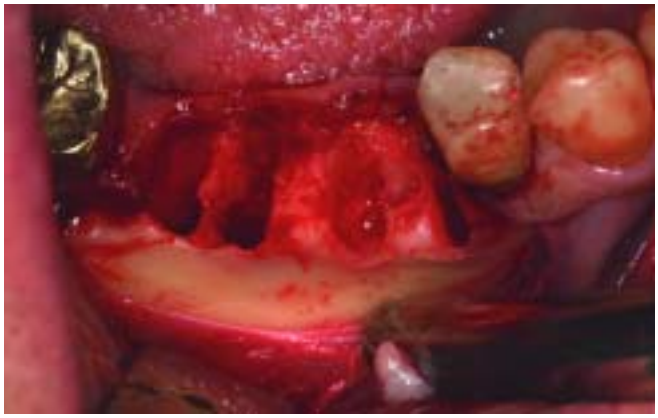

Fig. 2 Post extraction

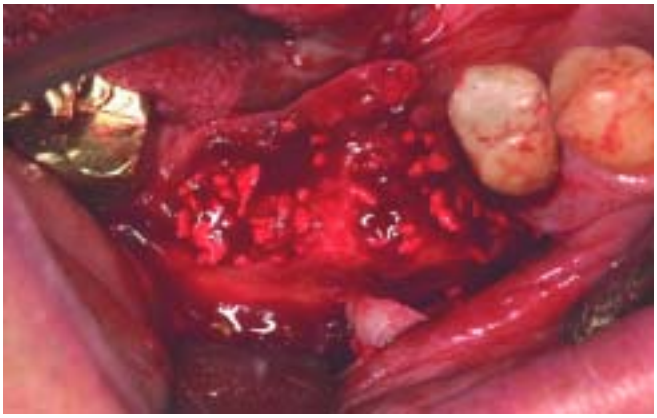

Fig. 3 Post grafting with Cerasorb M

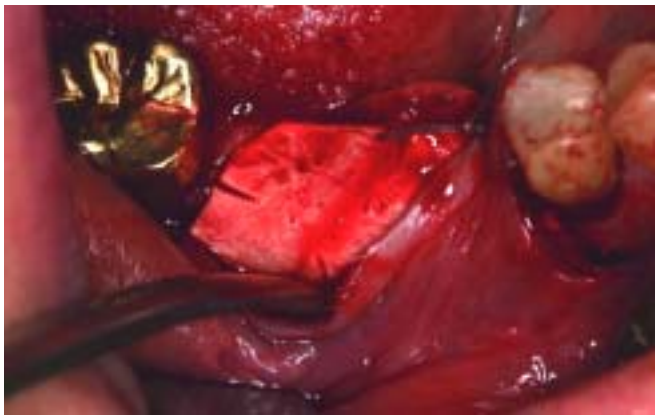

Fig. 4 Coverage with Epidguide membrane

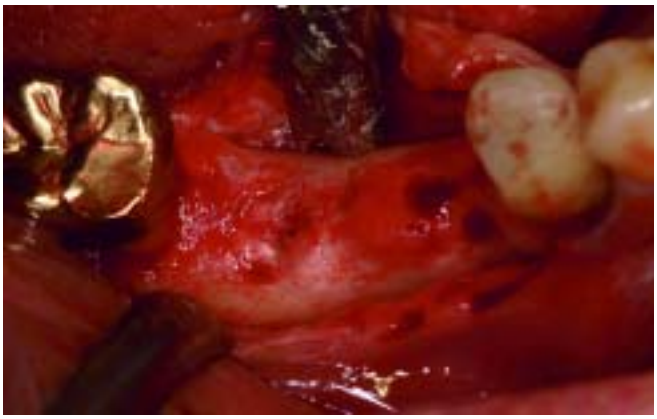

Fig. 5 Exposed alveolar ridge 6 months post grafting

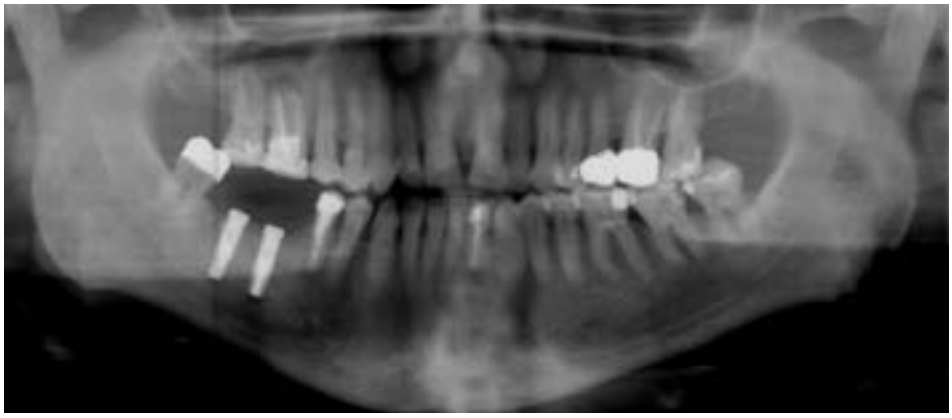

Fig. 6
OPG post implant placement

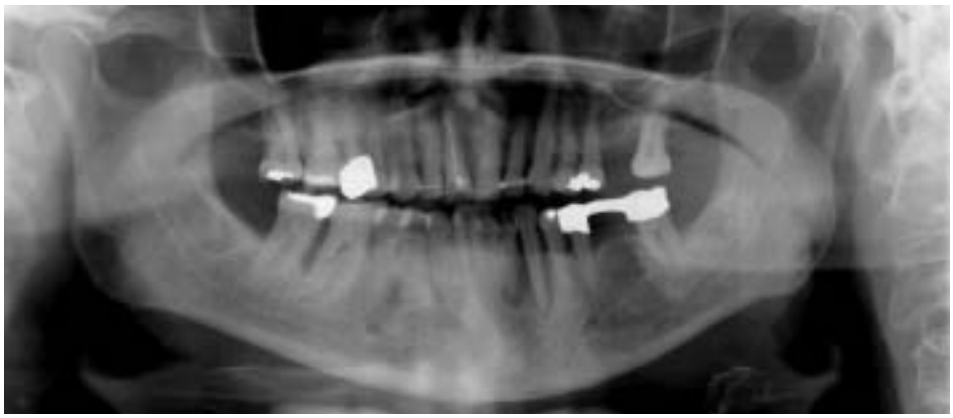

Fig. 7
Baseline OPG

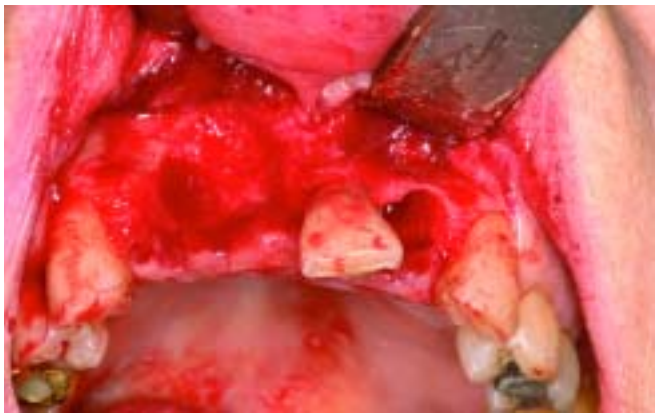

Fig. 8 Clinical view post extraction

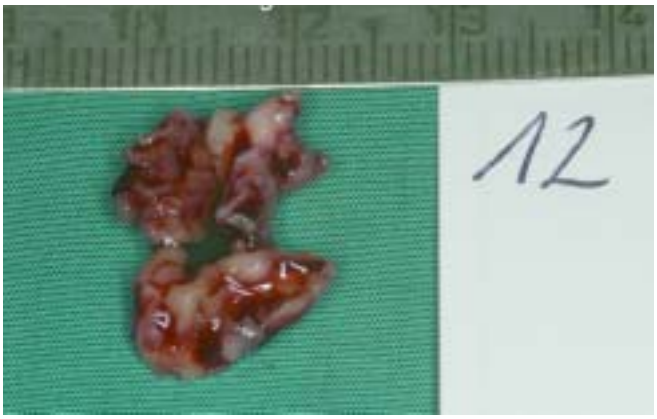

Fig. 9 Excised tissue

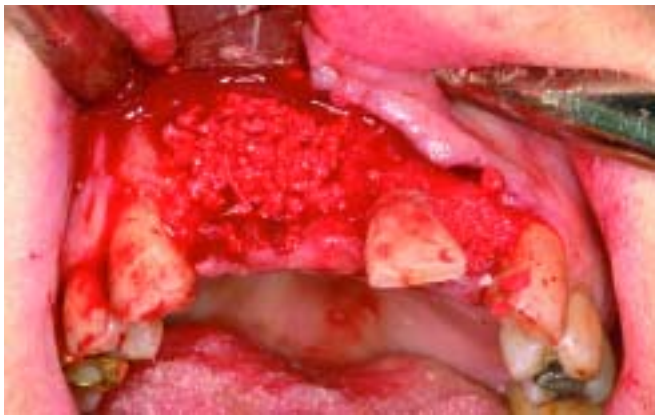

Fig. 10 Post grafting with Cerasorb M at sites of 12 + 11 + 22

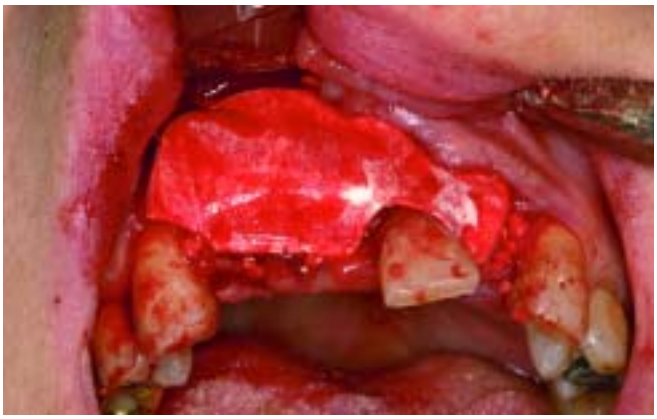

Fig. 11 Coverage with Epiguide membrane

Histology after 6 months: No bone grafting material detectable any more. Matrix of active, remodeling, partly lamellar bone present at the grafted site.

Patient 2 (see Figs. 7 to 15) – AB, age 63 years. Diagnosis: Localized profound marginal periodontitis around teeth 11, 12 and 22; extensive periapical osteolysis around 12, 11, 22 lost to restorative procedures. Treatment: Extraction, cystectomy 11, 12, 22; void filling with 2.0 ccm Cerasorb M, granule size 1,000 to 2,000 µm, covered with Epiguide membrane. Tissue sample sent for histology. Actinomyces missed pre-operatively impaired wound healing with minor augmentation loss.

In addition to the implants at sites 12, 11 and 22 shown clinically, the patient underwent ridge augmentation and implant placement at sites 26, 32, 33 (after extracting 31) and 43 as well as apicectomy of 46 with defects filled with Cerasorb M.

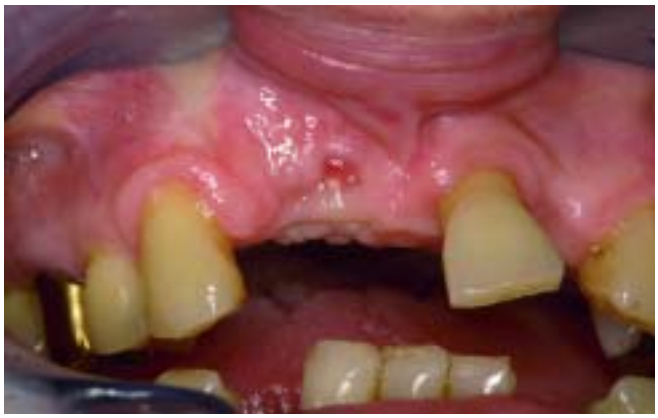

Fig. 12
Clinical view after 6 months

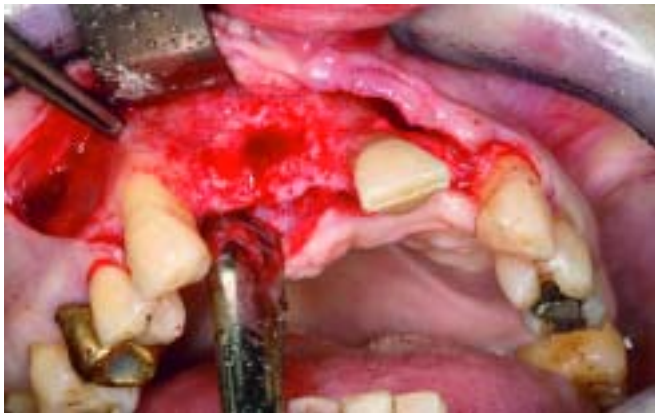

Fig. 13 Reconstructed defect after exposure

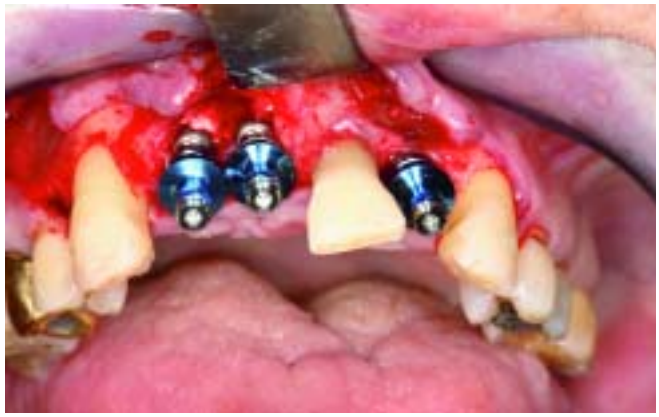

Fig. 14 Post implant placement at sites of 12 + 11 + 22

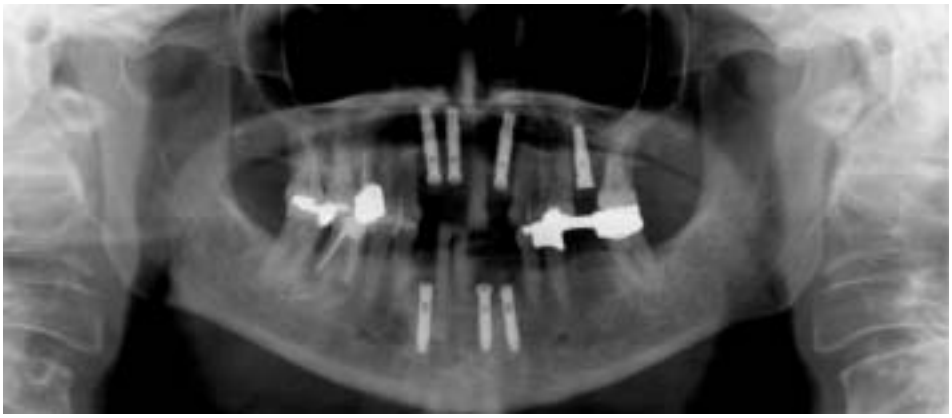

Fig. 15
Follow-up OPG post implant placement. Sites of 26, 32 and 33 (after extracting 31) and 43 were grafted at the same time with subsequent implant placement and apicectomy was done on 43. All defects were filled with Cerasorb M.

Histology: Cyst colonized by anaerobic organisms. Antibiosis: Clindamycin, 600 mg, q.i.d. for 8 days; doxicycline, 200 mg, q.d. for 20 days.

Follow-ups: Digital OPG postoperatively. Sutures drawn after one week. Digital OPG after 3 and 6 months. Implants placed after 6 months: 3i NT at site of 26, 3i OSS at all other sites.

Discussion

Fresh bone autografts are known to have the best growth and healing potential. They would continue to be the golden standard for reconstructing defects and would, no doubt, be the ideal material, if harvesting them would not disrupt the routine in the practice setting to a considerable extent. Various donor sites are available. These include the mandibular angle and the chin in the lower jaw, the retromolar

and palatal regions in the upper jaw, the tibial head and iliac crest whenever large-volume grafts are needed. No matter what the donor site, graft harvesting invariably requires minor or major secondary surgery. The rate of potential donor site complications can apparently be reduced by a subtle technique. But it is still reported to lie between 20% and 30% [1, 10]. The poorly predictable resorption pattern is another problem. Harvesting grafts from the tibia or iliac crest significantly increases personnel and material expenses. Needless to say that these should not go beyond what is economically feasible. Niedhart et al. [13] and St. John et al. [16] found that several hundred € to more than thousand US$ were needed for harvesting autogenous bone from the iliac crest in forensically and technically implacable procedures. This goes to show that synthetic bone regenerating materials also are an alternative to bone autografts cost wise. The absence of significant histologic and histomorphometric differences between Cerasorb M and bone autografts used for bilateral sinus lifting at the time of implant placement 6 months after grafting in a multicenter split-mouth trial recently conducted by Szabo and coworkers supports this assumption [17]. Non-autogenous grafting materials may be synthetic or semisynthetic, of bovine (animal) or human donor origin. The latter, i.e. bank bone, is uncontestedly associated with some residual risks for both the surgeon and the patient. A potential transmission of BSE, foreign proteins and priones as well as the potential sequels of grafting with bovine material have frequently been reported in the literature and cannot altogether be precluded [5, 6, 7]. Add to this a recent court decision mandating more comprehensive information of patients, who are candidates for grafting with bovine materials [14] and add further the risk of "stigmatizing" patients receiving bovine grafts as legally unfit for organ and blood donations at least in some counties/states.

Many synthetic bone grafting materials of hydroxyapatite or beta-TCP are either incorporated by contact osteogenesis after more or less extensive resorption or they are variably digested by macrophages in an inflammatory reaction. Ideally, a material should be resorbed by osteoclasts followed by remodeling by osteoblasts. This has so far only been documented for autografts. Cerasorb M largely fulfills these criteria. But what is known about the ultimate relation of allografts to the surrounding hard and soft tissue over time does not permit to definitely exclude any other class of materials at this point in time.

Together with the interconnecting pore system, the favorable primary configuration of Cerasorb M promotes and supports bland and efficient healing. Pores in the micrometer range are conducive to the ingrowth of bone forming cells and connective tissue fibers, which constitute the source of multifocal osteogenesis in the matrix. Macro-pores (100 to 500 µm in the case of Cerasorb M) permit the ingrowth of blood vessels, which supply the ingrown cellular and fibrillary elements and the newly formed bone. The high total porosity (about 65%) enhances the capillary effect thus serving as a basis for cell supply and resorption – from within. The polygonal canting granules facilitate handling and application and largely prevent undesirable micromovements. The surface is devoid of sharp edges and well rounded. Mixed with patient blood from the defect, the material is easily handled and reliably stays at the grafted site. Thanks to the low bulk density and high reconstructive volume, less material is needed for the void filling and space maker functions, so that both the resorption effort of the body and the material use by the surgeon are minimized.

Cerasorb M fulfills the criteria for low-risk routine use in the practice setting. These include insensitivity to potential or unavoidable transmission of infections; applicability for defects up to the critical size (= 5 ccm); high degree of resorption and replacement by bone; safe and easy handling in the practice setting at reasonable cost; radiopacity facilitating radiographic follow-ups; optimal safety forensically on account of high-purity, metal-free, fully synthetic production.

Suboptimal bone regeneration reported in a few cases was apparently attributable to the early ingrowth of connective tissue, which prevented a direct contact of the grafting material with the host bone. The high success rate, in turn, was no doubt due to routine vigorous bone freshening and the complete removal of soft tissue prior to void filling.

Recent cataloguing of Cerasorb with a measured phase purity of >99% has made the product the worldwide standard for ß-TCPs [8]. The reproducibly high phase purity guarantees reliable and predictable bone regeneration, because users can be sure to find the same material and chemical properties in every pack of Cerasorb or Cerasorb M at any time.

Conclusions

Cerasorb M is an ideal synthetic material for use in dental practice with a porosity largely mimicking that of natural cancellous bone. As it is fully synthetic, it does not expose surgeons and patients to the risks inherent in materials of biologic origin, i.e. potential allergy, infection, "stigmatization", nor does it require extensive pre-procedure patient information. It is characterized by ease of handling, optimal applicability and retention. Rapid resorption (determined by the underlying individual physiology) and simultaneous formation of new bone facilitate reconstruction even in problem patients, in those requiring immediate implant placement despite a reduced bone volume and – needless to say – in candidates for implant placement 4 to 6 months post reconstruction, depending on the site grafted. ■

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PRODUCT LIST

Indication	Product	Manufacturer/Distributor
Bone grafting material	Cerasorb M	Curasan
Implant system	Osseotite NT	3i
Non-resobable membran	TefGen	Curasan
Resobable membran	Epi-Guide	Curasan

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