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Research Paper
Dental Implants

Impact of particulate deproteinized bovine bone mineral and porous titanium granules on early stability and osseointegration of dental implants in narrow marginal circumferential bone defects

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Abstract. The use of two particulate bone graft substitute materials in experimental narrow marginal peri-implant bone defects was investigated with respect to early bone healing and implant stability. Porous titanium granules, oxidized white porous titanium granules (WPTG), and demineralized bovine bone mineral (DBBM) were characterized in vitro, after which the two latter materials were tested in experimental peri-implant bone defects in six minipigs, with empty defects as control. After mandibular premolar extraction, the top 5 mm of the alveoli were widened to 6 mm in diameter, followed by the placement of six implants, three on each side, in each pig. Six weeks of healing was allowed. The WPTG showed better mechanical properties. No significant differences in resonance frequency analysis were found directly after compacting or healing, and similar quantities of defect bone formation were observed on micro-computed tomography for all groups. Histomorphometric analysis demonstrated a more coronal bone-to-implant contact in the DBBM group, which also displayed more defect bone fill as compared to the WPTG group. The better mechanical properties observed for WPTG appear of negligible relevance for the early stability and osseointegration of implants.

Key words: dental implants; biomaterials; experimental study; bone regeneration..

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Fresh extraction sockets frequently present dimensions greater than the implant diameter, and immediate implant placement may therefore result in a gap between the implant surface and the marginal alveolar ridge. This is often referred to as the 'jumping distance', which may also be encountered in staged implantation procedures.[1] A review has recommended grafting for a jumping distance of >2 mm, but further disclosed that controversy remains regarding how big the gap should be (1–2 mm or wider) for potential benefit from bone graft substitute materials.[2] Also, there is no consensus on which bone graft substitute material is most suitable for the regeneration of bone and for dental implant support in marginal peri-implant bone defects.[1,3] Bone graft substitute materials for this indication should preferably enhance early stability and proliferate osseous support for the implants.[4]

White porous titanium granules (WPTG), a synthetic bone graft substitute material, may be a candidate material. WPTG is derived from the heat treatment and oxidation of porous titanium granules (PTG), and the process alters its physical characteristics and colour. According to the manufacturer, this material is intended for use in aesthetically sensitive areas. Although PTG has been characterized previously,[5] this has not been done for WPTG. However, previous experimental studies have demonstrated WPTG to have osteoconductive potential.[6,7] In the in vivo part of the present study, WPTG was preferred due to the risk of plastic deformation of the metallic PTG during application and potential implant load in the experimental model.[5]

Deproteinized bovine bone mineral (DBBM) is a naturally derived bone graft substitute material and one of the materials most studied and used in conjunction with implant dentistry. Several studies have been performed previously with a design similar to the present study, and the application of DBBM was found not to be advantageous for implant osseointegration in gaps of up to 1.25 mm, although a benefit was suggested for gaps exceeding 2 mm.[8–10] WPTG has not been evaluated in such a model and, furthermore, the impact of bone graft substitute materials on early implant stability and osseointegration before 8 weeks has not been extensively researched previously.

This study was conducted to characterize and evaluate the effects of two particulate bone graft substitute materials with different hypothesized mechanical properties applied in experimental marginal peri-implant bone defects, with respect to early bone healing and implant stability. DBBM and WPTG were compared in vivo, and PTG were included in the in vitro analysis for comparison. The hypothesis was that the stronger bone graft material would provide better primary implant stability and thus enhanced early bone healing and osseointegration in vivo.

Materials and methods

A scanning electron microscope (SEM) (TM-1000; Hitachi High-Technologies, Tokyo, Japan) and a commercially available micro-computed tomography (micro-CT) desktop scanner (SkyScan 1172; Bruker microCT, Kontich, Belgium) were used to visualize and analyze the pore structure of the materials. A fixed volume (0.5 ml) of the bone graft substitute material was placed in an Eppendorf tube and scanned at 8-μm voxel resolution using 100 kV and 100 μA source voltage and current, with standard Al + Cu filter. Structural characteristics of the pores were assessed as described previously,[5] in the middle of each scanned sample, within a volume of interest (VOI) measuring 3 mm in height and 8 mm in diameter. For SEM imaging, the bone graft substitute materials were viewed with backscattered electrons at 15 kV acceleration voltage.

Compressive mechanical testing (Zwicki; Zwick/Roell, Ulm, Germany) was conducted as described previously,[5] to evaluate the mechanical strength of the different bone graft substitute materials. Briefly, a confined column of 300 μl granules of each material was loaded at a rate of 2.5 mm/min until a fixed load of 850 N was reached ($n = 3$). Compressive strength was estimated from the load–displacement curves as theoretical load corresponding to the transition from the initial linear region, where the sample retains its porosity, to the linear compaction region, where porosity is eliminated. Compact volume was calculated as the reduction in volume due to the elimination of porosity.

The animal experimental study was performed using six female minipigs (Göttingen minipig, *Sus scrofa*; Ellegaard A/S, Dalmose, Denmark) aged 17–19 months and weighing 38–44 kg. The animals were acclimatized in the local facilities (University Hospital Malmö, UMAS, Malmö, Sweden). The preparation of animals and all animal management and care followed routine protocols approved by the institutional review board of UMAS. Ethical approval was obtained from the animal experiment ethics committee Malmö-Lund of the institutional review board at UMAS.

The animals were maintained under general anaesthesia using ketamine hydrochloride 50 mg/ml (Ketalar; Pfizer AB, Sollentuna, Sweden) and midazolam 5 mg/ml (Dormicum; Roche, Basel, Switzerland). After visual inspection of the animals, the pigs were shaved around the mouth, and the skin was rinsed with chlorhexidine 5 mg/ml in 60% ethanol (Apoteksbolaget, Stockholm, Sweden). Infiltration anaesthesia with 3.6 ml lidocaine 10 mg/ml and adrenalin 5 μg/ml (Xylocaine; Astra Zeneca, Södertälje, Sweden) was placed in the muco-buccal fold, following which deposits of plaque and calculus were carefully removed. After a marginal incision from the mandibular first premolar to the first molar, with distal and mesial releasing incisions, a mucoperiosteal flap was raised in order to expose the teeth and the alveolar bone to facilitate extractions of the premolar teeth P2, P3, and P4. Premolar teeth P2, P3, and P4 were carefully extracted and the empty alveoli were thoroughly inspected to make sure no root remnants were left in the sockets.

The marginal 5 mm of the alveoli were widened into standardized defects of 6 mm in diameter with a twist drill. A total of 36 implants (3.25 mm × 11.5 mm, Full Osseotite, MicroMiniplant; Biomet 3i Nordic AB, Malmö, Sweden) were installed into the extraction sites creating a marginal void between the lateral wall of the implant and the alveolar wall of approximately 1.4 mm (Fig. 1A). The most coronal part of the implant neck was placed flush with the crestal bone. The implant stability quotient (ISQ) was assessed by resonance frequency analysis (RFA) (Osstell; Osstell AB, Gothenburg, Sweden) at the time of implant installation. The measurement was performed four times in four directions and the average number was calculated and recorded.

Randomization was then performed on a quadrant level to graft the alveoli with heat oxidized PTG (Tigran White; Tigran Technologies AB, Malmö, Sweden) ($n = 12$) or DBBM (Bio-Oss; Geistlich Pharma AG, Wolhusen, Switzerland) ($n = 12$); control sites were left unfilled (sham), allowing a blood clot to form in

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