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Bioactive glass granules and polytetrafluoroethylene membrane in the repair of bone defects adjacent to titanium and bioactive glass implants

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An experimental animal model was used to investigate the effect of bioactive glass (BG) granules and nonresorbable polytetrafluoroethylene (PTFE) membrane on the repair of cortical bone defects adjacent to titanium and BG implants. Thirty-two Astra® (diameter 3.5 mm) dental implants were inserted bicortically and 42 conical BG implants (diameter 2.5–3.0 mm) monocortically, into fitted holes of rabbit tibia. Before implantation, a standardized bone defect was created by drilling an extra hole (diameter 3.0 mm) adjacent to each implant site. Twenty-eight defects were filled with BG granules (diameter 630–800 μm) (BG group) and 28 defects were left empty but covered with PTFE membrane (PTFE group). No material was used in 18 control defects (control group). Morphometrical evaluation with a digital image analysis system was used to measure bone repair as percentages of the defect area on scanning electron microscopy (SEM) and light microscopy pictures. Bone–implant contact was measured as percentages of the thickness of the cortical bone. At 6 and 12 wk, bone repair in defects in connection with titanium implants was 23.2% and 36.6% in the BG group, 23.2% and 32.4% in the PTFE group, and 47.2% and 46.2% in control defects. Corresponding figures for BG implants were 33.2% and 40.1% in the BG group, 16.6% and 33.5% in the PTFE group, and 25.7% and 54.9% in control defects. BG granules and new bone together filled 82.7% and 68.5% of the defect area adjacent to titanium implants, and 75.9% and 74.4% of the defect adjacent to BG implants at 6 and 12 wk, respectively. Better bone–implant contact was achieved at the defect side with BG than titanium implants (77.0% versus 45.0% at 12 wk). The results indicate that BG granules are useful in treatment of bone defects adjacent to dental implants. BG coating of the implant seems to improve osseointegration in the defect area.

1. Introduction

Bone resorption occurring after extraction of teeth reduces the height and width of the alveolar crest hindering the use of dental implants. Exposure of implant threads due to unfavourable bone anatomy may result in incomplete osseointegration of the fixture and a poor aesthetic result. Immediate implantation into fresh extraction sockets has been recommended in order to minimize bone loss and to shorten the time needed to complete the prosthetic treatment [1–4].

Various membrane techniques, originally developed for the treatment of bone loss due to periodontal disease [5], have been used to promote bone formation in bone defects around dental implants [6]. The following applications for membrane use have been suggested: treatment of dehisced defects at implant installation, treatment of fenestration defects at implant placement, augmentation of bone volume prior to implantation, and in connection with immediate installation of fixture in fresh extraction sockets [7]. One of the most documented barrier materials is nonresorbable polytetrafluoroethylene (PTFE) membrane.

Bioactive glass (BG), first introduced by Hench *et al.* in 1972 [8], is a surface-active glass which bonds chemically to bone minerals. The usefulness of BG in treatment of various bone defects in orthopaedic and oral and maxillofacial surgery has been shown in recent studies [7, 9–11]. BG used in this study (S54P4) is biocompatible and bone conducting [12].

The purpose of the study was to compare the effect of BG granules and PTFE membrane on repair of bone defects adjacent to titanium and BG implants in

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rabbit tibia. The experimental model used was designed to simulate immediate implantation in fresh tooth extraction sockets.

2. Materials and methods

2.1. Materials

The chemical composition of the BG (S53P4) used in this study as granules and cones is SiO_2 53.0, Na_2O 23.0, CaO 20.0 and P_2O_5 4.0 weight percentages. The preparation of BG has been described previously [13]. The size of the BG granules was 630–800 μm. Conical BG implants (upper diameter 3.0 mm, lower diameter 2.5 mm) were 4.5 mm long. Polytetrafluoroethylene (PTFE) membrane (Gore-Tex®, W.L. Gore and Assoc., Inc. Flagstaff, AZ, USA) was used without screw fixation. The titanium fixtures used were self-tapping dental implants (Astra®, Astra Meditec, Mölndal, Sweden) with a length of 7.0 mm and diameter of 3.5 mm.

2.2. Implantation procedure

Seventeen mature New Zealand White rabbits of both sexes (weight 3.5–4.5 kg) were operated under standard aseptic conditions. Pre-operatively, 50000 IU kg^{-1} benzylpenicillin procaine (Procapen® 300 000 IU ml^{-1}, Orion, Espoo, Finland) was given intramuscularly (i.m.) to each animal. General anaesthesia was induced by i.m. injections of 0.6 ml kg^{-1} ketamine hydrochloride (Ketalar® 50 mg ml^{-1}, Parke-Davis, Barcelona, Spain), 0.1 mg kg^{-1} medetomidine (Domitor® 1.0 mg l^{-1}, Lääkefarmos Oy, Turku, Finland) and 0.5 mg kg^{-1} xylazinum (Rompun® 20 mg ml^{-1}, Bayer, Leverkusen, Germany). Antiseptic polyvidon iodine solution (Betadine® 100 mg ml^{-1}, Leiras, Tammisaari, Finland) was used for cleaning the skin of the shaved anteromedial aspect of the tibia. The operation area was infiltrated with 0.9 ml 2% lidocaine/adrenalin (Xylocain adrenalin®, Astra, Södertälje, Sweden).

After careful soft tissue dissection, the anteromedial surface of the tibial diaphyse was exposed. Two to three holes were made in the medial border of the diaphyse under continuous sterile saline irrigation. Bicortical holes for the titanium implants were made with a twist drill (diameter 3.35 mm). Monocortical holes (diameter 3.0 mm) for BG implants were prepared with a conical drill (Frialit® 4–0, Friedrichsfeld GmbH, Mannheim, FRG). Before implantation, a standardized bone defect was created by enlarging the upper aspect of the hole using a round burr with a diameter of 3.0 mm.

In all, 74 implants were inserted (42 BG cones and 32 titanium fixtures), two to three in each tibia. Twenty-eight of the bone defects were filled with BG granules (BG group) and 28 were left empty but the area was covered with PTFE membrane (PTFE group) (Fig. 1). No material was used in connection with 18 defects (control group). All experimental areas were covered with periosteum attached to the soft tissue flap.

2.3. Sample preparation

Animals were killed after 6 and 12 wk with an overdose of ketamine hydrochloride and carbon dioxide. Resected bone specimens were fixed in 4% buffered formalin and embedded in methylmethacrylate (Technovit® 7200, Kulzer GmbH, Wehrheim, Germany). The blocks were cut longitudinally in two halves through the middle plane of the implants and adjacent defect holes with a diamond saw. Histological sections (15 μm) were prepared using a cutting–grinding method and stained with toluidine blue [14]. The other half of the blocks was used for scanning electron microscopy (SEM).

2.4. Morphometry

Morphometrical evaluation was made on SEM and light microscopy pictures using a computerized analysis system (Micro-Scale TC®, Digithurst Ltd, Royston, UK). Bone repair was measured as percentages of total defect area (*bone area*) (Fig. 2). In the defects filled with BG granules, bone and BG granules in direct contact with bone (*bone–biomaterial area*) was measured while loose single BG particles were excluded from the calculations. Bone–implant contact in the defect side and the opposite side was calculated as percentages of the cortical height.

2.5. Statistical analysis

The differences between the two implants, between the three material groups and between the two time points were statistically analysed using two-way and three-way analysis of variance (ANOVA). *P*-values less than 0.05 were interpreted as significant. Statistical computations were performed using an SAS statistical program package [15].

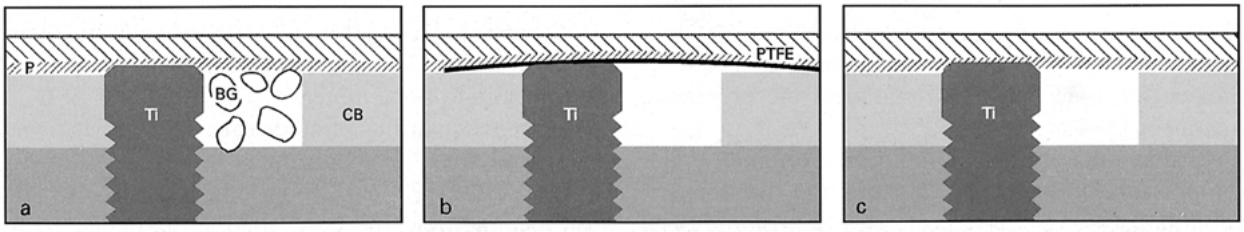

Figure 1 Experimental design. (a) Cortical defect filled with bioactive glass (BG) granules. (b) Defect covered with polytetrafluoroethylene (PTFE) membrane. (c) Control defect is left empty. Implant tap is either a titanium screw fixture or bioactive glass cone. All experimental areas are covered with intact periosteum attached to the soft tissue flap. CB, cortical bone; P, periosteum; Ti, titanium.

3. Results

Twelve specimens were excluded due to failure in laboratory process. Thus, a total of 62 implants were analysed (Table I). No post-operative infections or loose implants were observed clinically at the end of the follow-up time. Histologically, a mild mononuclear inflammatory reaction was found in a few samples in connection with BG granules at 6 and 12 wk. Multinuclear giant cells were not detected in any specimen.

Results of the histomorphometrical analysis of bone repair are presented in Table II. In statistical computation, the difference in bone repair (*bone area*) between three material groups was statistically significant regardless of the implant material used ($p = 0.02$). Adjusted means for bone area in respect of the time and implant effect show that less bone formation occurred in both BG ($p = 0.08$) and PTFE ($p = 0.0046$) groups than in the control group.

In the BG group, a tight contact between bone and the corrosion layer of the granules was observed. No resorption of BG was seen. Newly formed bone grew along the glass surface filling the space between the granules (Figs 3a and 4a). The difference in bone–biomaterial area (bone plus BG) in connection with titanium and BG implants was not statistically significant at different time points. If the area occupied by the granules (defect area minus area of BG granules) is not taken into consideration, 59.7% (S.D. 13.2) and 62.9% (S.D. 21.4) of the remaining defect area was covered by bone in connection with BG implants at 6 and 12 wk, respectively. The corresponding figures in connection with titanium implants were 56.2% (S.D. 15.8) and 54.4% (S.D. 14.0).

New bone formation and BG granules formed a continuous bridge in the BG group (Figs 3a and 4a). The bridge covered the whole defect adjacent to titanium and BG implant in 6/10 (60%) and 10/13 (77%) specimens, respectively. In the PTFE group, a thin bone bridge or single bone chips were seen in close proximity beneath the membrane (Figs 3b and 4b).

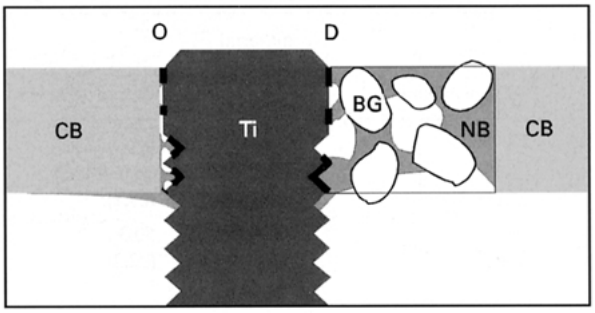

Figure 2 Morphometrical analysis. New bone (NB) formation (bone area) was measured as percentages of the total defect area. In defects filled with BG granules also bone–biomaterial area (bone and BG granules in direct contact with bone) was measured. Bone–implant contact (thick line) on the defect side (D) and the opposite side (O) was calculated as percentages of the thickness of the cortical bone. CB, cortical bone; Ti, titanium.

TABLE I Number of implants analysed in the three study groups

	BG granules (BG group)	PTFE membrane (PTFE group)	No material (control group)
Titanium implant			
6 wk	4	6	3
12 wk	6	6	4
BG cone implant			
6 wk	6	5	4
12 wk	7	6	5

TABLE II Bone repair (bone area) in the defects adjacent to implants in the three study groups given as mean percentages (S.D.) of the total defect area. Bone + BG (bone–biomaterial area) = area of bone and BG granules in direct contact with bone

	BG granules	PTFE membrane	No material
Titanium implant			
6 wk			
Bone	23.2 (9.4)	23.2 (24.5)	47.2 (6.6)
Bone + BG	82.7 (6.3)		
12 wk			
Bone	36.6 (10.7)	32.4 (25.6)	46.2 (21.0)
Bone + BG	68.5 (13.6)		
BG cone implant			
6 wk			
Bone	33.2 (6.4)	16.6 (10.1)	25.7 (13.2)
Bone + BG	75.9 (12.5)		
12 wk			
Bone	40.1 (12.3)	33.5 (25.0)	54.9 (19.6)
Bone + BG	74.4 (18.4)		

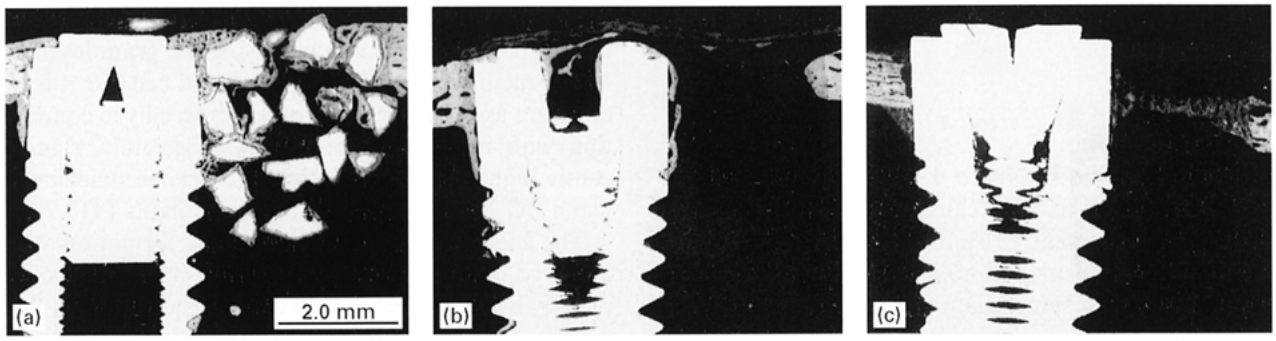

Figure 3 Scanning electron micrographs showing the healing in the study groups in connection with the titanium implant. (a) In the BG group, bone is growing along the reaction layer of granules connecting them together at 6 wk. (b) Scanty new bone formation is seen beneath the membrane and on the surface of the implant in the PTFE group at 6 wk. (c) New bone growth in the control defect at 6 wk.

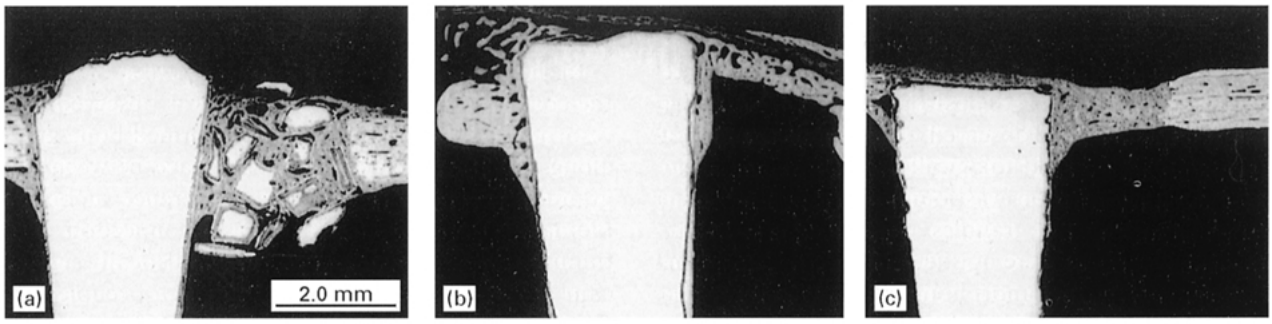

Figure 4 Scanning electron micrographs showing the healing in the study groups in connection with the BG implant. (a) Complete closure of the defect filled with BG granules has occurred at 6 wk (BG group). There is a tight contact between bone and the reaction layer of the implant. (b) Newly formed bone forms a thin and continuous bridge over the defect covered with PTFE membrane at 6 wk. (c) Rather thick and continuous bone bridge is seen in the control defect at 12 wk.

TABLE III Bone–implant contact in the three study groups given as the mean percentages (S.D.) of the thickness of the cortical bone on both sides of the implant

	BG granules		PTFE membrane		No material	
	Defect side	Opposite side	Defect side	Opposite side	Defect side	Opposite side
Titanium implant						
6 wk	70.6	58.0	45.3	70.6	41.5	56.0
	(–)[a]	(–)[a]	(37.8)	(25.0)	(19.8)	(27.1)
12 wk	45.0	52.3	30.5	56.8	53.8	50.3
	(11.6)	(23.7)	(27.9)	(24.3)	(30.6)	(22.2)
BG cone implant						
6 wk	69.7	81.2	70.9	76.5	59.4	62.3
	(11.8)	(9.1)	(21.2)	(14.4)	(41.7)	(10.1)
12 wk	77.0	64.5	77.5	55.8	83.2	61.0
	(13.2)	(30.2)	(22.0)	(29.6)	(11.7)	(34.0)

[a] Only one specimen in the group.

The bone bridge was complete in 5/12 (42%) defects in connection with titanium implant and in 4/11 (36%) defects adjacent to the BG implant. In control defects, a flat bridge of varying thickness was seen (Figs 3c and 4c). A full coverage of the defect by bone bridge formation was detected in 4/7 (57%) and in 4/9 (44%) specimens in connection with titanium and BG implants, respectively.

The amount of bone–implant contact on the defect side in different study groups was significantly higher using BG implant than titanium implant ($p = 0.0009$) (Table III). In this respect, a similar tendency, but no statistically significant difference, was noted on the opposite side of the implant. The comparison of the amount of bone–implant contact between the defect side and opposite side revealed no statistically significant differences.

4. Discussion

A healing period of up to 12 mon required before implantation of fixtures causes significant delay for prosthetic treatment [16]. In order to shorten the length of treatment and to prevent bone loss after tooth extraction, immediate implantation into fresh extraction sockets with or without a membrane technique has been suggested [1, 4].

PTFE membrane is clinically in common use in connection with guided bone regeneration (GBR). Nonresorbable PTFE is used as a mechanical barrier preventing the ingrowth of connective tissue into the bone defect, thus allowing the bone-forming cells to populate the defect site. However, variable results have been achieved using this membrane. Postoperative infections, membrane exposures to the oral cavity, and even partial necrosis of adjacent bone, have been reported [17, 18]. Furthermore, because PTFE is not resorbable, another operation is needed to remove the membrane from the tissue.

The results of previous animal and clinical studies indicate that bioactive glass can be used as a bone substitute in different bone defects (9, 10, 19–21). The design of the present study is based on these results. First, BG has been shown to enhance the new bone formation in cortical defects [19]. Although better bone repair has been obtained using BG granules than PTFE membrane, PTFE was included because it is in common use in oral implantology, especially in connection with immediate implantation. Secondly, significantly higher bone–implant contact has been achieved using BG implants than titanium implants [11].

The highest amount of new bone formation was achieved in control defects. However, if the area occupied by BG granules is taken into consideration in BG groups, the coverage of new bone exceeds that of the control group. Furthermore, if the area of new bone and BG granules in contact with bone (bone–biomaterial area) is taken into account, the best closure of

the defect was achieved in the BG group. This kind of comparison is justifiable, because BG is known to bond chemically to bone minerals [12]. The reason for the poorest bone repair in the PTFE group is that the membrane may disturb healing by preventing the migration of the periosteal cells into the defect area.

The finding of better bone repair and bone bridge formation in BG groups than in the PTFE group is in accordance with the results obtained in a study on the repair of cortical defects using BG granules and PTFE membrane [19]. Furthermore, the difference in bone formation between BG and PTFE groups is more distinct in connection with BG than titanium implant. This is probably due to the osteoconductive property of BG. When considering the chemical bonding between BG and bone, as demonstrated in earlier studies [13], a strong support is achieved for the implant. However, the biomechanical strength of bone–BG composite in connection of dental implants needs to be studied.

BG implants were used in this study to simulate the BG coating of the fixture. Because it is impossible to prepare threads in BG, conical bulks and a monocortical press-fit technique were used. However, regardless of weaker initial stability of BG cones than titanium implants, better bone–implant contact was achieved. Osteoconductive properties of BG seem to promote bone growth along the implant surface. No uniform finding was noted when the bone–implant contact on the defect side was compared to that of the opposite side in different study groups.

The results indicate that bioactive glass granules are useful in the treatment of fresh bone defects adjacent to dental implants. BG coating of the implant seems to improve osseointegration in the defect area.

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