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Cortical bone ingrowth in grooved implants with calcium phosphate coatings: a gap model study

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In *in vivo* experiments the gap healing of uncoated grooves and grooves coated with HA, HAH (heat treated hydroxylapatite) and FA was studied histologically and histometrically. Cylinders with grooves (0.25 mm, 0.50 mm, 0.75 mm or 1.0 mm depth) were implanted in cortical bone of goats for 3, 6 or 12 weeks. In the uncoated gaps after 3 weeks of implantation no bone ingrowth could be observed. Afer 6 weeks of implantation about 35% bone ingrowth was seen in the uncoated gap independent of gap depth. There was mostly no bone contact with the titanium surface. The presence of a coating enhanced bone ingrowth and initiated more bone contact. After 3 weeks of implantation there was more bone ingrowth and after 6 weeks the bone ingrowth and bone contact was increased, independent of the coating type. HAH showed the highest bone ingrowth. The bone ingrowth started from the periphery of the host bone.

1. Introduction

Despite the overwhelming immediate success that can be obtained with total joint replacements using methylmethacrylate bone cement for implant fixation, mechanical loosening of prosthetic components remains a serious problem.

Improvements in implant design and surgical techniques have enhanced the durability of cemented fixation, but the poor mechanical properties of methylmethacrylate bone cement and the long-term tissue reactions to this material compromise its use in younger and more active patients [1–6].

Biological prosthetic fixation using implants with porous surfaces is an attractive alternative to conventional total joint replacements. Bone is capable of growing directly into porous surfaces, thereby mechanically anchoring the prosthesis. Obtaining reliable fixation by bone ingrowth, however, remains a problem. Initial direct apposition of bone to the implant is often limited to relatively small areas.

If the mechanical methods used to gain initial fixation become ineffective during the early period the bone ingrowth may not be sufficient to provide adequate long-term prosthetic fixation. Retrieval studies have revealed that many of the components were fixed to the skeleton by fibrous tissue ingrowth, instead of bony ingrowth. Therefore, great efforts have been concentrated on enhancement of bony ingrowth into the non-cemented prosthetic surface. These include the use of osteoconductive substances such as calciumphosphate coatings and the use of osteo-inductive agents [7].

Under ideal interface conditions calciumphosphate plasmasprayed coatings significantly enhance host tissue adaptation and initial implant fixation. However, of greater clinical importance is the significant improvement in host tissue adaptation to coated implants in sub-optimal and clinically more realistic interface condition.

One approach is a combination consisting of the incorporation of osteo-inductive agents, such as growth hormone, in the bioactive calciumphosphate plasmasprayed coating. In earlier studies we have shown that growth hormone can be incorporated and released from dense calciumphosphate ceramics [8]. Recently we have shown that growth hormone can be loaded in calciumphosphate plasmasprayed coatings on titanium and subsequently released *in vitro* [9].

Before one can study the effects of growth hormone together with the coated implant in an *in vivo* model, one needs to know the minimal gap distance which an implant without growth hormone cannot overbridge sufficiently. We therefore created a new model. In this paper we present the results of bone ingrowth in grooved implants coated with different types of calciumphosphate, and with different groove depths.

2. Materials and Methods

2.1 Preparation of implants

Titanium plugs (5.1 mm diameter × 7 mm) were fabricated with four grooves; in each plug the groove depth was 0.25 mm, 0.5 mm, 0.75 mm or 1.0 mm and the width was 2.0 mm (Fig. 1).

Titanium plugs (5.1 mm diameter × 7 mm) were fabricated with two grooves, respectively 0.5 mm and 1.0 mm depth and 3.5 mm width (Fig. 2). The bottom of the grooves were uncoated or coated (C) with fluorapatite (FA), hydroxylapatite (HA) or hydroxylapatite with a heat treatment of 1 h at 600 °C (HAH). The coating thickness was about 50 μm.

2.2 Implantation procedure.

Four different plugs were implanted in the goat femur. Both femora were used in 12 goats ($n = 8$/period). The implantation periods were 3, 6 and 12 weeks.

Four different plugs were implanted in the goat femur. Both femora were used in four goats ($n = 4$/period). The implantation periods were 3 and 6 weeks.

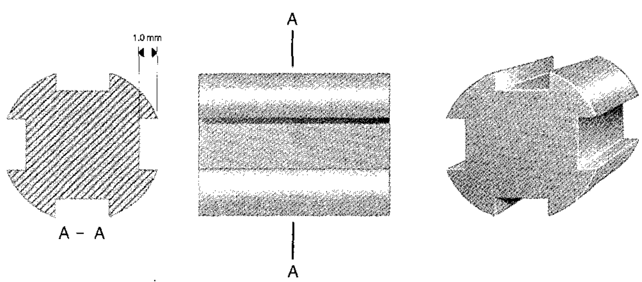

Figure 1 A schematic drawing of the titanium plugs (5.1 mm diameter) of the first experiment. In each plug the grooves have a depth of 0.25 mm, 0.5 mm, 0.75 mm and 1.0 mm. The width of the gap was 2.0 mm

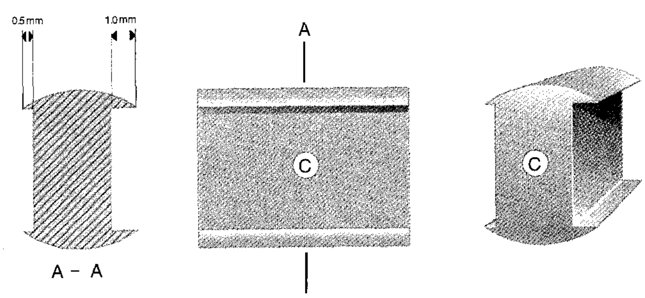

Figure 2 A schematic drawing of the titanium plugs (5.1 mm diameter) of the second experiment. In each plug two different grooves, respectively 0.5 mm and 1.0 mm depth, were fabricated. The width was 3.5 mm. The bottom of the grooves were uncoated or coated [C] with fluorapatite (FA), hydroxylapatite (HA) or hydroxylapatite with a heat treatment of 1 h at 600 °C (HAH). The coatings were 50 μm thick.

For the experiments healthy mature female goats, weighing 40–60 kg, and tested before for CAE/CL arthritis (Caprine Arthritis Encephalitis and Caseous Lymphadenitis) were used. Twenty-four hours prior to surgery, ampicillin 20% (2 ml/50 kg body weight/i.m) was administered to minimize infection risks. Surgery was performed under general inhalation anaesthesia. The anaesthesia was induced by an intravenous injection of Thiopental, and maintained by a mixture of nitrous oxide/oxygen/fluothane gas by a respirator. To minimize the risk of peri-operative aspiration, the stomach was drained with an oesophagus-stomach tube. The limbs were shaved, disinfected with providone-iodine and the femora were exposed by lateral skin incision and blunt dissection next to the quadriceps femoral muscle. Using pneumatically powered equipment (3M Maxi driver, < 150 rotations/min) four holes were drilled in the lateral cortex under cooling with saline. Each hole was drilled in three steps using drills with increasing diameter up to 5.1 mm. The distance between the holes was 2 cm. According to the statistical schedule, four different plugs were inserted into the femur. The implants were allocated to four positions, from proximal to distal in the femur. The implantation was performed using a press fit. The connective tissue and skin were closed in separate layers with 3–0 Vicryl sutures.

After 3, 6 or 12 weeks of implantation the animals were sacrificed. The samples were removed and subjected to a histological embedding procedure. Undecalcified sections (10 μm) were performed with a special saw technique [10]. The sections were stained with methylene blue and basic fuchsin and examined by light microscopy. To estimate the amount of bone ingrowth and bone contact with the deep surface, Vidas Imaging Analysis was used.

The histometry measurements were performed in 1–4 layers (0.25 mm/layer), depending on the gap distances, to estimate the direction of ingrowth. The layers were measured from periphery into the groove.

3. Results

The histometric data on bone ingrowth and bone contact after 3 and 6 weeks of implantation are shown in Figs 3–8.

The amount of bone ingrowth showed great variability between different animals, between the left and right femur of the same animal, and also between grooves of the same depth in one implant sample.

In the first experiment (uncoated samples) the histological and histometrical observations showed that after 3 weeks of implantation in the grooves, virtually no bone ingrowth had occurred. This was independent of the gap distances (0.25 mm–1.0 mm).

After 6 weeks of implantation about 35% of the groove area was filled with bone tissue. The percentage is independent of the gap distances (Fig. 3). The absolute amount of bone ingrowth increased with increase of gap distance.

The ingrowth started from the periphery of the surrounding host bone tissue into the grooves. The grooves showed no bone contact at the bottom of

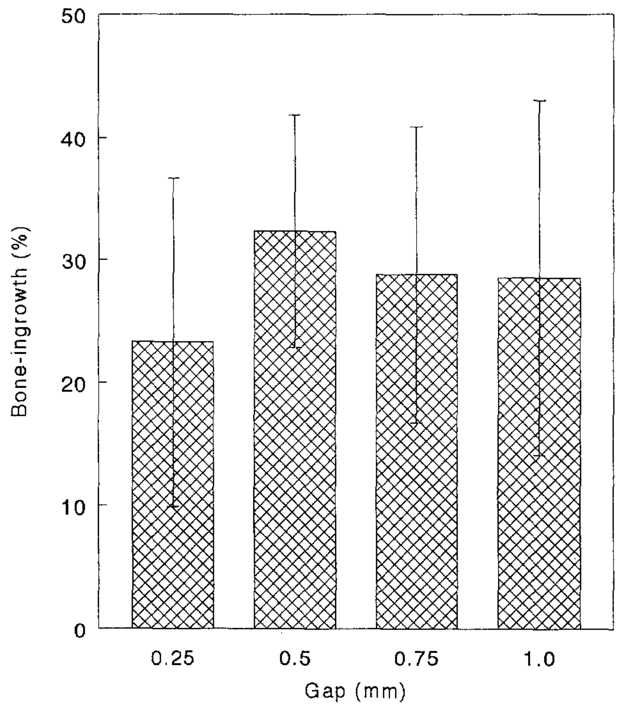

Figure 3 The bone ingrowth data (%) of the first experiment in the different uncoated gaps after 6 weeks of implantation.

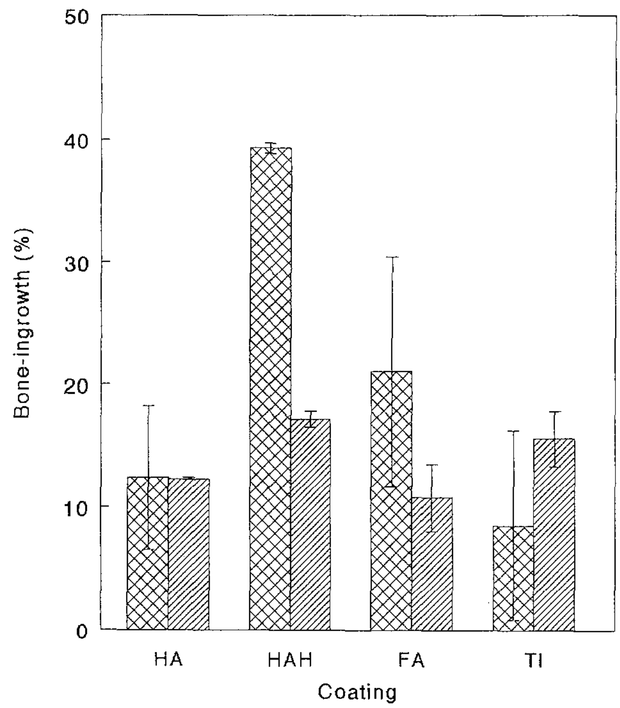

Figure 5 The bone ingrowth data (%) of the second experiment in the different coated gaps (0.5 mm ▩ and 1.0 mm ▨) after 3 weeks of implantation.

the grooves independent of the groove depth. In Fig. 4 the 6 weeks implantation data of the histometry measurements performed in 1–4 layers (0.25 mm/layer) are shown. One can seen that the 1.0 mm gap (4 layers), showed a decrease of bone amount in the layers from periphery to centre in the groove. After 12 weeks the amount of bone ingrowth was not increased significantly.

In the second experiment the histological and histometrical observations showed that after 3 weeks of implantation in the grooves (with or without coating) a small amount (about 10%) of bone ingrowth occurred. HAH and FA coated grooves of 0.5 mm depth showed the greatest bone ingrowth (Fig. 5).

The 0.5 mm coated grooves showed significantly more bone contact than the uncoated 0.5 mm grooves, and the 0.5 mm grooves showed significantly more bone contact than the 1.0 mm grooves (Fig. 6).

After 6 weeks of implantation (Fig. 7), in the case of the uncoated grooves, about 35% of the groove area was filled with bone tissue. The percentage was independent of the gap distances. The results were comparable with the first experiment. The ingrowth started from the periphery of the surrounding host

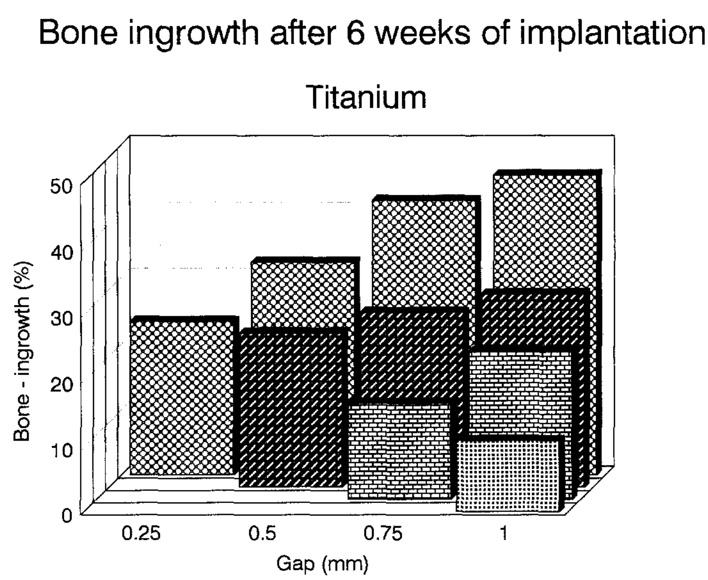

Figure 4 The bone ingrowth data (%) of the first experiment measured in layers 1–4 (from periphery to centre) in the different uncoated gaps after 6 weeks of implantation (▩ layer2; ▤ layer3; ▦ layer4)

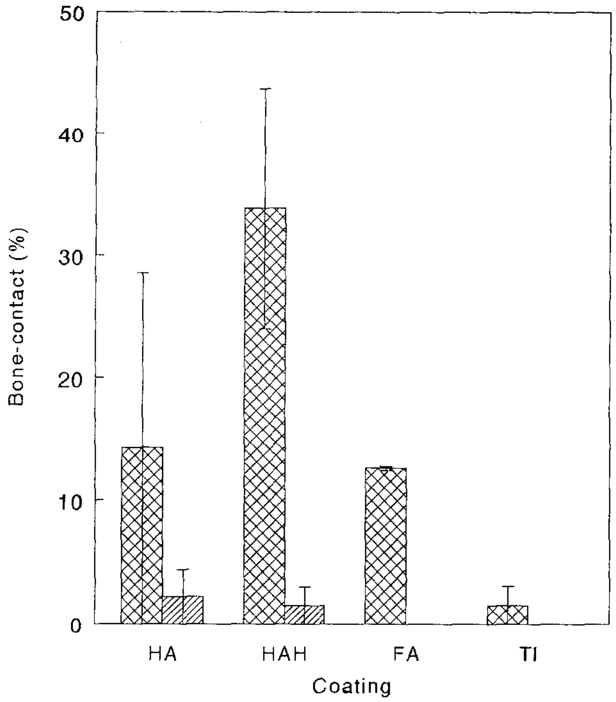

Figure 6 The bone contact data (%) of the experiment in the different coated gaps (0.5 mm ▩ and 1.0 mm ▨) after 3 weeks of implantation.

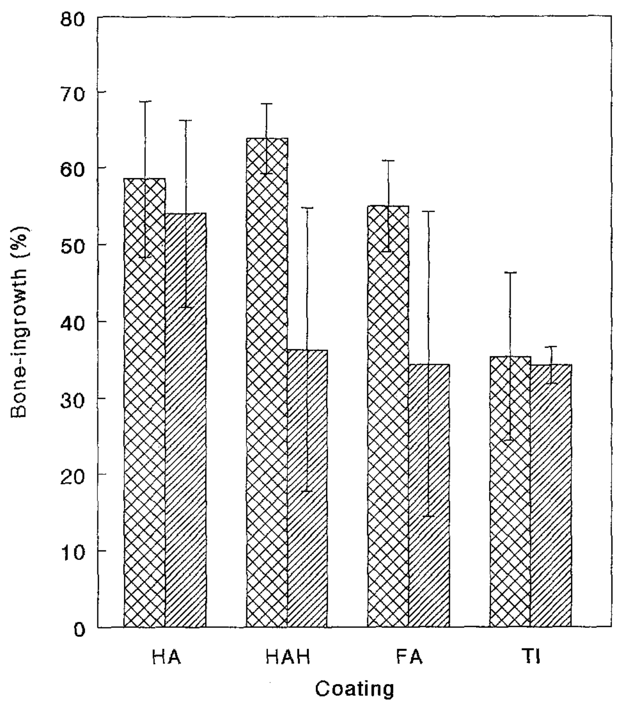

Figure 7 The bone ingrowth data (%) of the second experiment in the different coated gaps (0.5 mm ▩ and 1.0 mm ▨) after 6 weeks of implantation.

bone tissue into the grooves. The uncoated grooves showed a small amount of bone contact at the bottom of the 0.5 mm grooves, but no contact in the 1.0 mm grooves.

In the case of the coated plugs, the bone ingrowth was significantly higher than for the uncoated grooves, about 60% ingrowth in the 0.5 mm grooves. The 1.0 mm grooves showed a width variance, with an

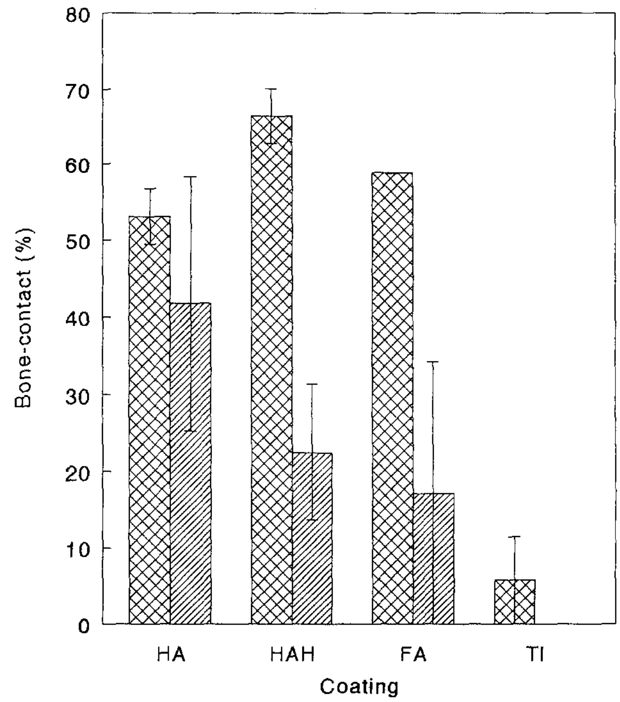

Figure 8 The bone contact data (%) of the second experiment in the different coated gaps (0.5 mm ▩ and 1.0 mm ▨) after 6 weeks of implantation.

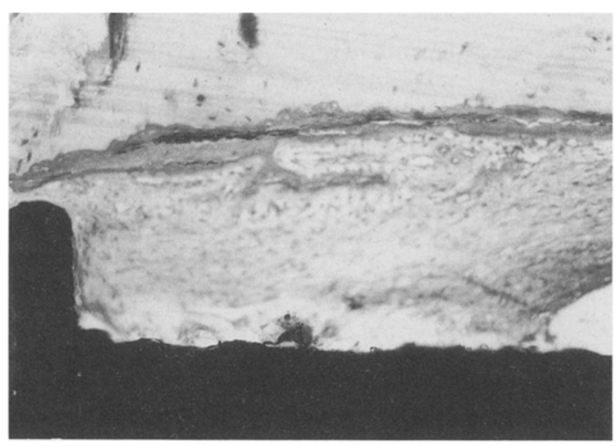

Figure 9 Histological photograph showed the bone growth near an uncoated groove (0.25 mm) after 3 weeks of implantation (first experiment).

average of 35%. The uncoated grooves showed significantly less bone ingrowth in the 0.5 mm grooves. The coated plugs showed bone contact, higher in 0.5 mm than in 1.0 mm grooves. There was slight bone contact in uncoated grooves of 0.5 mm but no bone contact in the 1.0 mm grooves. The coated grooves showed significantly higher bone contact than the uncoated grooves, independent of the groove distance (Fig. 8).

Photographs in the Figs 9–13 show some histology results. In Fig. 9 one can notice that after 3 weeks of implantation, uncoated grooves (in this case 0.25 mm) showed no bone ingrowth; only some bone healing can be seen.

The Figs 10 and 11 show the ingrowth and bone contact in HAH coated grooves of 0.5 mm depth after, respectively, 3 and 6 weeks of implantation. In the case of HAH coated grooves the amount of bone ingrowth

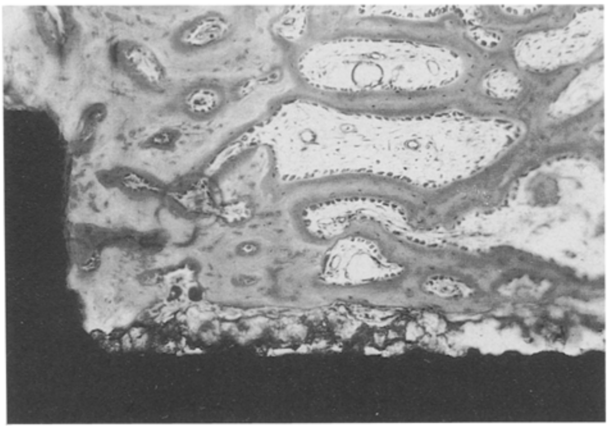

Figure 10 Histological photograph showed the bone ingrowth and bone contact in a HAH coated groove (0.50 mm) after 3 weeks of implantation (second experiment).

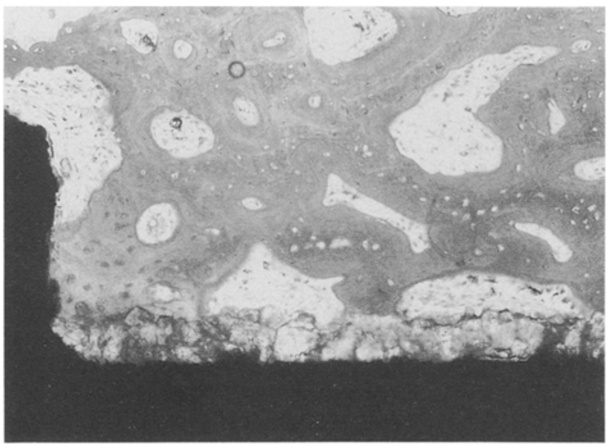

Figure 11 Histological photograph showed the bone ingrowth and bone contact in a HAH coated groove (0.5 mm) after 6 weeks of implantation (second experiment).

was increased a little after 6 weeks (see also Figs 5 and 7).

Figs 12 and 13 show the bone ingrowth and bone contact in HAH coated grooves of 1.0 mm depth after, respectively, 3 and 6 weeks of implantation. After 3 weeks a little bone contact can be seen, which increased significantly after 6 weeks of implantation to about 20% (see also Figs 6 and 8).

4. Discussion

To estimate the amount of bone ingrowth and bone contact with the bottom in the groove, Vidas Imaging Analysis was used. The bone ingrowth was measured by estimating the amount of dense bone. This means that remodelling lacunae, medullar features and connective tissue were excluded. The bone contact was expressed as a percentage of the surface length of the uncoated or coated groove bottom.

The amount of bone ingrowth showed a great variance between the different animals, between the left and right femur of the same animal and, also between the grooves of the same depth in one implant sample.

Figure 12 Histological photograph showed the bone ingrowth and no bone contact in a HAH coated groove (1.0 mm) after 3 weeks of implantation (second experiment).

Comparing the data of the bone contact of the second experiment it can be concluded that both the gap distance, the implantation period and the presence of a coating influenced bone contact behaviour. It was significant that the uncoated surface did not show bone contact in the 1.0 mm groove, and only a very small (2–5%) amount of contact in the 0.5 mm grooves (Figs 6 and 8).

The data of the first experiment showed that after 3 weeks of implantation (independent of the gap distance) bone contact was zero and bone ingrowth was too small ($\approx$ 10%) to observe any significant effect of the gap size.

The 6 weeks implantation data (Figs 3 and 4) showed that bone ingrowth in the first experiment was about 35%, and was independent of gap depth. These data were comparable with the uncoated groove data of the second experiment.

Comparing the data of Fig. 4 it can be concluded that bone ingrowth started from the periphery. The amount of bone decreased from the periphery to the centre in the gap (layer 1 to layer 4).

Expressing the percentage ingrowth in the different gaps in absolute figures, one could see an increase in bone growth as the gap size increased (Table I).

Because the 0.75 mm and 1.0 mm grooves showed bone ingrowth $>$ 0.25 mm, one would expect total bone ingrowth in the 0.25 mm groove. However, all uncoated grooves showed bone ingrowth only to within a certain distance of the groove bottom. An

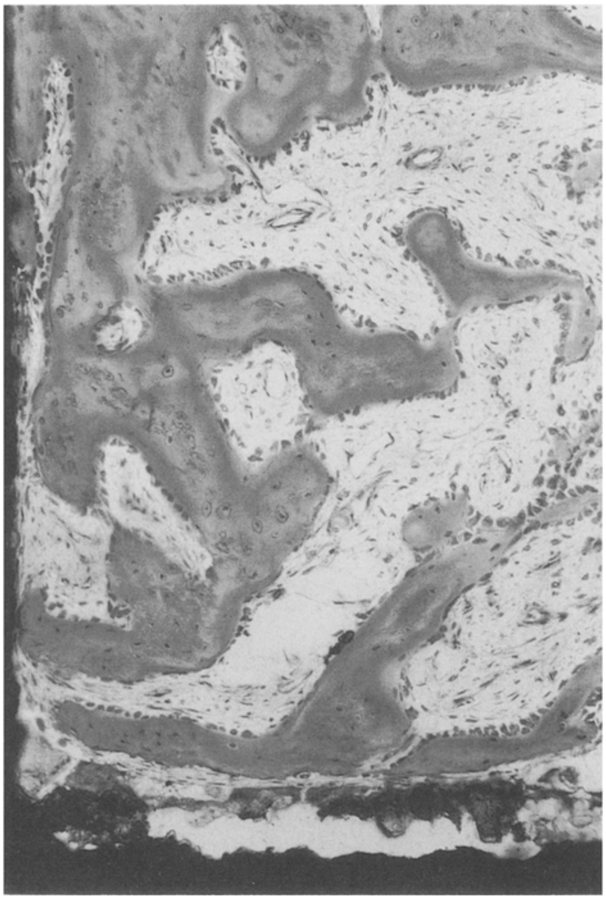

Figure 13 Histological photograph showed the bone ingrowth and some bone contact in a HAH coated groove (1.0 mm) after 6 weeks of implantation (second experiment).

unknown factor inhibited ingrowth to the groove bottom.

In this study a significant enhancement of bone ingrowth occurred after 3 and 6 weeks of implantation in the 0.5 mm grooves when a coating was present. In the 1.0 mm grooves no significant improvement occurred when a coating was present, except that the HA coated 1.0 mm grooves showed a higher ingrowth than the uncoated gaps after 6 weeks of implantation.

Bone contact enhancement occurred significantly in grooves of 0.5 mm and 1.0 mm after 6 weeks of implantation. After 3 weeks of implantation only the 0.5 mm grooves showed more bone contact when a coating was present. One can conclude that, especially for the larger 1.0 mm grooves, the improvement arising from the presence of a calciumphosphate coating will be more bone contact with the groove bottom, which means enhancement of the bridging performance.

TABLE I Bone ingrowth in different gaps expressed in percentage and absolute figures

Groove depth (mm)	Base ingrowth Percentage	Absolute (mm)
0.25	35	0.08
0.50	35	0.15
0.75	35	0.25
1.0	35	0.35

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