JOURNAL OF MATERIALS SCIENCE· MATERIALS IN MEDICINE 6 (1995) 14 - 18

Bioactive glass and glass-ceramic-coated hip endoprosthesis: experimental study in rabbit

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Co–Cr–Mo endoprostheses with a dual bioactive glass (BG) coating and titanium implants coated with a bioactive glass-ceramic (BGC) were studied under lead-bearing conditions in the rabbit hip. The dual BG coating contained an inner layer of high durability and an outer bioactive layer. Each type of coating improved the stabilization of prosthesis during the experiment period of 8 weeks compared to non-coated control implants. EDXA analysis confirmed the ability of BG and BGC coatings to bond chemically to bone. The BGC coating on titanium alloy proved superior to the dual BG coating on Co–Cr–Mo prosthesis with regard to bone formation on the surface of the implant. The bioactive top layer of the dual BG coating showed resorption, especially in the areas without direct bone contact. This is explained by partial crystallization of the glass during firing. Thermal discrepancy between BGC coating and titanium core caused cracking of the coating, which remains a major obstacle to its use as a bioactive coating.

1. Introduction

The mechanical strength of the interface between bone and bioactive glass, and the surface characteristics of solid bioactive glasses are well documented [1–5]. The surface reactions of bioactive glasses within tissue result in the formation of a subsurface silica-rich layer and a surface layer of hydroxyl-carbonate apatite to which bone attaches chemically. Compared to synthetic hydroxylapatite (HA), the surface apatite layer of bioactive glass resembles better the apatite of natural bone, and consequently higher bone bonding rate has been reported for bioactive glass than for HA [6, 7]. A further advantage of glasses is that the rate of bonding, as well as other properties, can be controlled by choice of composition. Properties of bioactive glass-ceramics can also be controlled to some extent. However, it is more difficult than with glasses, since glass-ceramics involve at least two phases, the compositions and proportions of which are determined not only by base glass composition but also by heat treatment.

Bioactive materials have usually been studied by implantation of cylinders or cones in bone under non-loaded conditions [5, 8–11]. The lack of loading during the time period needed for bone bonding limits the value of these tests in evaluating the applicability of the materials studied in functional implants.

One problem associated with the use of bioactive glass as a coating is the long-term ion exchange that may take place. The thickness of the silica-rich layer grows and reduces the strength of the material. If the leaching proceeds to the glass–metal interface the glass may scale off due to loss of adhesion. One way to solve this problem is to use a dual coating with an inner layer of high durability and an outer bioactive layer. The ground coating also protects the bioactive coating from contamination by metal ions which may dissolve from the metal core during firing. The purpose of this work was to study whether the performance of Co–Cr–Mo and titanium implants supporting a load-bearing joint can be improved by coating them with bioactive glass (BG) or glass-ceramic (BGC). The incorporation of Al_2O_3 in the ground coating and its possible negative effect on the bioactivity of the top coating were also investigated.

2. Materials and methods

2.1. Materials

Five implants cast at 1470 °C using a Co–Cr–Mo alloy (Wirobond®, BEGO Bremer Goldschlägerei Wilh. Herbst GmbH & Co., Bremen) and five titanium implants (Kirschner® Medical Corporation, Paterna, Spain) were used as hemiendoprosthesis in a rabbit hip. A dual BG coating was applied on the surface of three Co–Cr–Mo implants, whereas three titanium implants had an SiO_2–CaO–MgO–P_2O_5-based

BGC) (Patent pending) coating. Two uncoated implants of each types served as controls.

2.2. Coating

For the Co–Cr–Mo implant a non-active Al_2O_3-containing ground coating (HI-5) and a bioactive top coating (HI-6) (Table I) were optimized according to a method previously described [14]. The glasses were melted at 1360 °C for 3 h and quenched in water. They were then ground and sieved to a particle size of less than 45 μm and dispersed in ethanol. The implants were ultrasonically cleaned in the ethanol, dipped in glass–ethanol frit and allowed to dry. The inner layer was fired at 750 °C for 10 min. The dipping procedure was repeated for the outer layer, which was fired at 700 °C for 20 min.

A starting frit for the coating of titanium implant was prepared by mixing the glass powder (< 45 μm), ethanol and acetone. The cleaned titanium implant was dipped twice in the frit with a drying interval of 1 –2 min in a stream of warm air. The coated prostheses were then preheated for 1 h at 400 °C. Firing was carried out for 20 min in a protective Argon atmosphere at 900 °C. The coating was finished by cooling the implant (5 °C/min^{-1}) under Argon gas to 500 °C after which the cooling proceeded to room temperature with cooling of the oven without protecting gas. X-ray diffraction of the coatings showed HI-5 to contain only a small amount of $Na_2Ca_2Si_3O_9$, and HI-6 to contain a considerable amount of the same crystal. The BGC on titanium contained apatite, $Ca_{10}(PO_4)_6O$ and wollastonite as $SiCaO_3$.

2.3. *In vivo* tests

The experimental endoprostheses were implanted by posterolateral approach in the right hip of ten adult rabbits weighing 2650 to 2920 g. General anesthesia under a combination of fluanisone 10 mg/ml and fentanyl 0.2 mg/ml (Jansen, Beerse, Denmark) given intramuscularly 0.1 mg/kg + 0.3 mg/kg) and local 0.5% lidocain anesthetic (Orion, Espoo, Finland) were used. The implant was inserted by gently tapping it into the medullar canal after cutting the collum of the femur above the lesser trochanter corresponding to the implant collar. Intramedullar reaming was unnecessary as the prostheses were somewhat undersized. Rotational stability was deliberately not absolute. The animals were free to ambulate once they recovered from anesthesia and they resumed movement within a few hours.

The rabbits were killed after 8 weeks and radiographs were taken. The proximal end of the femur including the implant was then resected and the specimen fixed in 4% buffered formalin and embedded in plastic (Technovit Kulzer GmbH, Wehrheim, Germany). Histological sections (10 μm) were prepared perpendicular to the longitudinal axis of the implant at three levels (Fig.1) using a cutting–grinding method (Exakt-Apparatebau, Hamburg, FRG) developed for undecalcified hard tissue specimens [12]. The sections were stained with toluidine blue and evaluated by light microscopy. Furthermore, light microscopy together with a computerized analysis system (MicroScale TC, Digithurst Ltd, Royston, England) was used to measure the proportion of the implant surface covered by bone. Scanning electron microscopy (SEM) and energy-dispersive X-ray analysis (EDXA) on the remaining tissue blocks were used to analyse the chemical composition and the contact at the implant tissue interface.

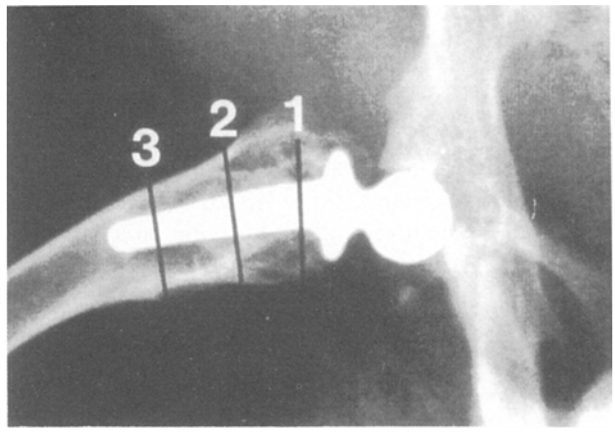

Figure 1 Radiograph of coated Co–Cr–Mo implant at sacrifice demonstrating the levels of cross-sections used for histological and SEM analyses (1 = proximal, 2 = middle, 3 = distal).

TABLE I Composition of the glasses used for the dual coating of Co–Cr–Mo implants (wt%)

Coating	SiO_2	Na_2O	CaO	Al_2O_3	B_2O_3
HI-5	64.0	23.0	10.0	3.0	0.0
HI-6	57.3	21.1	20 0	0.0	1.6

3. Results

3.1. Uncoated implants *in vivo*

At removal all four controls (two Co–Cr–Mo and two titanium alloy implants) were found to be loose on manual testing. Histological examination showed lack of osseointegration and no further analyses were made.

3.2. Coated implants *in vivo*

One rabbit in the BGC coating group had an unnoticed but healed periprosthetic fracture. All coated implants were clinically and radiologically tightly

TABLE II Proportions of the implant surface covered by bone at different section levels

Section level	Glass-ceramic coated titanium		Dual-glass coated Co–Cr–Mo alloy	
	mean (%)	range	mean (%)	range
Proximal (1)	55	(37–74)	6.7	(0–20)
Middle (2)	45	(31–66)	5.3	(0–16)
Distal (3)	27	(1–36)	4.7	(0–14)

fixed to the femur. On sample removal two of the three animals with the dual BG-coated Co–Cr–Mo implant were found to have increased amount of discoloured joint fluid.

Histological evaluation of Co–Cr–Mo implants with dual BG coating showed that limited areas of implant surface were covered by bone at each studied section level (Table II). Narrow bone lamellas were often seen around the implants, but direct contact with the coating material was mostly lacking (Fig. 2a). Usually, loose connective tissue with mild to moderate chronic inflammatory reaction consisting of lymphocytes and histiocytes was found between bone lamellas and implant. Resorption of the outer coating layer (HI-6) (Fig. 2c), often accompanied by foreign-body giant cells, was a rather prominent finding, especially in the areas that were not in contact with bone.

Histological analysis of BGC coated titanium implants revealed that 27–55% of the implant surface was covered by bone (Table II and Fig. 2b). The lowest bone coverage was found at the distal section level. Narrow bone lamellas, mostly in contact with the coating material, were forming around the implant shaft projecting to the marrow space. A tight contact between the reaction layer in the surface of BGC coating and bone was a recurrent finding (Fig. 2d). No resorption of the coating material was seen. Occasionally, small clusters of mononuclear inflammatory cells were seen in bone marrow close to the areas of implant surface not covered by bone.

SEM investigation demonstrated resorption of the HI-6 layer of dual BG coating in the areas without direct bone contact (Fig. 3a). In the areas with intimate bone contact, the bone was bonded to glass through the apatite surface layer of the coating. The ground coating was found to be nearly bubble-free and well adhered to the alloy. Also the interface between the ground (HI-5) and top (HI-6) coatings was intact.

The area of dual BG coated Co–Cr–Mo implant shown in Fig. 3a was further analysed by EDXA. Composition profiles over the interface in areas with (Fig. 3b) and without (Fig. 3d) bone contact showed that calcium phosphate formation extended to the vicinity of the ground coating (HI-5). Where bone contact existed (Fig. 3b) the calcium phosphate content in the surface was considerably higher than in areas without contact (Fig. 3d). In the latter areas the

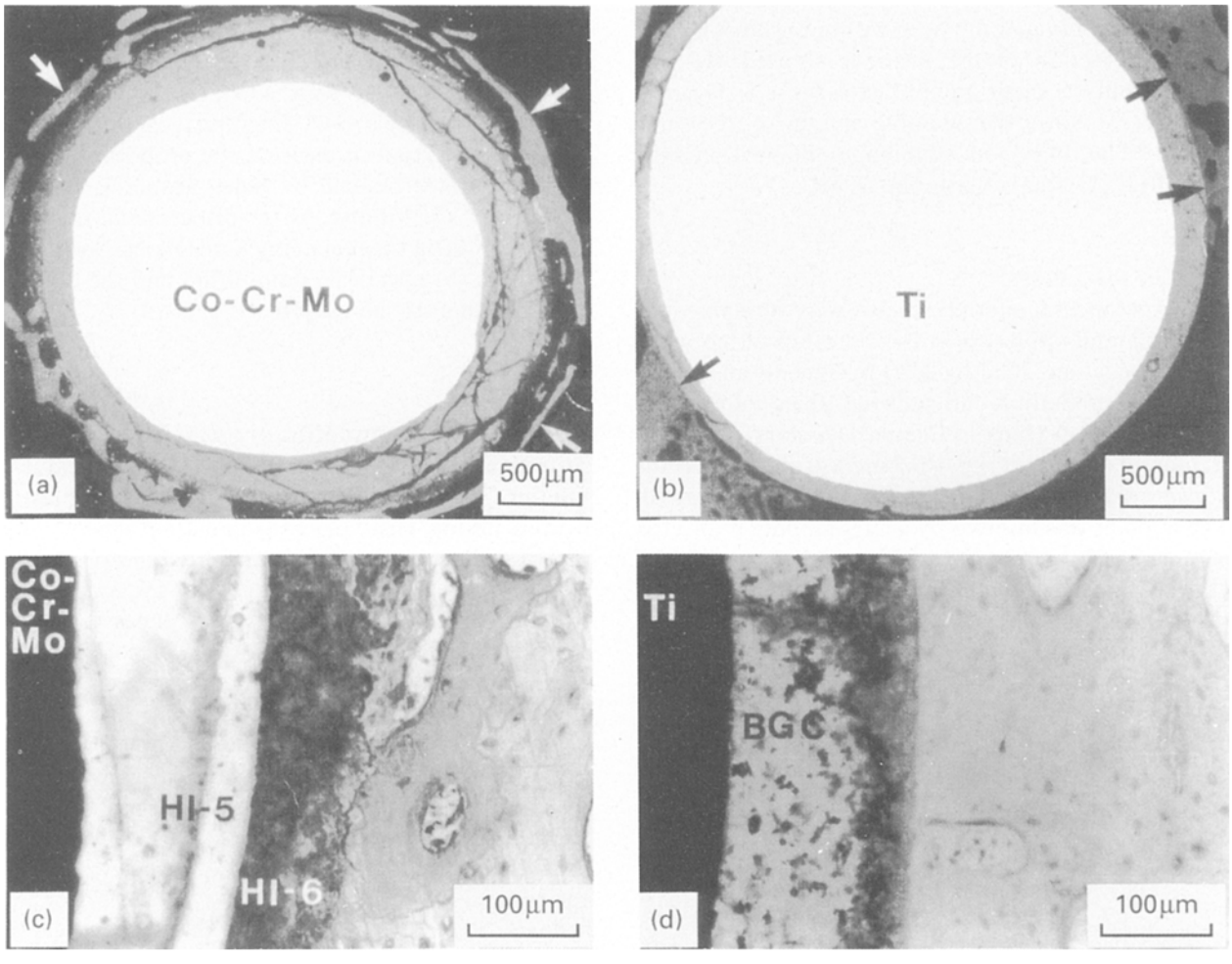

Figure 2 (a) Overview SEM picture of coated Co–Cr–Mo implant at level 3 shows formation of narrow bone lamellas around the implant (arrows). Contact between bone and coating material can be seen in only a few areas. (b) Overview SEM picture of coated titanium implant at level 1 shows tight contact between bone and coating material (arrows). (c) Histological picture of Co–Cr–Mo implant coated with two layers of glass (HI-5 and HI-6) shows tight contact with bone in the lower part of the picture. Note resorption of the outer coating layer (HI-6). (d) Histological picture of a titanium implant coated with bioactive glass ceramic (BGC) shows tight contact with bone. No resorption of coating material can be seen. Note the dark reaction layer of BGC.

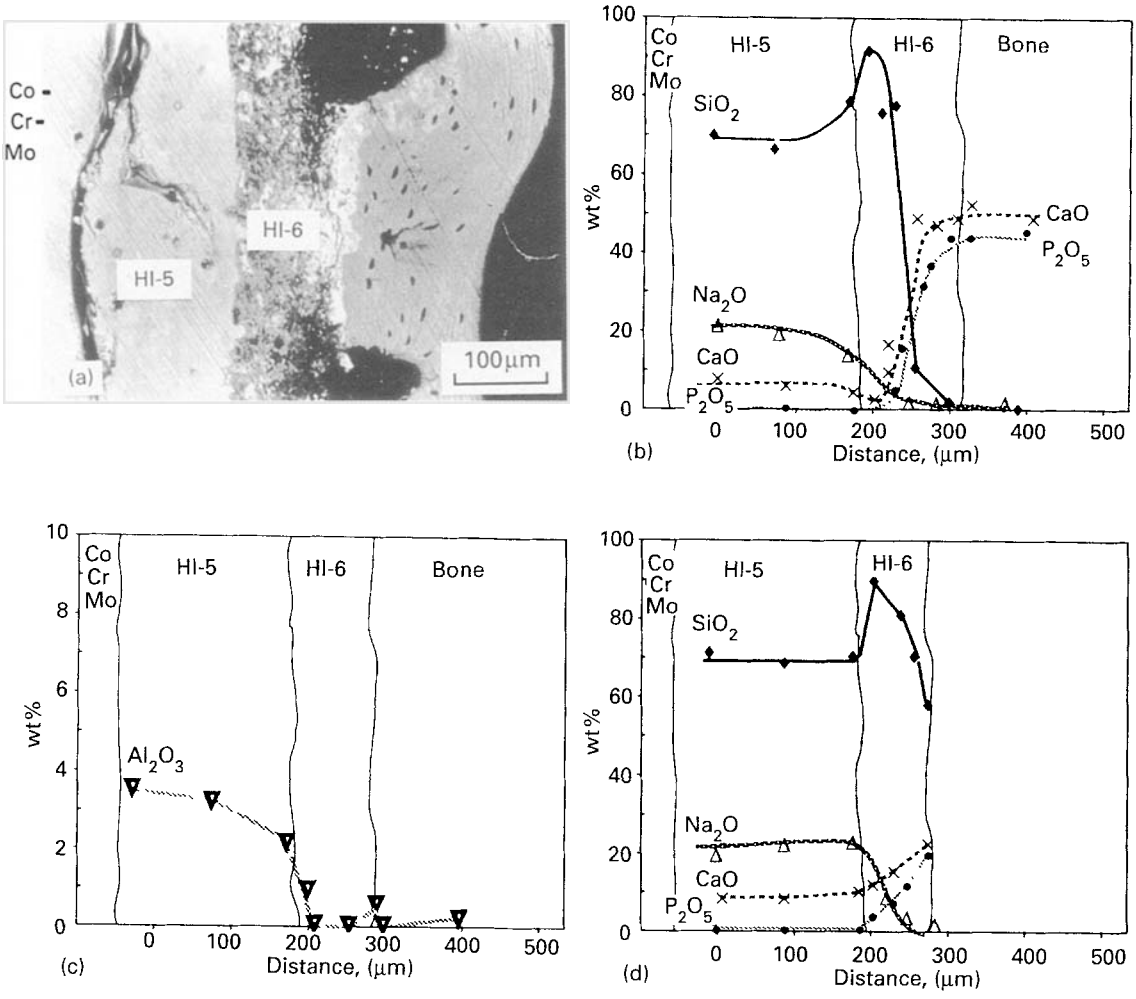

Figure 3 (a) SEM picture of coated Co–Cr–Mo implant demonstrates resorption of the outer coating layer (HI-6). Note also direct contact with bone in the middle of the picture. (b) and (c) Composition profiles in the dual coating and over the bone interface. (d) Composition profiles of the coating layers in the area without bone contact

glass was also slowly resorbing. The reactions in the HI-6 coating had extended down to the interface with the ground coating (HI-5). However, no reactions were seen in the HI-5 coating. EDXA analysis showed that a slight dissolution of alumina from the HI-5 coating into the HI-6 coating had occurred during firing (Fig. 3c). This extended about 10 μm into the HI-6 coating. Furthermore, a slight enrichment of alumina was seen on the glass surface (Fig. 3c).

SEM/ EDXA analysis of BGC-coated titanium implants confirmed bioactive bonding to bone. Furthermore, EDXA revealed a slight decrease in the MgO content and a corresponding increase in the P_2O_5 content towards the surface of the BGC coating. The thickness of this phosphate-enriched layer is about 15–20 μm. The coating was slightly cracked. Some bubbles were noted within the coating but it was properly adhered to titanium.

4. Discussion

The present results demonstrate that coating with BG or BGC can improve the stabilization of a hip endoprosthesis under load-bearing conditions. This indicates the potential of bioactive glass and glass-ceramics for coating of metal implants.

The top (HI-6) layer of the dual BG coating on the Co–Cr–Mo implant behaves differently in areas with bone bonding compared to areas without contact. In the latter areas the glass is slowly resorbing. Bonding seems to inhibit or at least slow down this process. Experience has shown that this kind of resorption does not occur in homogeneous glasses with similar composition [4]. Thus, resorption is related to crystallization during firing. It has been reported that the glassy matrix of Ceravital®-type, partly crystallized glass-ceramics, resorbs slowly [13]. It is probable that the partial crystallization of HI-6 changes the composition of the glassy phase making it resorbable.

Formation of calcium phosphate in the top coating shows that the bioactivity of HI-6 has not been lost during firing. The reactions extend down to the interface with the ground coating. However, no reactions were seen in the ground coating. This indicates that the composition of HI-5 glass is durable enough to stop the leaching at the interface between the two coatings.

The BG coatings used in the study contain originally no phosphate. Thus, phosphate in the calcium phosphate layer originates from the body fluid. Where bone contact exists the calcium phosphate content in the surface is considerably higher than where no contact exists. This may be related to the slow resorption of HI-6 coating. The ground coating contains 3

wt% of Al_2O_3. It is known that alumina may interfere with the bone bonding process [4, 5, 13, 14]. Andersson *et al.* [4] reported recently a three-fold increase in alumina content in the surface of glass implants in a rabbit tibia as compared to bulk glass. This alumina enrichment completely inhibited calcium phosphate formation and consequently bone bonding. For the present dual BG coating a slight dissolution of alumina from the HI-5 ground coating into the HI-6 top coating occurs during firing needed for sintering, this extending only about 10 μm into the top coating. It is, however, also seen that a slight enrichment of alumina in the glass surface occurs. The level of Al_2O_3 in the surface is only about 0.3 wt% and has apparently inhibited neither apatite formation nor bone bonding.

The BGC-coated titanium implants showed at each level studied a distinctly larger circumferential proportion of bone bonding than BG-coated Co–Cr–Mo implants. Mobility of implants at the beginning of mobilization of the study animals did not inhibit bonding between the thin surface reaction layer of the BGC coating and bone as confirmed by SEM/EDXA. As could be expected, the proportion of implant surface covered by bone seems to attenuate in proportion to the distance of the tapered implant shaft from the endosteum. The poor result for the dual BG coating is most likely due to the resorption of the outer HI-6 layer.

Only HA coatings have shown their applicability in clinical use with reliable chemical bonding to bone. Plasma-sprayed coatings of HA, however, are known to be subject to some amount of resorption [15] and their long-term performance has not yet been proven. The same problem of resorption also applies to the dual BG coating used in the present work. On the other hand, it has been proposed that resorption of a coating may not be a major problem [16, 17] as the main purpose of the bioactive coating is to improve implant primary stabilization by bone bonding. If this is true, a glass coating may prove to be useful even if it is slowly resorbing. Long-term stabilization of the implant should then be provided by mechanical osseointegration. Slight cracking of the BGC coating indicates that its coefficient of thermal expansion is too high. Consequently further efforts are needed to solve these problems while preserving the bioactive characteristic of the glass-ceramic coating on titanium.

Acknowledgements

The authors gratefully acknowledge the technical assistance of M. D. Timo Puolakka and Mr Clifford Ekholm. The titanium implants were kindly provided by Kirschner® Medical Corporation, Paterna, Spain. The funds in support of the study were received from the Emil Aaltonen Foundation.

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Received 16 February 1993
and accepted 12 January 1994