Surface properties of hydroxyapatite ceramic as new percutaneous material in skin tissue

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Hydroxyapatite ceramic (HAC) was studied for utilization as a percutaneous device to prevent exit-site and tunnel infection along peritoneal dialysis catheters. As a result, it was found that HAC had good compatibility with skin tissue compared with silicone rubber and glassy carbon. In the present study, the surface properties of HAC after long-term implantation in skin of dogs was evaluated by scanning electron microscopic observation, solubility and bending tests. At 12 weeks after implantation, the surface of HAC was eroded severely by body fluid or cells, and the grain boundaries were clearly relieved. Ingrowth and adhesion of collagen into the etched ditch of HAC were observed. At 12 months, the eroded surface had been tightly covered and adhered to by a collagenous layer in spite of ripping off the surrounding fibrous capsule. In solubility tests, HAC dissolved at the rate of 0.23 mg cm^{-2} HAC surface area per year. On the other hand, the bending strength decreased by about 10% at 4 weeks and scarcely decreased after that time. From these results, it was confirmed that the solubility of HAC produced tight contact and strong adhesion with skin tissue to prevent bacterial infection, and HAC was practical for a permanent percutaneous device.

1. Introduction

One of the most serious problems unsolved in continuous ambulatory peritoneal dialysis (CAPD) is exit-site and tunnel infection along chronic silicone peritoneal catheters [1]. Infection is related to interactions between biomaterials and living tissue [2].

Hydroxyapatite ceramic (HAC) has been evaluated as a practical percutaneous device to prevent such infection along peritoneal catheters. HAC showed slight epidermal downgrowth of less than 1.0 mm and bacterial infection was not observed long-term. It was confirmed that HAC had good compatibility with skin tissue as compared with silicone rubber and glassy carbon [3–5]. In animal trials using a new catheter with an HAC percutaneous device (PD), two dogs were able to survive for a long time, 3, 6 and 19 months, respectively, without any bacterial infection (Fig. 1) [6].

In the present study, the surface properties of HAC after long-term implantation in skin of dogs was evaluated by scanning electron microscopic observation, solubility and bending tests, related to interaction between HAC and skin tissue.

2. Experimental procedure

Hydroxyapatite was prepared by a wet synthetic method using $Ca(OH)_2$ and H_3PO_4 as starting materials. Hydroxyapatite was sintered at 1200 °C by the usual ceramic processing technique to get a dense ceramic (HAC) [7]. The relative density of HAC was 98.5%. HAC-PD for investigating compatibility with skin consisted of a flange of ϕ 20 × 2 mm and a stem of ϕ 7 × 10 mm. The dimensions of samples for solubility and bending tests were 7 × 7 × 0.7 mm and 4 × 20 × 2 mm, respectively. HAC-PDs were percutaneously implanted in the dorsal skin of adult mongrel dogs. The samples for solubility and bending tests were implanted in subcutaneous tissue of dogs.

At 2 weeks, 1, 2, 3, 6, 12, 15 months and 3 years after implantation, the implants were extracted. Subcutaneous tissue and the fibrous capsule surrounding the implants were removed. The implants were washed in distilled water, cleaned in an acetone bath and dried. PDs were cut up into small pieces for the scanning electron microscopic observations. The weight of the pieces for solubility tests was precisely measured using a balance. Bending strength was measured by the three-point bending test method with a span of 15.0 mm and at a crosshead speed of 0.1 mm min^{-1}.

3. Results and discussion

HAC, $Ca_{10}(PO_4)_6(OH)_2$, is one of the basic calcium phosphates that have some slight solubility into physiological salt solution *in vitro* [8]. As implanted into a living body, HAC was directly touched by blood or other body fluid and cells. As a result, the surface of HAC was gradually dissolved and eroded.

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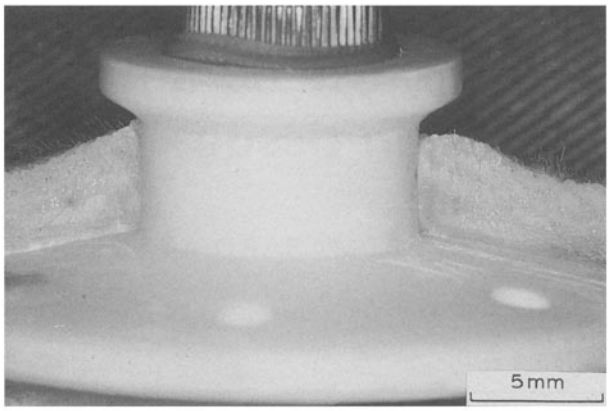

Figure 1 HAC-PD and dorsal skin of dog extracted at 12 weeks after implantation.

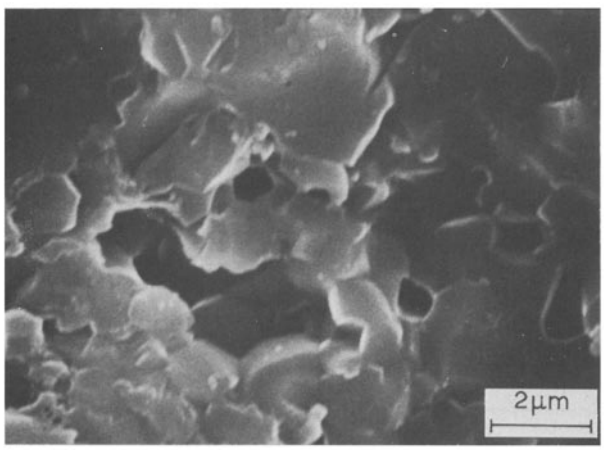

Figure 2 Scanning electron microscopic representation of the raw surface of HAC before implantation.

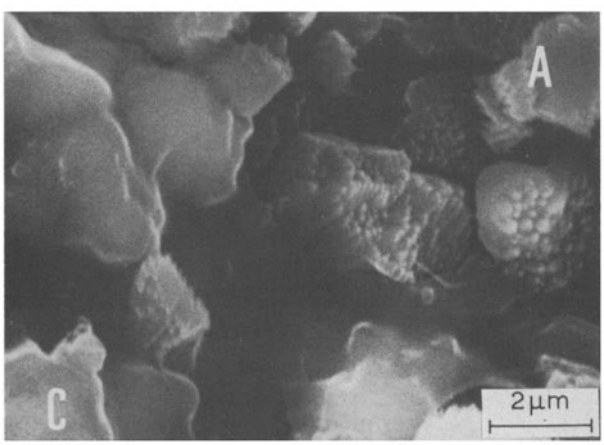

Figure 3 HAC surface implanted in subcutaneous tissue at 12 weeks: (A) part shows the relieved grain boundaries of HAC, (C) part of connective tissue adhered to HAC.

Figures 2 and 3 show scanning electron microscopic representations of the surface of HAC before implantation and of HAC-PD at 12 weeks after implantation, respectively. HAC was eroded severely and the grain boundaries were clearly relieved. Ingrowth and adhesion of fibrous connective tissue into the etched ditch of HAC were observed at 12 weeks.

At 12 months after implantation, a collagenous layer had covered the eroded HAC surface and adhered strongly in spite of ripping off the fibrous capsule surrounding HAC (Fig. 4). It was confirmed that dermis and subcutaneous connective tissue was tightly in contact with HAC.

In histological observations, it was found that the fibrous capsule surrounding HAC was thin, 50–100 μm in thickness, and mature tissue without infiltration of inflammatory cells (Fig. 5). In amino acid analysis, the fibrous capsule surrounding HAC during long-term implantation in subcutaneous tissue was composed of pure collagen that had a very similar amino acid composition to femur periosteum of the same dog [4].

The weight loss of HAC samples for solubility tests was precisely measured during implantation in subcutaneous tissue and was plotted for each duration of implantation (Fig. 6). The surface of HAC dissolved linearly at the rate of 0.23 mg cm^{-2} per year. This indicates that the dissolution rate of dense HAC was slight, only 0.75 μm depth per year. On the other hand, the bending strength decreased by about 10% at 4 weeks and scarcely decreased after that time (Fig. 7). It was found therefore that there is no serious degradation so as to decrease the mechanical strength extremely in skin tissue, and no problem in utilizing it for a permanent PD.

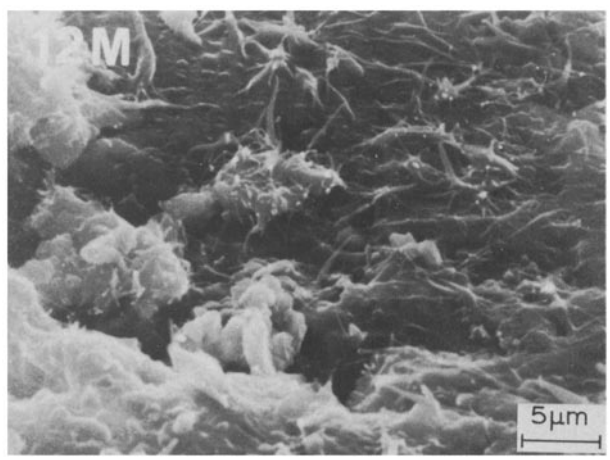

Figure 4 HAC surface at 12 months. Collagenous layer had strongly adhered to HAC surface in spite of ripping off the fibrous capsule.

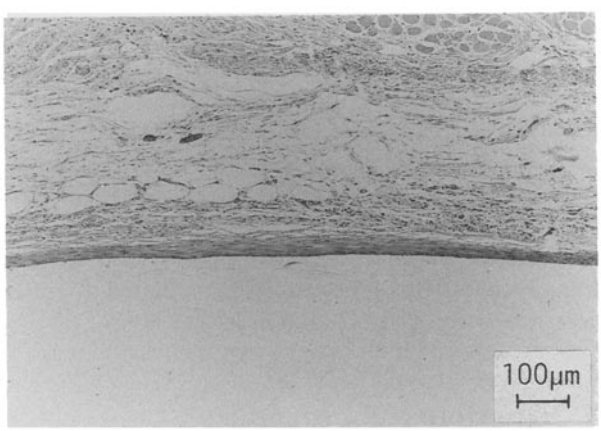

Figure 5 Histological representation of the fibrous capsule interfaced on the flange of HAC-PD at 4 weeks. The fibrous capsule was thin and mature tissue without infiltration of inflammatory cells occurred.

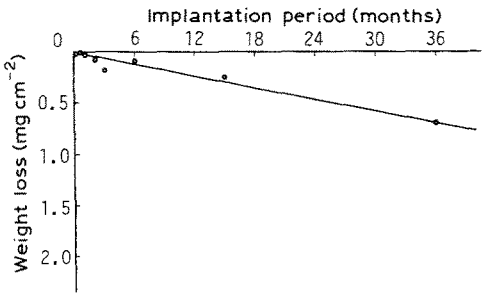

Figure 6 Weight loss of HAC plotted for each duration of implantation. Surface of HAC dissolved linearly.

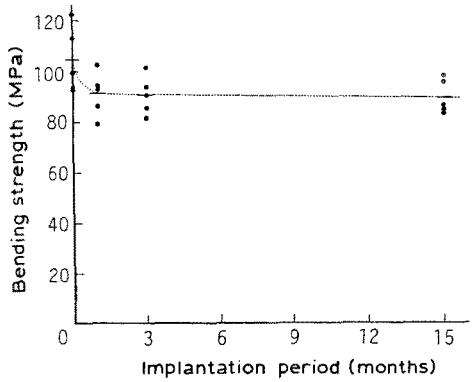

Figure 7 Change of bending strength versus implantation period. Bending strength decreased by about 10% at 4 weeks and scarcely decreased after that time.

4. Conclusion

It was confirmed that the solubility of HAC produced tight contact and strong adhesion with skin tissue to prevent bacterial infection, and that HAC was practical for a permanent percutaneous device.

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