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Stability of zirconia-toughened bioactive glass-ceramics: *in vivo* study using dogs

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The strength of zirconia-toughened glass-ceramic composite was measured after subcutaneous implantation in dogs. The bending strength was not degraded at all 12 weeks after implantation. Scanning electron microscopy revealed that the composite reacted very slowly with body fluid. The thickness of the reaction layer was about 10 μm in depth after 12 weeks, and was less than the critical flaw size (approximately 30 μm) estimated from the bending strength and the fracture toughness. We found that the zirconia-toughened glass-ceramic composite exhibited high strength in living body fluid for a long period.

1. Introduction

Apatite- and wollastonite-containing glass-ceramics in the system $MgO–CaO–SiO_2–P_2O_5$ can form a tight chemical bond with living bone tissues and show relatively high strength (250 MPa in bending) [1, 2]. This glass-ceramic has already been applied clinically to dental implants and artificial bone. However, some artificial hard tissues require higher strength. We have reported [3–7] that glass-ceramic composites toughened with zirconia were prepared for widespread prosthetic applications. Their strength increased with increasing zirconia content. This bioceramic exhibited extremely high bending strength (400–1000 MPa) for 30–80 vol % zirconia [6, 7]. On the other hand, the bioactivity of zirconia-toughened glass-ceramic composites was evaluated by their bonding strength to living bones, the femora and tibiae of dogs [8, 9]. The bonding strength of the composite containing 30 vol % zirconia was as high as that of the glass-ceramic, whereas that of the composite containing 50 vol % zirconia was very low. Therefore, we determined that the optimum zirconia content to prepare high-strength and bioactive ceramics was 30 vol %. The glass-ceramic composite has great potential for use in biomedical applications.

In bioactive glasses or glass-ceramics, some ions dissolve from the surface to react with ions supplied from body fluid. The surface change may degrade the strength of the material. The strength of bioceramics should not be degraded during implantation in living bodies as artificial hard tissues. In this study we measured the strengths of the composite after implantation in dogs. This paper discusses the degradation.

2. Experimental

A powder mixture of nominal composition (wt %) CaO 47.7, P_2O_5 6.5, SiO_2 43.8, MgO 1.5 and CaF_2 0.5 was melted at 1550 °C in a platinum crucible. The melt was then quenched to form the glass. The resultant glass was reheated until it crystallized, i.e. after 2 h at 1150 °C. The glass-ceramic, which contained 15% apatite [$Ca_{10}(PO_4)_2(O,F_2)$] and 60–70% wollastonite ($CaSiO_3$) crystals [7, 10], was pulverized to powder of particle size < 7 μm (average size 1–2 μm). The resultant glass-ceramic powder was blended with partially stabilized zirconia powder [TRZ(W)2.6Y-15, prepared by Nippon Soda Co.] by ball-milling. The mixture was composed of 70 vol % glass-ceramic powder and 30 vol % zirconia powder. The mixture was cold isostatically pressed at 196 MPa and then presintered at 1200 °C for 2 h. The presintered body obtained was post-isostatically hot-pressed at 1200 °C for 1 h under a pressure of 196 MPa [7]. As a control material, the base glass-ceramic of the above-mentioned composite was prepared. The glass (wt %: CaO 47.7, P_2O_5 6.5, SiO_2 43.8, MgO 1.5 and CaF_2 0.5) was pulverized to powder of particle size < 7 μm (average size 1–2 μm). The powder was cold isostatically pressed at 196 MPa and then the compact was heated at 1150 °C for 2 h for sintering and crystallization. This glass-ceramic (denoted "base glass-ceramic") contained no zirconia.

Rods of these materials (4.1 mm in diameter) were ground using a #400 diamond wheel. The rod specimens were washed well in ethanol and then sterilized by a conventional "ethylene-oxide gas method". Epidermal incisions, which penetrate the dermis, were made in the back of a healthy mongrel dog. The rod-

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shaped materials were implanted into the subcutaneous tissues. We expected to observe changes in the materials in moving body fluid. After 7, 28, 56 and 84 days the specimens were extracted. The three-point bending strength was measured at a loading rate of 0.5 mm min^{-1} and a span length of 15 mm in water at 37 °C.

The specimens were cut perpendicularly to the surfaces. The cut surfaces were polished with 1 μm diamond and observed by scanning electron microscopy (SEM). Furthermore, microchemical analysis by energy-dispersive spectroscopy (EDS) was performed on the cross-sections over a spot approximately 2 μm square.

3. Results and Discussion

Fig. 1 shows an SEM micrograph and EDS spectra of the cross-section of the base glass-ceramic after subcutaneous implantation for 84 days. The reaction layer with body fluid was 40–50 μm in depth from the surface. It was found that the layer was composed of the CaO/P_2O_5-rich phase (part B) and the SiO_2-rich phase (part C). These phases were continuous with interlocking. Bioglass by Hench [11] forms these two phases in living body or simulated body fluid. Glass-ceramic A-W by Kokubo and co-workers (see, for example [12, 13]) forms the CaO/P_2O_5-rich phase but does not form the SiO_2-rich phase. The base glass-ceramic in this study also contained apatite and

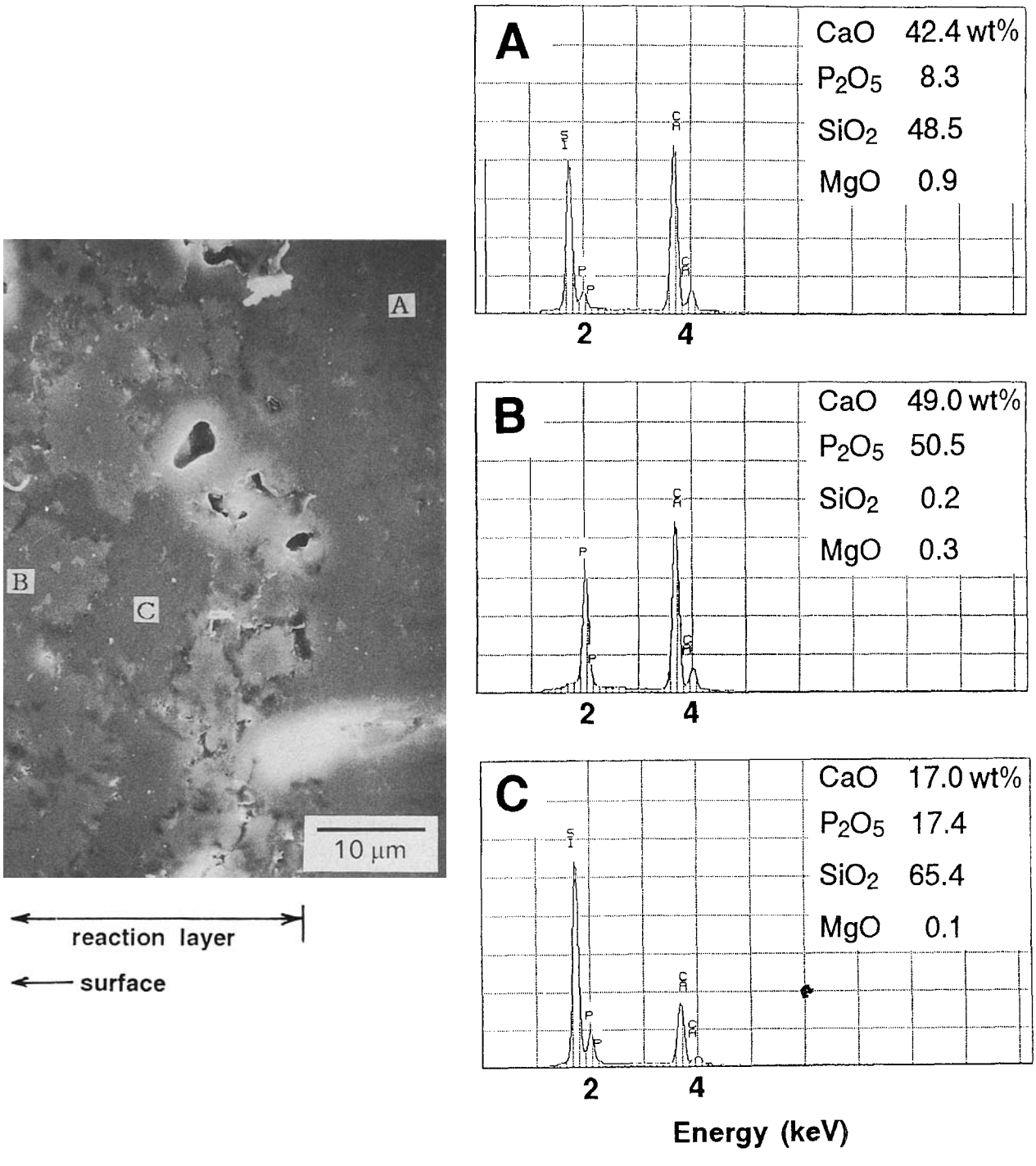

Figure 1 SEM micrograph and EDS spectra of the cross-section of the glass-ceramic after subcutaneous implantation for 84 days.

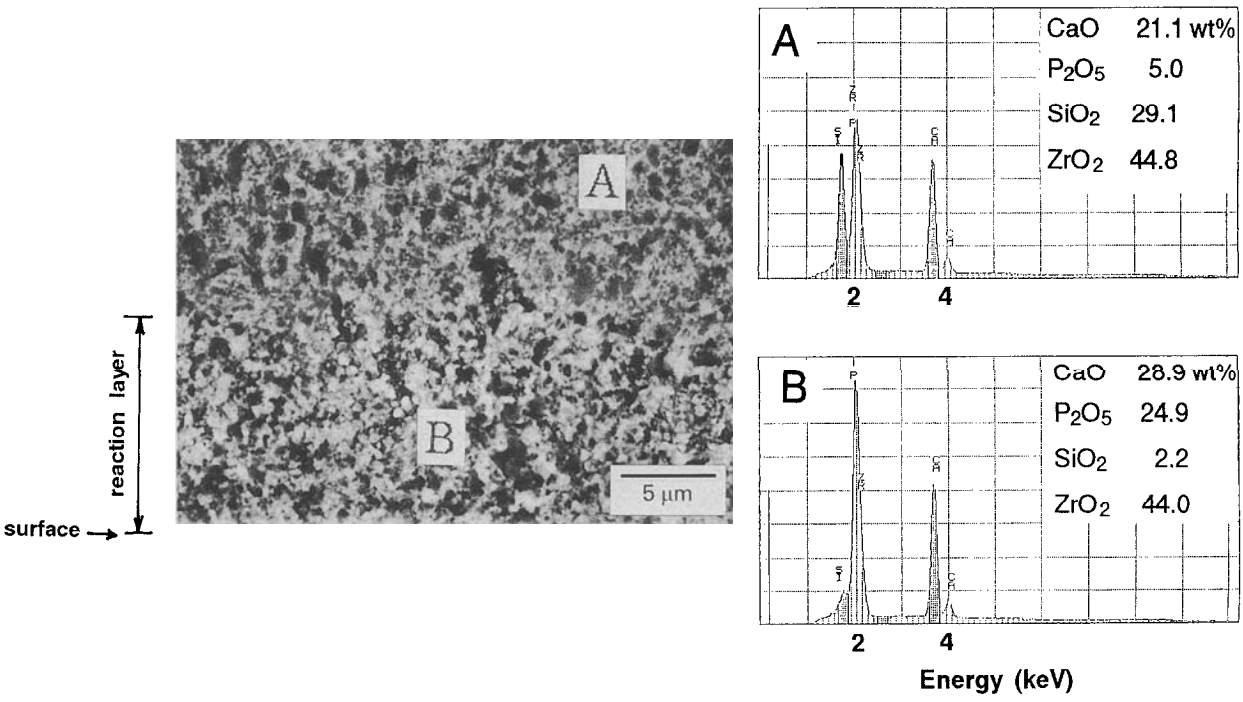

Figure 2 SEM micrograph and EDS spectra of the cross-section of the zirconia-toughened glass-ceramic after subcutaneous implantation for 84 days. The quantity of Mg was so small that it was neglected in this analysis.

wollastonite crystals. However, the SiO_2 content in the base glass-ceramic was higher than in glass-ceramic A-W. Therefore, it is suggested that the mechanism of reaction to the living body varies with the composition of glass-ceramics.

Fig. 2 shows an SEM micrograph and EDS spectra of the cross-section of the glass-ceramic composite after subcutaneous implantation for 84 days. Zirconia appears bright due to a difference in atomic number contrast. The layer reacting with body fluid was about 10 μm in depth from the surface. According to the EDS spectrum, the reaction layer B was composed of a CaO/P_2O_5-rich phase containing a small amount of SiO_2. The SiO_2-rich phase, shown in Fig. 1, was not found. The crystallized glass in the composite was partitioned into many sections by zirconia particles. In these small sections, CaO/P_2O_5-rich phases and SiO_2-rich phases may exist. Therefore, we considered that the reaction phase was detected as a CaO/P_2O_5-rich phase containing SiO_2, based on the EDS analysis.

Parts A in Figs 1 and 2 have not yet reacted with body fluid. The CaO/SiO_2 ratio of part A in Fig. 2 is 21.1/29.1 (namely 42.0/58.0). Compared with that in Fig. 1 (CaO/SiO_2 = 42.4/48.5), the CaO content is less. During the sintering of the composite, the crystallized glass particles react with the zirconia particles to decrease the Ca concentration [9]. The ability of glasses or glass-ceramics to form apatite in the system $CaO–P_2O_5–SiO_2$ decreases with decreasing CaO content [14]. Therefore, we suggest that the reaction of the composite with body fluid was restricted by the decrease in Ca concentration in part of the crystallized glass, compared with that of the base glass-ceramic.

Fig. 3 shows the relationship between the implantation period and the thickness of the reaction layer. The layer thickness of the glass-ceramic increased with

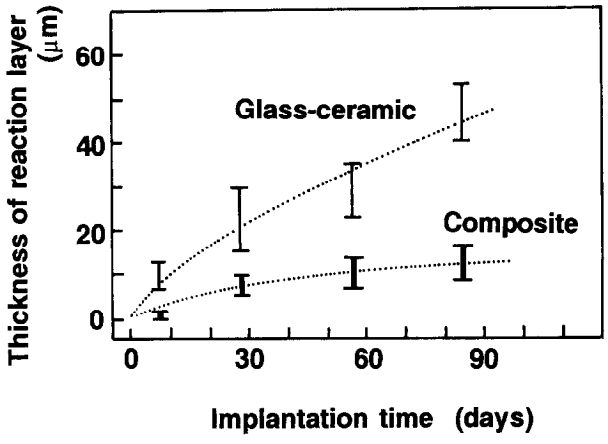

Figure 3 Thickness of the reaction layer as a function of the implantation time: I, glass-ceramic and I, zirconia-toughened glass-ceramic composite.

increasing implantation period. On the other hand, the composite reacted slowly with body fluid.

Fig. 4 shows the bending strength of the glass-ceramic and the composite after subcutaneous implantation. The strength of the glass-ceramic after implantation for 84 days was 60–70% that of the as-prepared glass-ceramic, whereas the strength of the composite did not decrease. It is assumed that the thick reaction layer of the glass-ceramic reduces the strength, and that will be the origin of fracture with loading. The composite formed a reaction layer of 10 μm for 84 days implantation. The thickness of the layer was less than the critical flaw size (about 30 μm) [15] estimated from the bending strength and the fracture toughness, i.e. approximately 500 MPa and 3 MPa $m^{1/2}$ [5, 7], respectively. Therefore, the strength will not decline.

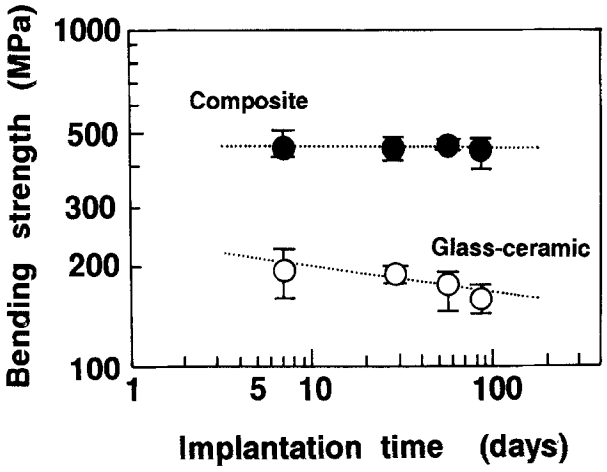

Figure 4 Bending strength of (○) the glass-ceramic and (●) the zirconia-toughened glass-ceramic composite after implantation.

4. Summary

Zirconia-toughened glass-ceramic has been showing high strength in living bodies. As reported previously, the bonding strength of the composite is as high as that of the glass-ceramic containing no zirconia. Therefore, we consider that the composite can be used clinically for a long period.

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