

## Acceleration and Deceleration of Bone-Like Crystal Growth on Ceramic Hydroxyapatite by Electric Poling

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The electric properties of HAp have long since been investigated for the understanding of its bioactive characteristics from the viewpoint of materials science.<sup>1–10</sup> The mass transport mechanism was first studied by a complex impedance method for the crystallographical analysis of tooth caries, and the ion transport through the HAp structure has been attributed to the exchange of lattice positions of OH<sup>−</sup> ions with lattice defects thereafter.<sup>1,3,4</sup> An important hypothesis was also made based on the piezoelectric effect, that osteogenesis occurs by an ionic process driven by mechanical stress applied to bones;<sup>5</sup> some studies have attributed the piezoelectricity of bones to incorporated water and fibrous collagens.<sup>6–8</sup> Further analysis has thereafter been made through a series of thermally stimulated current studies, which have revealed that the polarizability of HAp originates from the reorientation of the dipole moments between O<sup>2−</sup> and H<sup>+</sup> of lattice OH<sup>−</sup> ions.<sup>9</sup> We have very now discovered the acceleration and deceleration of bone-like crystal growth on polarized ceramic HAp, depending on the electric polarization conditions.

We report here the phenomenological effects of polarization on the acceleration and deceleration of bone-like crystal growth on HAp ceramics. Considering the role of dipole moment in the crystal growth, we extended this study to a variety of materials such as apatites extracted from wasted cattle bones, non-hydroxide calcium phosphate, ferroelectric barium titanate and calcium titanate with a medium dielectric constant. On the basis of these results, a model is proposed for the enhanced crystal growth.

HAp ceramic specimens were prepared by sintering the compacted bodies of wet-chemically synthesized powders at 1200 °C for 1–5 h under a flow of steam in order to maintain lattice OH<sup>−</sup> ions during sintering<sup>10</sup> or in air as is usual. Those specimens sintered under steam or in air are named as HAp(w) and HAp(a), respectively. For further study, the ceramic specimens of tricalcium phosphate (TCP) and apatite extracted

from cattle bones (designated c-Ap(w)),<sup>11</sup> barium titanate (BaTiO<sub>3</sub>, BT) and calcium titanate (CaTiO<sub>3</sub>, CT) were also prepared, since TCP contains no lattice OH<sup>−</sup> ions, while spontaneous polarization takes place in BT and CT has medium polarizability. c-Ap(w) was also sintered under steam. These specimens, with a size of 10 mm diameter × 1 mm thickness, were sandwiched between platinum plates, heated to 300 °C in air, then subjected to the polarization treatment in a dc field of 1 to 1000 V for 2 min or 1 h, and thereafter cooled to room temperature under polarization.<sup>12</sup> Considering its tetragonal-cubic phase transition temperature, the BT specimens were polarized at 200 °C. These polarized specimens were immersed in a simulated body fluid (1.5SBF)<sup>13</sup> with pH = 7.25, which contains the 1.5 times concentration of inorganic ions in the human body, at 36.5 °C for several hours to 1 week. Grown layers were analyzed by scanning electron microscopy (SEM), X-ray diffraction (XRD), FT-infrared spectroscopy (IR) and energy dispersive X-ray (EDX) analysis. Prior to the experiments of crystal growth, dielectric measurements were also carried out on all the ceramic specimens using the ac frequency of 10 kHz at temperatures of 25–350 °C for the evaluation of polarizability. A dielectric constant measured at 36.5 °C is shown below as  $\epsilon_s$ .

Figure 1 phenomenologically demonstrates the effect of polarization on the crystal growth on HAp ceramics: While slow crystallization was dispersively observed on nonpolarized HAp(w) (Figure 1a), large crystals of 1–4  $\mu\text{m}$  in diameter covered the surface of polarized HAp(w) under 120V (Figure 1b) after an immersion in 1.5SBF for only 12 h. The crystal growth was dependent upon the dc field strength, temperature, and time for polarization. As a whole, higher field strength gave rise to faster crystal growth; sizable agglomerated crystals of 10  $\mu\text{m}$  in diameter were observed in some spots on polarized HAp(w) under 1000 V, and the acceleration effect was confirmed even for a polarization as weak as 12 V/cm. The importance of the polarization temperature is suggested by the fact that the polarizability of HAp is attributed to the ordering of lattice OH<sup>−</sup> ions due to the reorientation of protons around O<sup>2−</sup>, which is activated at an elevated temperature (200–300 °C).<sup>9</sup> Although the polarization at 300 °C was most effective for the acceleration of crystal growth, we also identified an acceleration effect by polarization at 200 °C. The polarization time is also considered to have an influence on the crystallization, as is shown in comparison with the results (Figure 1b,c), in which the formation of thick layers is seen on HAp(w) polarized for 1h (Figure 1c), whereas 2 min polarization resulted in the deposition of disperse crystals (Figure 1b). An experiment confirmed that a 1 h polarization is sufficient for the optimum acceleration of crystal growth; under these conditions the surfaces of HAp(w) were already coated with thick bone-like layers within 6–12 h (Figure 1d,e). Under the optimum polarization conditions (120 V, 1

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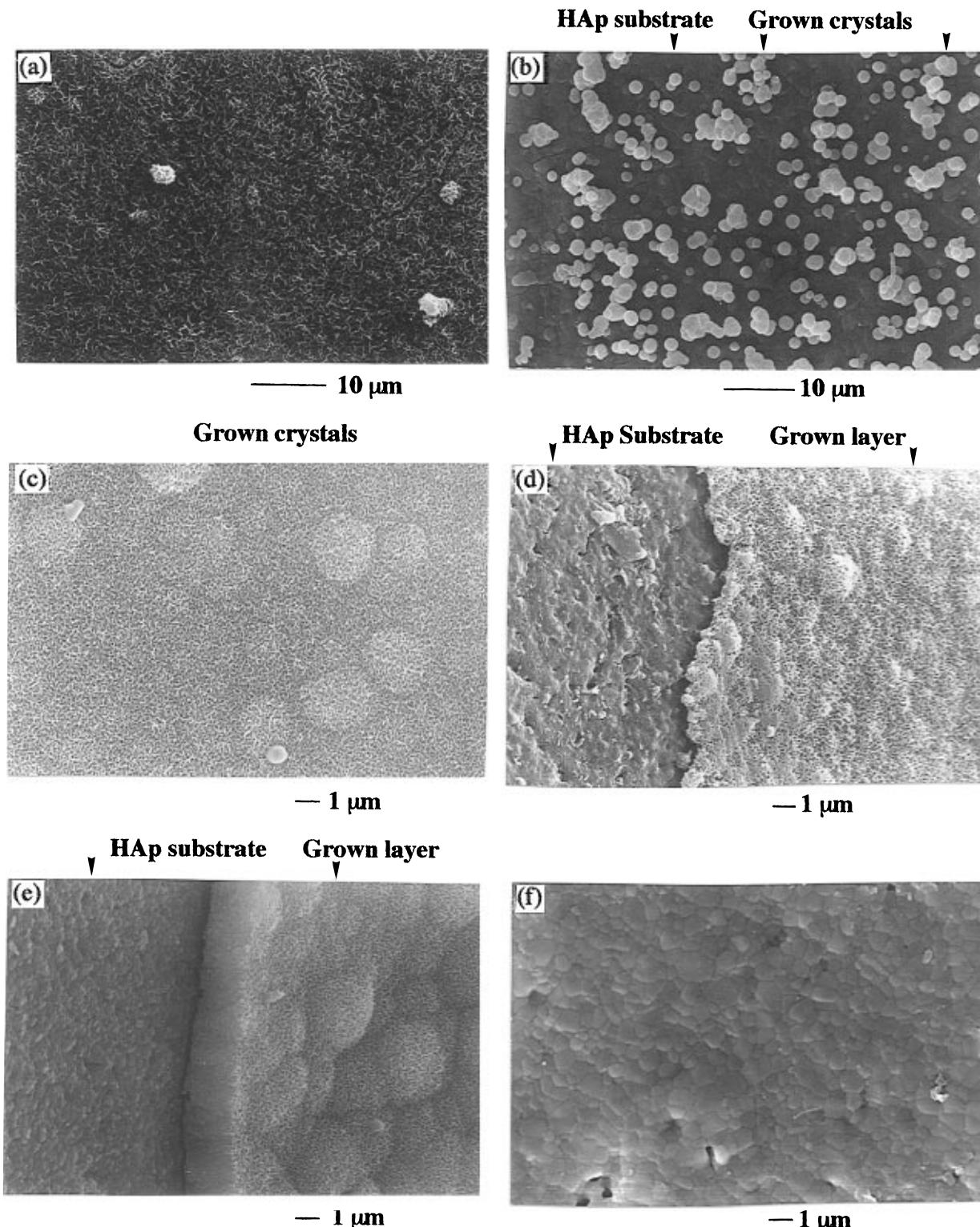
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(11) The apatite was supplied by T. Akazawa and co-workers at Hokkaido Industrial Institute, who prepared the powders by 120 °C hydrothermal treatment of spongy and cortical bones cut from waste cattle femur for reuse.

(12) As the previous study reported that poling at a limited range of temperatures for short time was relaxed,<sup>9</sup> we kept applying dc voltage until the specimen had cooled to room temperature.

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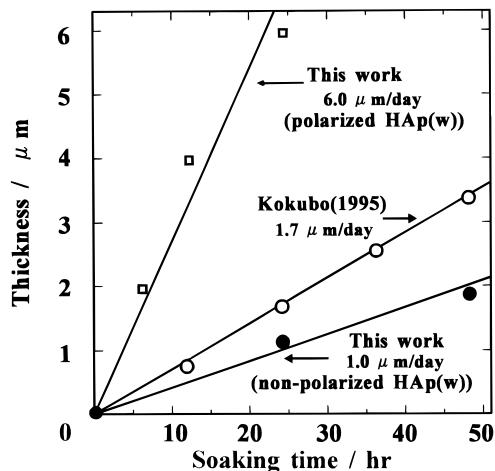


**Figure 1.** Scanning electron micrographs of the surfaces and fractured surfaces of the hydroxyapatite ceramic specimens (HAp (w)) immersed in the simulated body fluid (1.5SBF) at 36.5 °C, showing the electric polarization effect on bone-like crystal growth, where the photographs show nonpolarized (a), negatively polarized surfaces (b–e), and positively polarized surface (f). Polarization conditions (electric field/applied time) and immersion time in 1.5SBF: (0 V/0 h)/(12 h) (a), (120 V/2 min)/(12 h) (b), (120 V/1 h)/(12 h) (c), (120 V/1 h)/(12 h) (d), (120 V/1 h)/(24 h) (e), (120 V/1 h)/(3 day) (f).

h), the growth rate was estimated as 6  $\mu\text{m}/\text{day}$ , almost 3 times of the result obtained by the biomimetic method (1.7  $\mu\text{m}/\text{day}$ ).<sup>13</sup> Here another characteristic result concerning this polarization effect is seen in Figure 1f: All of the accelerated crystal growth mentioned above was observed on negatively charged surfaces (abbreviated as N surface), whereas Figure 1f shows that no crystal growth ever took place on the positively charged surface

(P surface) even after a 3-day immersion in 1.5SBF. This will be mentioned and discussed below.

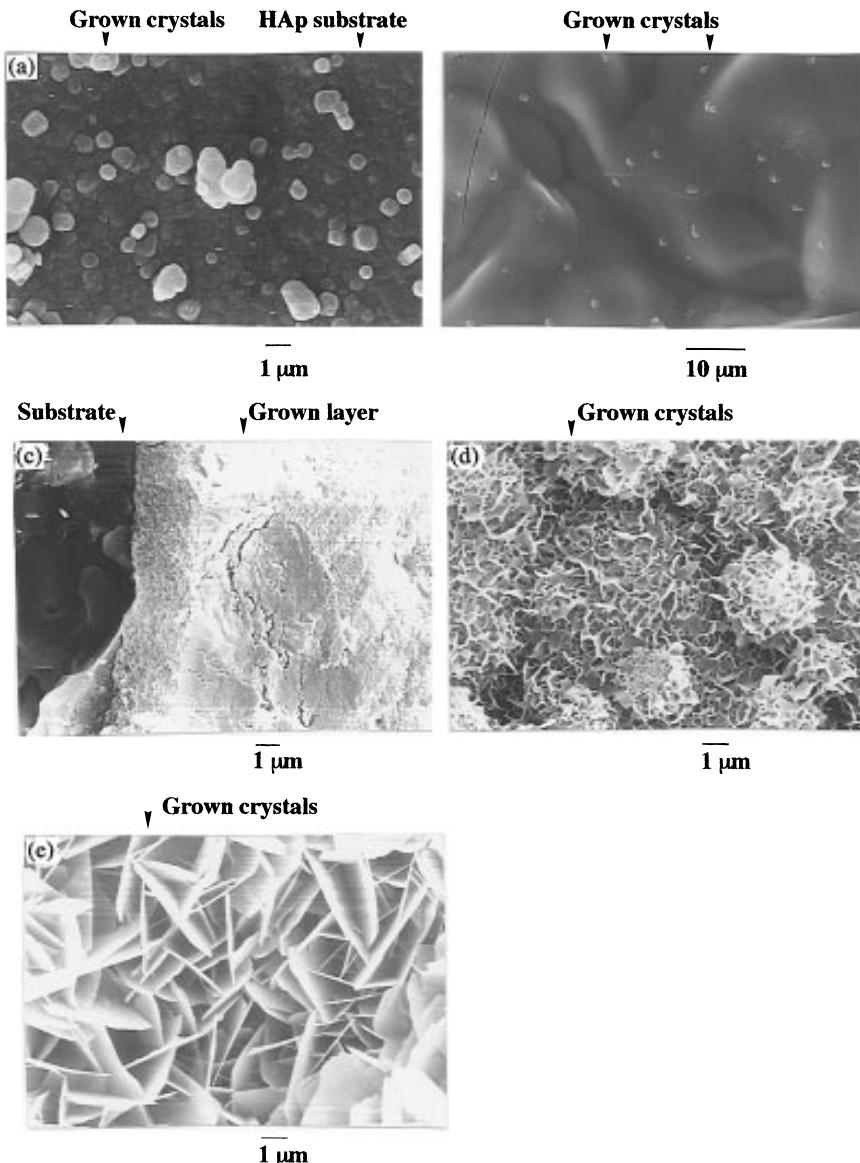
The growth rate obtained under the polarization condition of 120 V/mm for 1 h at 300 °C was experimentally estimated as 6.0  $\mu\text{m}/\text{day}$ , corresponding to 6 times that of nonpolarized HAp(w) and 3 times that of a reported value obtained by the biomimetic method<sup>13</sup> (Figure 2). The growth rate was observed to ap-



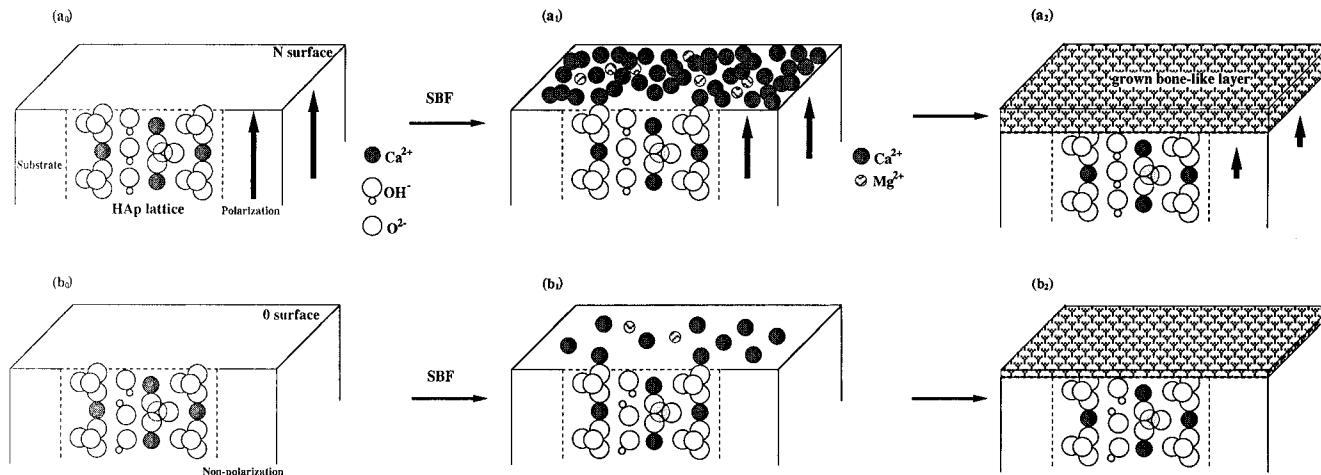
**Figure 2.** Comparison of the crystal growth rate of this work with the biomimetic method carried out by Kokubo and co-workers.<sup>1</sup> Also shown is the time change of crystal growth on nonpolarized HAp(w).

proximately linearly increase with polarization field strength. The grown crystals and layers were analyzed by XRD, EDS, and FT-IR. XRD and EDS confirmed that the grown crystals and layers were apatitic calcium phosphate crystals including a small amount of Mg. The layers were also confirmed by FT-IR to contain carbonate ions. These analytical results indicate the formation of bone-like crystals of partially carbonated calcium hydroxyapatite.

As mentioned above, the existence of lattice OH<sup>-</sup> ions is essential for polarization of HAp. To verify this claim, HAp(a) ( $\text{Ca}_5(\text{PO}_4)_3\text{O}_x(\text{OH})_{1-2x}$ ), which underwent partial dehydration because of lack of sufficient H<sub>2</sub>O vapor during sintering,<sup>10</sup> and unhydrated calcium phosphate TCP ( $\text{Ca}_3(\text{PO}_4)_2$ ), were subjected to the same experiments. Figures 3a,b supports the inference; although accelerated crystal growth was observed on the N surface of HAp(a), the polarization effect was not as distinctive as in the case of HAp(w). The deterioration of polarizability by partial dehydration is backed by the



**Figure 3.** Scanning electron micrographs of the surfaces and fractured surfaces of the ceramic specimens of HAp sintered in air (a),  $\text{Ca}_3(\text{PO}_4)_2$  (b), apatite extracted from wasted cattle bones (c),  $\text{BaTiO}_3$  (d), and  $\text{CaTiO}_3$  (d), immersed in 1.5SBF. Polarization conditions (electric field/applied time) and immersion time in 1.5SBF: (120 V/2 min)/(12 h) (a), (120 V/1 h)/(12 h) (b), (120 V/1 h)/(3 day) (c), (120 V/1 h)/(1 week) (d), (120 V/1 h)/(1 month) (e).



**Figure 4.** Model for the accelerated bone-like crystal growth on ceramic hydroxyapatite at the early (a<sub>1</sub>) and intermediate stages (b<sub>1</sub>) in comparison with that of a nonpolarized specimen (a<sub>2</sub>, b<sub>2</sub>), where the arrows express the direction and strength of dipole moments. Polarized state is shown by the orientation of OH<sup>-</sup> ions (a<sub>0</sub>) in comparison with nonpolarized or randomly distributed state (b<sub>0</sub>).

smaller measured dielectric constant of HAp(a) ( $\epsilon_s = 30$ ) than that of HAp(w) ( $\epsilon_s = 40$ ). As expected, no crystal growth was observed either on the P surfaces of HAp(a) or on TCP. Actually the polarization treatment essentially had no significant influence on TCP because of its small polarizability ( $\epsilon_s < 10$ ). Whereas on c-Ap(w) ( $\epsilon_s = 25$ ), accelerated crystal growth was observed (Figure 3c). To generalize the polarization effect on crystal growth, this experiment was also applied to ferroelectric BT, which has spontaneous polarization ( $\epsilon_s = 3000$ ), and CT ( $\epsilon_s = 150$ ). Interestingly, considerable crystal growth was observed on the N surface of polarized BT (Figure 3d) and CT (Figure 3e) after a 1-week immersion in 1.5SBF.

On the basis of the above results, we propose a model for the accelerated and decelerated crystal growth on HAp in comparison with the usual crystal growth (Figure 4): At first cations are more rapidly adsorbed on N surface due to polarization (Figure 4a<sub>0</sub>, 4a<sub>1</sub>) than on a surface of nonpolarized HAp (0 surface (Figure 4b<sub>0</sub>, 4b<sub>1</sub>), and the counterions of HPO<sub>4</sub><sup>2-</sup>, HCO<sub>3</sub><sup>-</sup>, and OH<sup>-</sup> are attracted around the cations. At this stage, Ca<sup>2+</sup> ions are predominantly adsorbed on N surface because of the superior binding affinity for HAp to the other cations of Na<sup>+</sup> and Mg<sup>2+</sup> in 1.5SBF.<sup>14</sup> Nucleation takes place among these supersaturated ionic groups, and the remaining dipole moments accelerate the growth of

nuclei due to the attraction of these ions on the N surface (Figure 4a<sub>2</sub>). On the positively charged surface, on the other hand, chloride ions appear to be mainly adsorbed, which may be unfavorable for crystal growth of HAp. This model is under further study.

Because of its unparalleled bioactivity with surrounding tissues in the human body, numerous works on crystal growth of HAp have recently been undertaken with a view toward the biological applications. The biomimetic crystal growth is reportedly a viable method for this purpose, which enables the coating of strong materials with bone-like HAp through a low-temperature process.<sup>13,15</sup> The present result is expected to greatly contribute to the development of biomimetic HAp coating methods on implant materials.

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