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The Effect of Electrical Stimulation on Bone Formation Around Hydroxyapatite Implants Placed on the Rabbit Mandible

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Nonresorbable, nonporous, particulate hydroxyapatite (HA) was implanted on the mandible in rabbits and stimulated electrically, 4 hours per day, during the first postoperative week. Stimulated and control implant sites were recovered 8 weeks postoperatively and examined histologically. The HA migrated into the mandible in the electrically treated specimens, and was routinely found in intimate association with preexisting mandibular bone. In the controls, the HA remained superior to the mandibular surface. In further studies (without electrical stimulation) in which the implant site was recovered 26 weeks postoperatively, HA was observed in the mandible: some HA particles migrated completely through the mandible and were found in the adjacent soft tissue. It was concluded that, under the conditions studied, electrical stimulation does not promote bone growth into HA, but rather produces the opposite result–it promotes more rapid movement of HA particles into the mandibular bone. The HA particle migration into the mandible observed (longer postoperative times) in the absence of electrical stimulation suggests that migration is a general property of HA particles when placed over bone under muscle.

Various forms of synthetic hydroxyapatite (HA) have been shown to be biocompatible[3] and useful in reconstruction and augmentation of the mandible.[4–7] Hydroxyapatite functions as a spaceoccupying substance. but does not enhance regeneration of bone": the pores (in block HA) and the interstices (in particulate HA) become filled with connective tissue.

A mixture of autogenous cancellous bone and HA may result in bone growth in regions that would otherwise be filled with connective tissue.[5] Because electrical stimulation can also promote osteogenesis,[9] we studied the possibility that such stimulation could function as a substitute for autogenous bone in promoting bone growth around HA particles. To facilitate the study of electrically stimulated bone (in distinction to trauma-induced reparative bone growth), a model was developed that did not involve an osseous defect. Observations made 8 weeks after HA implantation (7 weeks after cessation of electrical stimulation) led to a second experiment (not involving electricity) designed to explore the initial results.

Methods

SURGICAL PROCEDURE

Twelve female, white New Zealand rabbits (3 to 5 months of age) were used in these studies. The masseter muscle was exposed via an extraoral incision, the attachment was cut, and the muscle was reflected superiorly to expose the mandible (Fig 1). A porous polyvinyl-chloride ring (Tygon, S5OHL 11, Norton. Akron. OH), 5 mm high, 13 mm inner diameter. 19 mm outer diameter, was placed on the bone and filled with approximately 1.2 g of HA

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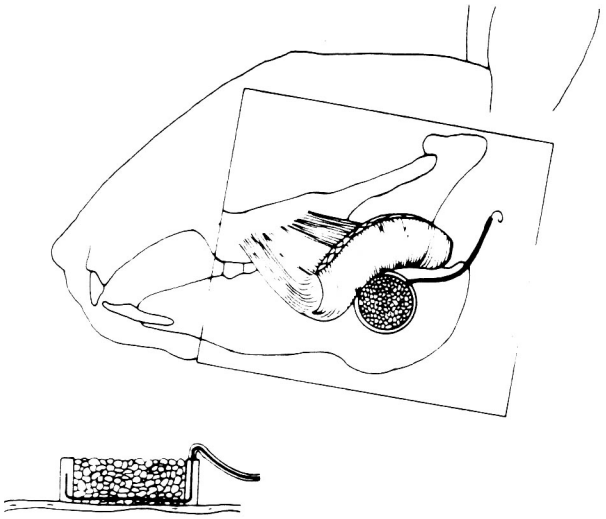

FIGURE I. Diagram showing placement of HA on the rabbit mandible. A ring of polyvinvl chloride containing the electrode was placed under the masseter muscle and the electrode "as exteriorized through the skin incision.

(Calcitite 2040. Calcitek. Inc. San Diego. CA). Stainless steel ligature wire 10.5 mm in diameter) was then passed through one wall of the ring and terminated in the opposite wall (Fig 1). The wire electrode (insulated with polyethylene tubing along its entire length. except for the portion in contact with the bone) was externalized through the incision and secured to the skin over the jaw. The muscle was closed over the top of the implant and sutured along the mandibular ridge with 4-0 absorbable sutures: the skin incision was then closed with the same suture. The procedure was performed bilaterally except that the wire was placed only on one side.

Electrical treatment consisted of a current of 20 μA, administered 4 h/d, for 5 of the first 7 postoperative days. with the jaw electrode operating as the cathode and a platinum needle electrode (E2. Grass Instrument Company, Quincy. MA) placed in the muscles of the hip acting as the anode. Electrical stimulation was delivered to one of the implants, and the contralateral implant served as the control. The current was supplied by a constant-current source (Model 224. Keithley. Cleveland. OH) and both the current and voltage were monitored continuously throughout the treatment with autoranging multimeters (Model 175, Keithley. Cleveland, OH). The voltage varied automatically (0.9 to 1.5 V) to maintain the current at its preset value. Following cessation of electrical stimulation (I week postoperatively), the cathode was removed by gently pulling it perpendicularly to the mandibular surface.

The rabbits were killed 8 weeks postoperatively (unless noted otherwise), and the implant site was removed, fixed in formalin, dehydrated, embedded in epoxy (SPI Chem, SPI Supplies, Westchester, PA), and cut on a diamond saw (Model 650. South Bay Technology, Inc. Temple City. CA) at 125 μm in a plane orthogonal to the mandibular surface: 15 to 25 sections from the central one third of the implant were stained with toluidine blue and basic fuschin. and analyzed.

Results

Six rabbits were treated five times during the first postoperative week and killed 8 weeks postoperatively. In one instance (on the control side) the implant became elevated from the mandible, resulting in disbursal of the HA. In another animal, the implant (on the treated side) was lost during tissue processing: thus, a total of 10 implants from 6 animals were available for analysis.

The typical appearance of an unstimulated implant is shown in Figure 2; the mandible was essentially unaffected by the presence of the HA, and the interstices between the particles were filled with

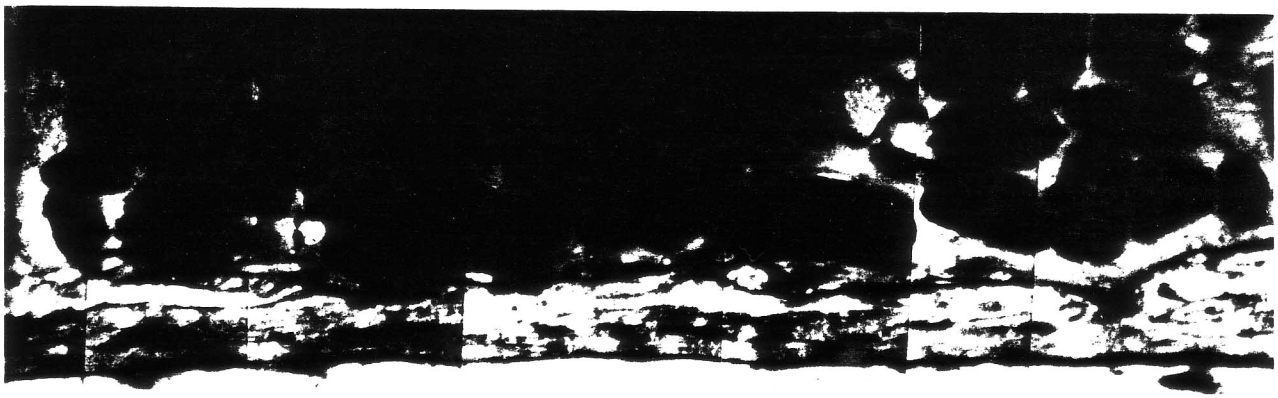

FIGURE 2. Characteristic tissue reaction to HA implant after 8 weeks. The view corresponds to that depicted in the insert in Figure I the mandible at the bottom, in cross-section). The implant was enveloped by connective tissue and significant changes in the bone were not observed.

connective tissue. Growth of bone from the mandible into the implant was not observed. Occasionally (in fewer than 10% of the sections examined), HA particles partially penetrated the bone (Fig 3). On the stimulated side, the characteristic observation was that of significant migration of HA particles into the mandible (Fig 4). The remaining region of the HA implant was filled with connective tissue indistinguishable from that on the control side.

The results are summarized in Table 1. For each implant, HA was listed as being in the mandible only if it occurred in the bone along 50% or more of the length of at least two of the sections analyzed. Hydroxyapatite was routinely found in the mandible on the stimulated side, but not on the control side. Passage of HA into the bone bore no constant relationship to position of the HA particles in the implant; in two cases. HA was observed in bone in the section taken through the diameter of the implant, but in the other two cases it occurred at other places in the implant. Similarly, HA migration was not related to the location of the electrode.

Because it was not possible to determine whether the electrical treatment actually initiated the movement of HA into bone or merely potentiated an ongoing process, a second group of six rabbits was implanted bilaterally and killed 26 weeks postoperatively. None of these implants were electrically stimulated. Three implants were lost (two because the HA particles became disseminated, one because of infection). In each of the remaining nine cases, significant migration of HA into the mandible was observed; a typical result is shown in Fig 5. In four instances HA particles migrated through the mandible, and were found in the adjacent soft tissue. Approximately 20% of the mandibular area under the implant contained HA particles that projected from the inner surface.

Discussion

Electrical stimulation of the type used (20 μA, negative polarity) has previously been shown to elicit osteogenesis in rabbits that had undergone a mandibular slot osteotomy.[10] Based on this observation, and on an analysis of the pertinent literature, a model of electrically stimulated osteogenesis was proposed in which the stimulus results in an acute inflammatory response having one or more components that are mitogenic for osteoprogenitor cells.[9] The osteoprogenitor cells then proliferate, differentiate, and form the osteoblasts responsible for the stimulated growth.

In our study, the initial hypothesis was that the osteoblasts recruited by the electrical treatment would form bone around the HA particles, thereby effectively increasing mandible thickness. We observed the opposite result. When evaluated 8 weeks after surgery, HA was found in the mandible occupying regions previously occupied by the mandibular bone. Because observations were not made prior to 8 weeks postoperatively, one can only speculate regarding the mechanism by which the HA entered the bone. The range of electrical current that produces osteogenesis is relatively narrow and model dependent.[9] Osteonecrosis rather than osteogenesis occurs if the current is too high. Perhaps the current employed in this study was too high for the uninjured mandible, and resulted in bone necrosis during the first postoperative week. During the subsequent 7 weeks (between cessation of electrical stimulation and sacrifice), resorption of the dead bone

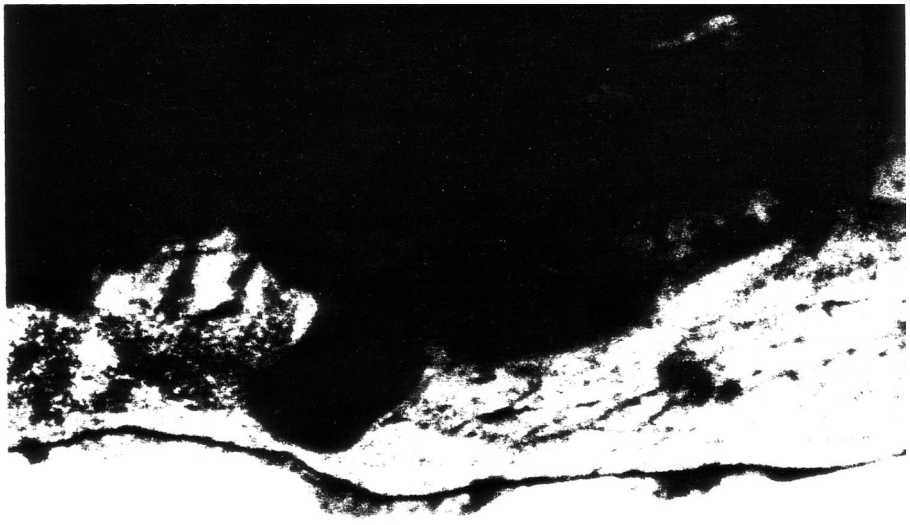

FIGURE 3. An HA particle in the mandible on the unstimulated side after 8 weeks. The view corresponds to that depicted in the insert in Figure 1 (the mandible at the bottom, in cross-section).

FIGURE 4. Characteristic tissue reaction to HA implant and electrical stimulation after 8 weeks. The view corresponds to that depicted in the insert in Figure1 (the mandible it the bottom, in cross-section). The mandibular outline is altered and HA particles in the bone can he seen.

and elaboration of new matrix permitted migration of HA particles into the regenerating area as a result of pressure from the overlying masseter muscle on the HA.

Accelerated remodeling is an alternative possibility and it is supported by observations made on the unstimulated side, where migration of HA into the bone apparently occurred even in the absence of electrical stimulation (Fig 3). This observation prompted the second experiment in which no electricity was applied, and the rabbits were killed 26 weeks postoperatively. In this instance, the presence of HA particles was routinely observed in the mandible; in four cases, the particles passed through the mandible into the underlying tissues. It seems likely, therefore, that the electrical stimulation potentiated. but did not initiate, HA particle migration through the mandible.

One of the salient characteristics of the HA particle migration was its focal nature; it occurred in a localized region of the implant (averaging about 20% of the available surface area). This pattern is consistent with a mechanism involving the application of force at a particular point on the surface of the implant. Particles can shift their relative position, thereby minimizing the lateral spread of the load. At whatever point the force is applied to the implant by the muscle, that force is transmitted to the hone via the column of HA particles directly underlying the point of application of the force.

Table 1. Movement of HA Particles in Electrically Stimulated and Unstimulated HA Implants on Rabbit Mandibles

	8 Weeks (n = 6)		26 Weeks (n = 6)
Observation	E	C	C
HA in bone (anywhere)	4/5	0/5	9/9
HA in bone (center)	2/5	0/5	5/9
HA through bone	0	0	4/9
Percent surface area of HA through bone	0	0	20 ± 10%

Abbreviations: C. controls: E. electrically stimulated group.

The question arises as to why HA migration into hone as not observed in previous animal or clinical studies. Chang et al implanted HA along the lower inner border of the mandible in dogs[11] and at 3 to 9 months some of the HA particles were attached to the hone, but their presence in the bone was not reported. Block and Kent performed a radical alveolectomy in dogs, and reconstructed the alveolar ridge using HA.[12] Sixteen weeks postoperatively, some bony ingrowth into the HA was observed (particularly in implants that were augmented with autogenous hone), but the occurrence of HA in the original hone was not described. In both studies, the HA implant was apparently not subjected to continuous or intermittent compressive forces (the HA vas not covered with muscle, and the implant site was not subjected to forces associated with mastication). The involvement of the mandibular hone that we observed 26 weeks postoperatively may have resulted from the continuous pressure by the masseter muscle, as transmitted by the implant to the mandible. An apparently similar remodeling phenomenon occurs when the mandible is subjected to compressive forces by a silicone rubber chin implant.

Block and Kent found that HA-augmented alveolar ridges exhibited negligible loss in height 1 to 4 years postoperatively.[5] This may indicate that the phenomenon described here does not occur in patients when HA is used to augment atrophic mandibular ridges. Perhaps HA particle migration occurs only when the implant is subjected continuously to pressure, such as when it is implanted under muscle. Alternatively, after longer follow-up, patients with augmented atrophic ridges may eventually show a phenomenon similar to that described here.

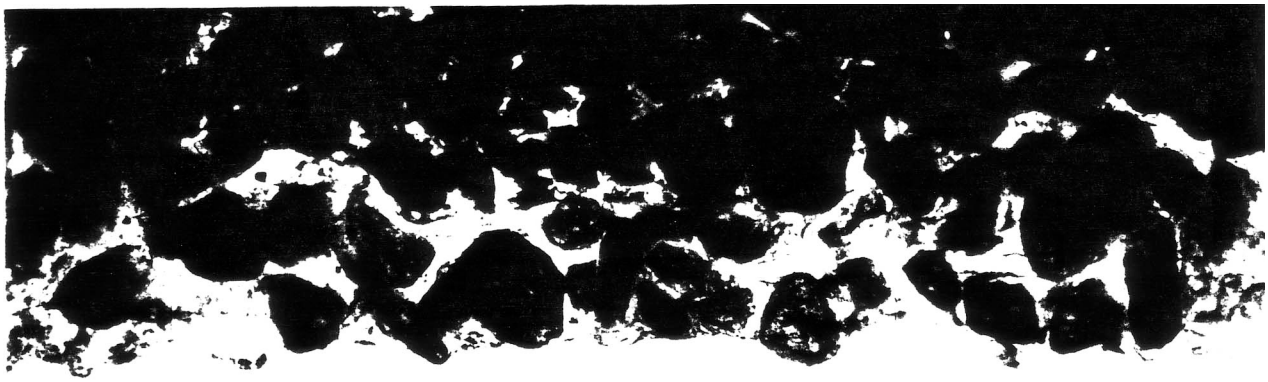

FIGURE 5. Characteristic tissue reaction to HA implant after 26 weeks. The view corresponds to that depicted in the insert in Figure 1 (the mandible at the bottom, in cross-section). Penetration of numerous HA particles into the mandible is seen.

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