CORALLINE HYDROXYAPATITE KERATOPROSTHESIS

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Abstract

The ideal prosthesis will let the tissue grow in to the supporting material and have a similar curvature as the recipient cornea. We developed a new support for a keratoprosthesis (KPro) made of porous hydroxyapatite (HA), which is highly biocompatible, biointegrable, nonbiodegradable and colonizable. It was implanted unilaterally in eyes of twelve New Zeland rabbits, intralamellarly and between an homologous episclerokeratoplasty (with and without conjunctival flap) for twelve months. Various pathology studies and Technetium-99 bone scans have revealed good vascularization, no signs of infection or extrusion, no epithelial downgrowth and no adverse tissue reaction. This type of HAKPro has been accepted by rabbit corneas for twelve months, and a clinical trial on selected patients is justified in the near future.

Key words: Keratoprosthesis, hydroxyapatite, corals, episclerokeratoplasty.

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Introduction

The concept of KPro in the treatment of corneal blindness was suggested by Pallier de Quengsy in 1789-90. Since that time, several designs have been developed using many kinds of materials. The first and well established biological haptic for KPro made of living human tissue was Strampelli's second technique of osteoodonto fixtion, in use since 1964. Failures of most KPro is due to the lack of biological and mechanical integration, leading to many postoperative complications

and short lasting implant retention. The most common complications are melting of tissue around the optical core, with leakage and extrusion of the implant, and formation of retroprosthetic membranes. In order to prevent those complications, we present a support material that is well incorporated into the tissue, obliterating the interface between tissue and KPro.

Coralline HA porous ceramic (transformed by an hydrothermal exchange reaction), has been under investigation as an alloplastic bone substitute since 1975. HA is a calcium phosphate based compound that has been used as bone replacement material for maxillofacial inlay grafting, alveolar ridge augmentation, cranial reconstruction over bare dura, middle ear reconstruction, laryngeal framework support, and as an ocular implant to improve motility following enucleation and evisceration. It is highly biocompatible, causes minimal tissue inflamation, is not reabsorbed and allows rapid host tissue ingrowth, resulting in a close approximation to normal human bone.

Materials and Methods

Stage 1:

We obtained two different kinds of coral of the genus Porites from the Caribean Colombian Coast: Porites Porites (PP) (fig. 1) with pores ranging between 80 and 200 microns in diameter, all interconnected in a trabecular pattern, and Porites Astreoides (PA) (Fig.2), also with a regular system of interconnecting pores of aproximately 120 microns, both resembling the haversian system of normal lamellar bone. In our laboratory, the coral skeletal carbonate was transformed into HA by an hydrothermal exchange reaction. The porous HA was then shaped to obtain this new support for the KPro. Curvature radiuses similar to those of the normal cornea were used. In the first

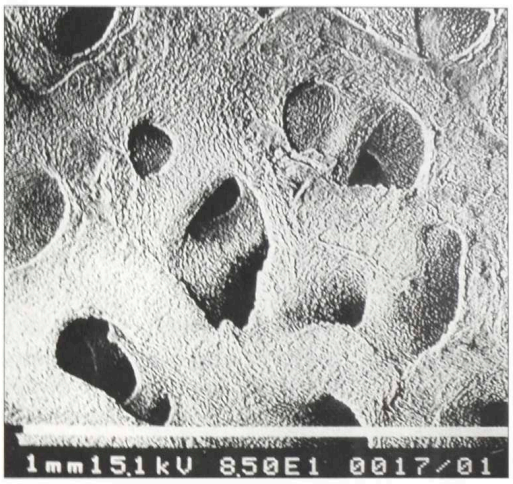

Fig. 1 Electron Microscopy of Porites Porites coral showing pores ranging from approximately 80 to 120 microns in diameter, interconected in a trabecular pattern.

Fig. 2 Electron Microscopy of Porites Astreoides coral showing a regular system of interconecting pores approximately 120 microns in diameter.

model, both curvature radiuses were 7 mm, where as in the second model, the internal radius was 8 mm. and the external radius 7 mm, in order to minimize border thickness. The diameter used was 10 mm, with a 1 to 1.5 mm. thickness and a 3 mm. central opening in to which the optical cylinder was fitted and fixed with a cement (Glass-Ionomer) that did not affect the vitality of HA (Fig.3). The 15 diopter optical cylinder was made of polymethylmethacrylate (Perspex CQ).

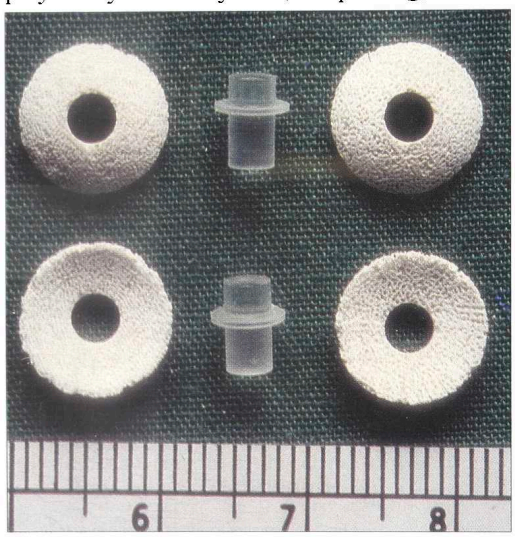

Fig. 3 Coralline hydroxyapatite haptic showing the smoothness in both faces and methacrylate optical cylinder

Stage II:

The KPro were implanted unilaterally in the right eye of 12 New Zeland rabbits. These rabbits were grouped into three different sets. Each group of four rabbits underwent a different surgical technique and in each group the two kinds of corals (P. Porites and P. Astreoides) were used. The first group received an intralamellar KPro (1*) (Fig.4), (only the haptic was implanted in two rabbits). The same technique was performed on the second

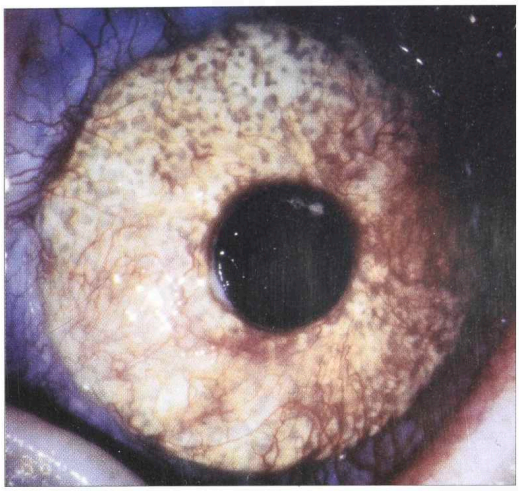

Fig. 4 Hydroxyapatite haptic and optical cylinder in a rabbit 9 months post-op, showing vessels growing through the pores.

group (2*) although supplemented with a sliding conjunctival flap; the last group(3*) underwent an episclerokeratoplasty (Fig. 5) in which the KPro was implanted in between

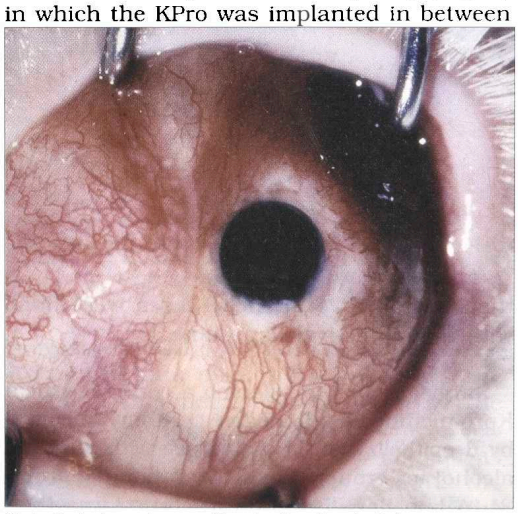

Fig. 5 A keratoprosthesis implanted between an episclerokeratoplasty and the cornea; 12 months after surgery.

Table 1

RABBIT	KPro	CORAL TYPE	PATHOLOGY	T-99 BONE SCAN	MONTHS
1 I.L.1	HAPTIC	PP	9 months		9
1 I.L.2	HAPTIC	PP			13
1 I.L.3	HAKPro	PP			12
1 I.L.4	HAKPro	PA	2 months		2
2I.L.+C.F.1	HAKPro	PP			11.5
2I.L.+C.F.2	HAKPro	PP	7 months		7
2I.L.+C.F.3	HAKPro	PA		9 months	12
2I.L.+C.F.4	HAKPro	PA			13
3 E.1	HAKPro	PP			12
3 E.2	HAKPro	PA		7months	12
3 E.+C.F.3	HAKPro	PP		5 months	12
3 E.+C.F.4	HAKPro	PA	5 months		5

I.L: Intralamellar. C. F.: Conjunctival Flap. E: Episclerokeratoplasty. HAKPro: Hydroxyapatite Coralline Keratoprosthesis.

the corneas; two of these cases were done with a conjunctival flap (table 1).

Surgical steps for placing a central corneal Kpro included a 360 degree peritomy, followed by deepithelization of the cornea with absolute alcohol for group 2* and two rabbits of group 3*. A lamellar dissection of cornea was then performed including 1 mm of sclera for 1* and 2*.

Superior and inferior rectii muscles were exposed over a 10 to 14 mm. lenght by blunt dissection leaving the sheath undisturbed. A fragment, one third the thickness of the muscle, was then split with scissors and sectioned 10 mm away from its insertion; the distral portion was tied with fine catgut and the proximal portion was freed from all adhesions. The flaps were inverted by swinging them over onto the cornea in order to promote

rapid vascularization. A 3 millimeter threphine opening into the center of the cornea was performed, followed by anterior vitrectomy, lens aspiration and sectorial iridectomy.

The posterior flange of the KPro was slipped through the trephine opening, and on top of the two inverted flap muscles previously tied together.

A 3 millimeter trephine opening into the anterior lamellar cornea was performed for 1* and 2*, and into the donor cornea for 3*. The cornea was placed on the KPro and sutured with twelve peripheral stiches using 10-0 nylon; the conjunctiva was sutured with 7-0 vycril.

We implanted the optical cylinder in all but two rabbits of the first group. The optical cylinder was left exposed in one rabbit of each group receiving the conjunctival flap at the time of surgery, and in the remaining rabbits it was exposed on the twentieth postoperative day. Daily prophilactic antibiotics, analgesics and artificial tears were used in all cases. Pathology studies were performed at 2, 5, 7 and 9 months (Fig. 6) and technetium-99 bone scans (Fig.7) at 5, 7 and 9 months.

Results

The three groups were analized at intervals of ten to twenty days up to twelve months. Each group was observed for vascularization of the support (pathology and technetium-99 bone scans), tissue response to the two different types of corals and a variety of complications associated with the KPro.

All rabbits showed adequate vascular response. As shown in Table 1, some rabbits were euthanized and their eyes were sent to hystopathologycal study (Fig. 6); revealing

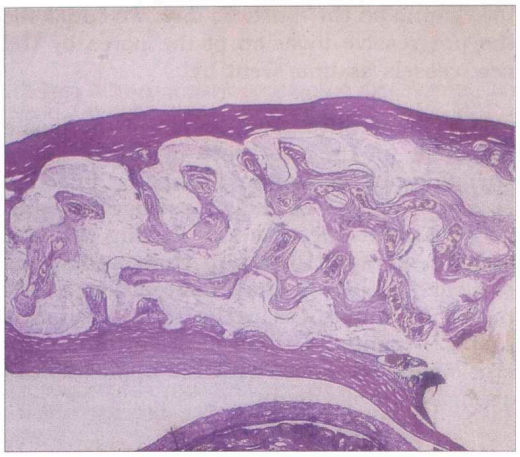

Fig. 6 Pathology sample at 2 months; the study revealed a hydroxyapatite layer interposed between layers of corneal stroma. hydroxyapatite spaces appear filled with fibrovascular tissue throughout. (Process by Prof. Richard Green)

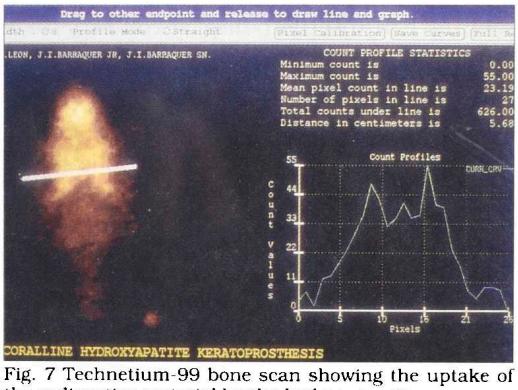

Fig. 7 Technetium-99 bone scan showing the uptake of the radioactive material by the hydroxyapatite.

fibrovascular tissue ingrowth in all the pores. The technetium-99 bone scan shows the uptake of the radioactive material by the hydroxyapatite (Fig. 7). Growth of new vessels was seen inside the pores of the implant as of the tenth postoperative day, around the periphery at first. These advanced towards the mid periphery around the twentieth day and were finally seen to enclose the total area of

the haptic on the fourtieth day. We could see the progressive invasion of the pores by the new vessels as time went by.

The comparative visualization of the tissue response to the two types of corals shows adequate vascularization, no signs of infection or extrusion, no epithelial downgrowth and no adverse tissue reaction. During the first months, all rabbits in group 1* showed a good corneal response, except for one of them which had a PP implant. On the tenth day, this rabbit presented a small paracentral corneal erosion that resolved with the application of artificial viscous tears.

At nine months, all rabbits in group 1* presented a small inferotemporal melting or erosion area of 0.5 mm. which required a sectoral conjunctival flap. Two of the rabbits in group 2* and one in group 3* received a sliding conjunctival flap secondary to a superficial traumatic erosion, between the 4 and 6 months.

We also encountered some complications common to all KPro: In group 1*, one rabbit with a PA implant presented a superior half moon shaped corneal melting or erosion secondary to an excess protrusion of the optical cylinder which undermined the normal humidity on the edge of the implant's opening. In three other rabbits from groups 2* (PP-PA) and 3* (PP) there was a conjunctival growth over the optical cylinder caused by a lack of protrusion of this optical part. We observed similar vascularization between the two kinds of corals (PP and PA) used.

Discussion and Conclusion

As the years go by, ophtalmic surgeons encounter great difficulty in finding an adequate support for the KPro. The ideal support should be well tolerated by the receptor tissues. This material must be higly biocompatible, cause minimal tissue swelling, must not be reabsorbed and must allow rapid host tissue ingrowth. All of these requeriments are met by the well known HA. Although the study was performed with a view at observing vascular response to the porous HA haptic, we had to standarize the surgical technique in order to minimize other keratoprosthetic complications. We noticed a good vascularization in all KPro supports, and a good tolerance by the rabbit corneas. We did not find any significant difference between the two kinds of corals (PP and PA).

Pathological analysis revealed fibrovascular tissue ingrowth in all samples, and at two months, one rabbit showed some osteoblasts lining the hydroxyapatite material. It would be interesting to know the origin of these cells. In three rabitts we performed a technetium-99 bone scan as a kind of analysis that allows us to see the rate of vascularization.

In terms of biological function we obtained a biocompatible KPro, a biointegrable, nonbiodegradable and colonizable haptic; in terms of mechanical function we encountered good alignment with the macula and reliable fixation of the optical part.

We conclude that this type of HAKPro has been accepted by rabbit corneas for twelve months, and a clinical trial on selected patients could be justified in the near future.

The next step in the research is to increase the diameter of the optical part, and to find other kinds of corals for use in different parts of the world.

In humans, we recommend using either periosteum, fascia lata or sclera with conjunctival flap, or oral mucosa to cover the

haptic. Surgery should be done in one step, and the power of the optical cylinder should be increased. We recommend technetium-99 bone scan as the method of choice for determining vascularization.

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