Clinical Evaluation of a Bilayered Collagen Membrane (Bio-Gide) Supported by Autografts in the Treatment of Bone Defects Around Implants

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The aim of this study was to determine the efficacy of a bioresorbable collagen membrane (Bio-Gide) in combination with autogenous bone grafts in the treatment of peri-implant dehiscences, fenestrations, or limited vertical defects. Eighteen titanium dental implants with exposed threads placed in 17 patients were studied. Autogenous bone was used in all cases to fill the defect and maintain the space underneath the barrier. The collagen membrane was trimmed and adapted to cover the defect in a saddle configuration. The membrane absorbed the blood and easily covered and adhered to the underlying bone. It was not stabilized by any retentive means. Sixteen to 32 months postoperatively, the sites were reentered and the amount of bone regenerated was measured. The results showed significant bone gain (average 87.6%) in the treatment of peri-implant defects with Bio-Gide and autogenous bone. (INT J ORAL MAXILLOFAC IMPLANTS 2001;16:857–863)

Key words: *autologous transplantation, bioresorbable membrane, guided bone regeneration, peri-implant defect*

A sufficient quantity of bone is an essential prerequisite for the long-term success of implant therapy. The placement of endosseous implants in sites where the bone volume is equal to or less than the size of the implant results in part of the implant surface not being covered by bone, with possible peri-implant soft tissue irritation, decreased bone-implant contact surface, and potential implant failure.[1–5]

The need for bone regeneration in cases of limited dehiscences or fenestrations with machined-surface implants has been questioned. A 5-year follow-up on implants with exposed threads at the time of placement did not show any soft tissue irritation or further bone loss when oral hygiene measures were carefully applied.[6]

Large bony defects may appear when implants are placed in areas of deficient bone volume at the predetermined implant site. Sizeable reductions in the bone-implant contact area and large peri-implant defects may be a more specific indication for bone regeneration. However, there are no references in the literature known to the authors concerning defect size as a definitive indication for guided bone regeneration (GBR) nor any indications for such a treatment when surfaces other than machined, commercially pure titanium are used.[6]

Guided bone regeneration has been successfully applied to treat peri-implant bone defects[3,7,8] and to augment the height and the width of atrophic alveolar ridges prior to implant placement.[3,7–9] Dehiscences, fenestrations, peri-implant intrabony defects, or vertical augmentation concomitant to implant placement have been successfully managed with autogenous bone or bone substitutes as spacers and nonresorbable or resorbable barriers.[10] The barrier prevents invasion of the defect by surrounding soft tissue, offers protection and stabilization to the blood clot as well as the filling material, and gives the bone cells sufficient time to proliferate and regenerate bone.[3,11,12]

Nonresorbable expanded polytetrafluoroethylene (e-PTFE) membranes (Gore-Tex, W. L. Gore and Associates, Flagstaff, AZ) have been used successfully since the 1980s. However, this material has 3 definite disadvantages. First, postoperative membrane exposure can occur and compromise the

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regenerative process.[3] Second, an extensive second operation is often necessary for removal of the membrane. Finally, when the membrane is removed after 6 months, newly formed bone can react to exposure by resorption.[13] To avoid the inherent disadvantages of nonresorbable membranes, resorbable barriers have been introduced in GBR. For bone regeneration to occur, the following requisites[14] should be satisfied: bioresorbability, absence of foreign body reaction, no residues after degradation that may interact with bone regeneration, and efficient barrier function for 5 to 6 months.[15]

Bio-Gide (Geistlich Biomaterials, Wolhusen, Switzerland) is a bioresorbable collagen barrier made of fiber protein, which consists of hydroxyproline with the structure of a triple helix. Collagen fibers provide structural elasticity during the crystalline phase of bone regeneration. The properties of collagen ensure optimal tissue integration and adequate wound healing.[16] The 2 disadvantages of this material are insufficient space-making ability and the possibility of antigenic reaction.[17] The problem of space creation can be solved by using bone or bone substitutes, while the development of antigenicity can be prevented by establishing excellent quality control during fabrication. The degradation rate of Bio-Gide has been tested in experimental models and varies from a few days to several weeks.[18,19] The Bio-Gide collagen membrane is simple to apply and rapidly conforms to the underlying tissues.[16] For bone regeneration to occur, membranes must be stabilized by pins or tacks to prevent any micromovement that may compromise the regenerative process.[9]

The aim of the present study was to evaluate the efficacy of a collagen membrane (Bio-Gide), used in conjunction with autogenous bone grafts, for the treatment of peri-implant dehiscences, fenestrations, or limited vertical defects. Such defects were recognized at phase I surgery and resulted from implant placement at sites with insufficient bone volume; Bio-Gide membranes were placed without stabilization other than the inherent properties of collagen to adhere to the underlying tissues when adequately adapted to the defect.

MATERIALS AND METHODS

A total of 17 patients (10 females and 7 males, mean age 47 years, range 24 to 85 years) were included in this study. Preoperative examination consisted of periapical radiographs, a panoramic radiograph, and a clinical examination to evaluate bone volume at the proposed implant sites. No computed tomography as a diagnostic tool was used in the present series. None of the patients in the present series were smokers. All implants were screw-type with a machined surface (Nobel Biocare, Göteborg, Sweden) and were placed in a 2-stage procedure. The patients were informed of the necessity for a second surgery to evaluate the bone gain obtained after the regenerative therapy, to perform any soft tissue procedures needed to enhance esthetics, and to connect the abutment.

The types of defects found are reported in Table 1 and were classified as dehiscences, fenestrations, or intrabony defects. The number of implant sites exposed was recorded (buccal/labial, mesial, distal), along with the number of walls involved (1, 2, 3, or circumferential defect) in the case of intrabony defects.

Eight implants were placed in the maxilla and 10 in the mandible. After the implants were placed, during phase I surgery, a number of threads were found exposed. Twelve defects were dehiscences involving 3 sides (mesial, buccal/labial, and distal) of the implant. One defect was a fenestration, one was a combination of intrabony defect and dehiscence on the buccal, and 2 were wide circumferential intrabony defects that appeared following immediate implantation.

The height and width of the defects were measured with a periodontal probe (PCP-UNC15, Hu-Friedy, Chicago, IL). The shoulder of the implant was used as a reference for height, and the bony edge of the defects at 2 distinct levels was used for the width both at the platform of the implants and at mid-distance between the top and the bottom of the defect, in cases of a V-shape type defect. The mean values for the width recorded at phase I surgery and at reentry are reported in Table 1. All measurements were made by one calibrated operator.

Autogenous bone was used in all cases to fill the defect and maintain the space underneath the barrier, since the membrane has no inherent rigidity and collapses over the defect when pressed, leaving no room for the regenerating tissues. Cortical bone from adjacent sites was shaved with a rongeur. No bone from the prepared osteotomies was used for grafting. Small particles of dense cortical bone were thus harvested and gently packed over the defect (Figs 1 and 2). No cortical penetration at the site of the defect was done. The collagen barrier (Bio-Gide) was trimmed and adapted to cover the defect and extended 2 to 3 mm sideways, being laid over the implant in a saddle configuration (Fig 3). It was tucked underneath the palatal or lingual flap to cover the ridge and buccal defect, moistened, and pressed gently in place with gauze to adapt to the

Table 1 Clinical Data for Pre- and Postoperative Defects

Patient	Age	Sex	Implant Location	Implant length × diameter (mm)	Type of defect	Initial value (mm)		Second value (mm)		Defect fill (mm)		Time of second operation (wk)	Percent bone regeneration	Clinical healing
						Height	Mean width	Height	Mean width	Height	Mean width			
1	45	F	42	15 x 3.75	DhB	5.0	4.0	2.0	4.0	3.0	0.0	24.0	60	Exposed
			32	15 x 3.75	DhB	5.0	4.0	2.0	4.0	3.0	0.0	24.0	60	membrane
2	31	F	21	15 x 3.75	DhBMD	4.0	4.0	0.0	0.0	4.0	4.0	24.0	100	Uneventful
3	49	M	47	8.5 x 3.75	DhB	3.0	2.0	2.0	2.0	1.0	0.0	24.0	33.3	Uneventful
4	35	M	22	15 x 3.3	W3	8.0	4.0	3.0	4.0	5.0	0.0	28.0	62.5	Uneventful
5	36	M	44	15 x 3.75	DhB	5.0	2.0	0.0	0.0	5.0	2.0	20.0	100	Uneventful
6	85	F	32	15 x 3.75	DhB	5.0	3.0	0.0	0.0	5.0	3.0	16.0	100	Uneventful
7	51	M	34	15 x 3.75	DhB	5.0	1.0	0.0	0.0	5.0	1.0	18.0	100	Uneventful
8	59	M	25	12 x 5	W3	5.0	4.0	0.0	0.0	5.0	4.0	28.0	100	Uneventful
9	42	F	45	11.5 x 5	DhB	3.0	3.0	0.0	0.0	3.0	3.0	24.0	100	Uneventful
10	69	M	33	15 x 3.75	DhB	8.0	4.0	0.0	0.0	8.0	4.0	16.0	100	Uneventful
11	45	F	23	15 x 3.75	DhB	7.0	2.0	0.0	0.0	7.0	2.0	30.0	100	Uneventful
12	28	F	11	15 x 5 (WP)	FBM	10.0	4.0	0.0	0.0	10.0	4.0	28.0	100	Uneventful
13	24	F	22	13 x 3.75	DhBMD	3.0	4.0	0.0	0.0	3.0	4.0	24.0	100	Uneventful
14	64	F	43	15 x 3.75	DhB	5.0	3.0	2.0	3.0	3.0	0.0	18.0	60	Exposed membrane
15	55	M	32	15 x 3.3	DhB	5.0	1.5	0.0	0.0	5.0	1.5	18.0	100	Uneventful
16	48	F	21	15 x 3.75	DhB	3.0	4.0	0.0	0.0	3.0	4.0	18.0	100	Uneventful
17	33	F	23	18 x 3.75	W1	6.0	2.5	0.0	0.0	6.0	2.5	32.0	100	Uneventful
Mean	47					5.28	3.11	0.61	0.94	4.67	2.17	23.0	87.5	
SD						1.93	1.04	1.04	1.63	2.14	1.66		21.5	

Dh = dehiscence; B = buccal; M = mesial; D = distal; F = fenestration; W1 = intrabony defect—1 wall; W3 = intrabony defect—3 walls; Second value = value at second operation; SD = standard deviation.
For difference in means between pre- and postoperative height values: $t = 9.24$; df = 17; $P = 4.85 \times 10^{-8}$.
For difference in means between pre- and postoperative width values: $t = 5.53$; df = 17; $P = 3.68 \times 10^{-5}$.
Width value represents the mean of the 2 measurements made.
Implant locations (International System): 11 = maxillary right central incisor; 21 = maxillary left central incisor; 22 = maxillary left lateral incisor; 23 = maxillary left canine; 25 = maxillary left second premolar; 32 = mandibular left lateral incisor; 33 = mandibular left canine; 34 = mandibular left first premolar; 42 = mandibular right lateral incisor; 43 = mandibular right canine; 44 = mandibular right first premolar; 45 = mandibular right second premolar; 47 = mandibular right second molar.

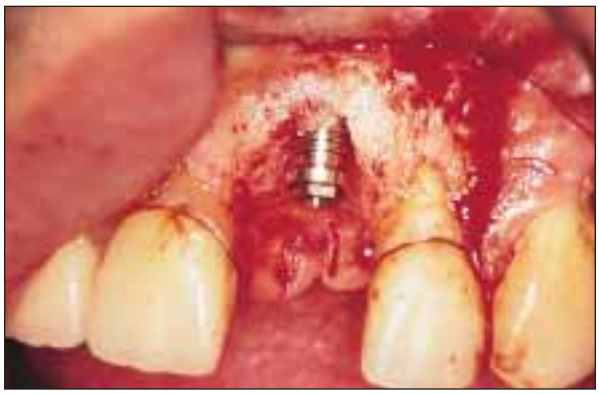

Fig 1 Implant placed to replace the maxillary left central incisor. The dehiscence measured 4 mm on the labial side. A 1-wall vertical defect was present on the mesial and distal sides.

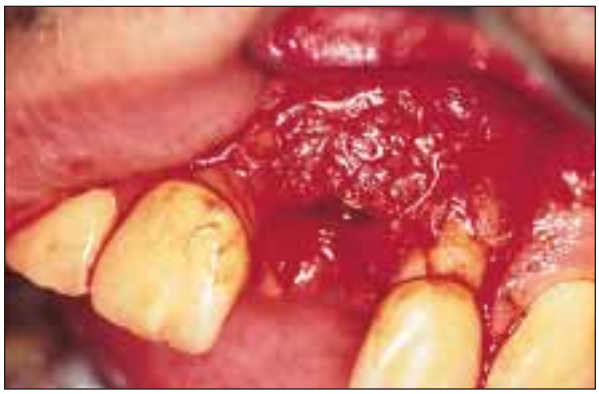

Fig 2 Autogenous bone was gently packed into defect.

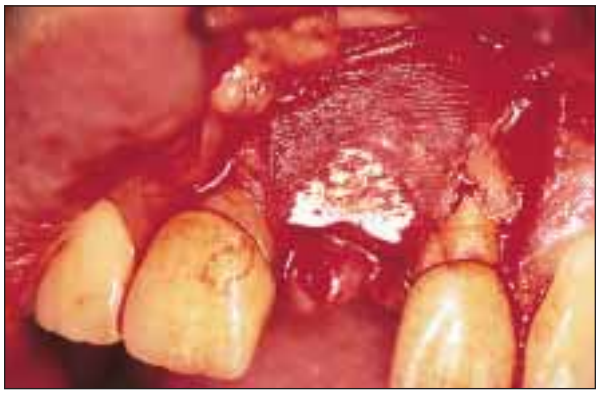

Fig 3 The membrane was placed in a saddle configuration, covering the defect.

underlying bone. The membrane absorbed the blood and easily covered and adhered to the underlying bone. It was not stabilized by any direct retentive means. The flaps were then readapted to cover the membrane and sutured without tension. In cases where the flaps remained tense during suturing, a periosteal releasing incision was made to ease handling of a tension-free flap. Nonresorbable 5.0 nylon sutures were used for suturing. Gentle compression over the defect was applied for 2 minutes, after which the patient was released.

Postoperative care consisted of a 5-day course of antibiotics (amoxicillin 500 mg 3 times daily) and rinsing twice a day with a 0.12% chlorhexidine solution (Oroclense, Germiphen, Brantford, Ontario, Canada) for 2 weeks postoperatively. Sutures were removed 10 days after surgery. One patient was completely edentulous and was asked not to wear her prosthesis for the first 4 postoperative weeks. She was put on a liquid diet. After that, her denture was relined with a resilient liner (Coe Comfort, GC America, Alsip, IL) and was used only for esthetic purposes and eating of soft food. Checkups were done at a biweekly interval for the first month and then bimonthly until the time of abutment connection.

Approximately 6 months postoperatively, the sites were reentered through a crestal incision, with vertical incisions avoided to limit the undesirable exposure of bone and potential soft tissue recession. The amount of regenerated hone was measured using the same periodontal probe and the measurements were compared to the initial values.

Statistical analysis was done to evaluate the difference between the initial and the final values using the Student *t* test for paired samples.

RESULTS

The initial values and the data collected at abutment connection are reported in Table 1. Sixteen remaining sites healed without complications, and 2 membranes were exposed. In 1 patient, the membrane became exposed after 2 weeks. Mouth rinsing was continued for the following 3 weeks. The cover screw appeared and the gingiva healed around it with no visible signs of inflammation and no trace of the membrane clinically. The healing continued uneventfully until the sixth postoperative month. In the second patient, a flap dehiscence occurred 2 weeks postoperatively. Tentative resuturing of the flaps was successful. The membrane was not removed, and rather good closure of the soft tissue

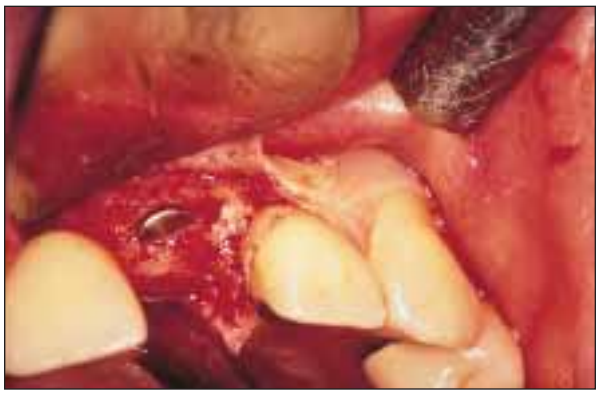

Fig 4 Healing at 6 months. The defect is filled with bone that has regenerated; bone has also regenerated over the cover screw.

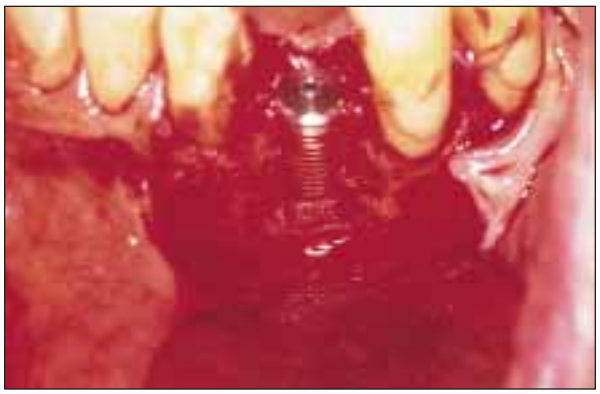

Fig 5 A 9-mm labial dehiscence on the implant placed in the mandibular left canine site.

occurred, with no signs of inflammation. Four months later, a limited 1- to 2-mm fenestration of the cover screw on 1 of the patient's implants was present, without clinical evidence of inflammation.

Two sites showed thin buccal osseous healing, while the newly formed tissue at all other sites showed bony consistency clinically similar to the local adjacent sound bone. Timing of the second operation varied between 16 and 32 weeks after membrane placement (mean value 23 weeks). The height of the initial defects varied between 3 and 10 mm (5.28 ± 1.93 mm). The height of the residual defect varied between 0 and 3 mm, with a mean value of 0.61 ± 1.04 mm. The vertical gain in bone varied between 1 and 10 mm, with a mean value of 4.67 ± 2.14 mm. The difference between the pre- and postoperative values was statistically significant ($P < .001$). At the time of implant placement, the width of the defect varied between 1 and 4 mm, with a mean value of 3.11 ± 1.04 mm. At the time of abutment connection, the width varied between 0 and 4 mm, with a mean value of 0.94 ± 1.63 mm. The gain in new bone mesiodistally varied between 0 and 4 mm, with a mean value of 2.17 ± 1.66 mm, and was statistically significant ($P < .001$).

The overall percentage of bone regeneration varied between 33.3% and 100%; 13 of the 18 defects showed 100% regeneration (Figs 4 to 6). Significant bone gain (average gain 87.5%) was achieved after 16 to 32 weeks.

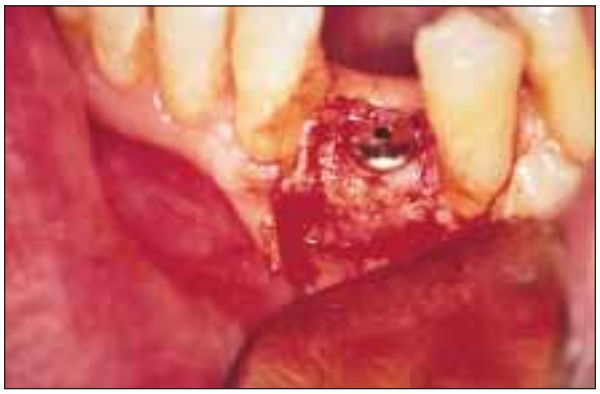

Fig 6 Reentry at 4 months showing bone regeneration.

DISCUSSION

The purpose of this clinical study in humans was to evaluate the efficacy of a resorbable membrane (Bio-Gide) associated with autogenous bone chips in promoting bone regeneration around peri-implant bony defects. The overall results of the regenerative treatment of the 18 defects showed significant new bone formation, with a mean reduction in defect height and width of 87.5%. This is in accordance with other clinical studies that demonstrated similar percentages of bone fill. Simion and coworkers[20] obtained 93.38% gain in the treatment of implant dehiscences and fenestrations using polylactic acid/polyglycolic acid membranes in association with autogenous bone chips as a space-maker and stabilized with fixation screws or nails. Zitzmann and associates[21] found collagen membranes very effective in the treatment of peri-implant defects in comparison to e-PTFE. In that study, the membranes were stabilized with pins, and Bio-Oss (natural bone mineral substitute, Geistlich Biomaterials)

served as a spacer. A mean bone gain of 92% for Bio-Gide and 78% for e-PTFE was obtained. In other studies,[3,10,22] the overall reduction of peri-implant defects using e-PTFE membranes ranged between 82% and 93.6%. However, when no barriers were applied over the defects, an average of 3.5% of the exposed implant surface was covered with bone, whereas 75% of the implant defect regenerated when e-PTFE membranes were used.[5]

The collagen membrane itself cannot contain a cavity because it lacks the necessary stiffness to maintain enough space under the membrane to fill the defect. It is therefore desirable to use a grafting material when applying resorbable membranes.[23] Autogenous bone is the ideal material for use in regenerative therapy.[24] It is generally available adjacent to the implant site.[25] It is believed to exhibit both osteoconductive and osteoinductive properties[24,26] and can maintain adequate space under the membrane for a sufficient period of time for hard tissue regeneration and to integrate with the preexisting bone.[26]

Bone substitutes have been used extensively as spacers under membranes.[27–29] However, in this study, autogenous bone was used exclusively for this purpose because it was readily available in the quantity needed to treat the defects. It can always be collected from adjacent sites, or if needed, from a remote site in the oral cavity or from the prepared implant site to meet the specific treatment needs.

Degradation of the Bio-Gide barrier occurred without clinical signs of inflammation, even where wound dehiscence occurred postoperatively. The mean average percentage of bone fill is influenced by membrane exposure and averaged 60% in the 2 exposed sites in this series. It should be noted that membrane degradation occurs faster in case of incomplete wound closure.[30]

When soft tissue dehiscence occurs, Lorenzoni and colleagues[30] found that a self-reinforced polyglycolic acid membrane (Biofix, Biocon, Tampere, Finland) was progressively resorbed, with consequent spontaneous healing of the soft tissues in 3 to 6 weeks. The absence of soft tissue coverage caused significant reduction in the quantity of bone regeneration (45% vs 75% for unexposed membranes).

Removal of a resorbable barrier is not necessary in case of wound dehiscence, while exposure of an e-PTFE membrane, which occurs in 16% to 41% of sites,[3,22,26] requires its removal before 6 weeks because of contamination and potential damage to the underlying newly formed tissues.

Using Bio-Gide membranes, Zitzmann and associates[21] obtained an average bone fill of 94% for sites with uncomplicated wound healing and 87% for sites with incomplete wound closure after 6 weeks. With e-PTFE membranes, the average bone fill was 98% for sites with uncomplicated wound healing and 65% for sites where membrane exposure required their early retrieval.

The usefulness of bioresorbable pins to stabilize a collagen membrane may be questioned. It has been stated that absolute stability of the membrane is fundamental to the whole concept of GBR and a vital prerequisite for therapeutic success, and that the tiniest movement on the granulating tissue underneath the membrane is to be avoided.[9] In the present study, it was possible to obtain stability of the collagen membrane without additional fixation because of the inherent properties of collagen to adhere and conform to underlying tissues when gentle pressure is applied to it. However, it was not possible under the present conditions to verify whether micromovements had any deleterious effects on the percentage of regenerated bone-to-implant contact. The clinical results confirm that when handled cautiously, the soft tissues will cover the membrane and maintain it in place, with no need for further stabilization. In 2 patients, a thin layer of bone was found covering the implant threads that were underneath. This may have been caused by displacement of the autogenous bone underneath the membrane or by collapse of the membrane over the defect.

CONCLUSIONS

Significant bone gain was obtained in the treatment of peri-implant defects using Bio-Gide and autogenous bone. The results compared favorably to those reported in the literature with e-PTFE. The decrease in defect size was significant. This indicates that Bio-Gide has the potential to facilitate bone growth. The material possesses certain properties that facilitate clinical handling and permit uneventful healing, and it may be used without additional stabilization. However, the effect of micromovements on the percentage of regenerated bone-to-implant contact needs to be investigated. The barrier must be supported to prevent its collapse into the bone defect or onto the implant surface.

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