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A comparative study of barrier membranes as graft protectors in the treatment of localized bone defects

An experimental study in a canine model

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Abstract: Guided bone regeneration is a predictable and well-documented surgical approach for the treatment of deficient alveolar ridges prior to endosseous implant placement. The purpose of this study was to compare a new resorbable membrane (GORE RESOLUT ADAPT Regenerative Membrane, i.e. 67% glycolide (PGA) : 33% trimethyline carbonate (TMC)) with Bio-Gide®, a resorbable collagen membrane. Five canines were used in the study. Three saddle-type osseous defects were created bilaterally in edentulous areas of the mandible. The defects were filled with assayed, canine demineralized freeze-dried bone (DFDB) in a thermoplastic gelatin matrix. Using a randomized block design, four sites were covered with PGA : TMC membranes of four different porosities, one site was covered with a collagen membrane and one site consisted of DFDB alone (control). At 3 months, the animals were euthanized and the mandibles were removed *en bloc* for laboratory processing. A total of 30 sites were reviewed microradiographically and underwent histomorphometric analysis for bone regeneration, soft tissue presence and remaining graft material. All sites exhibited uneventful healing. A significantly higher percentage of bone regeneration was seen in the sites protected by the PGA : TMC membrane. A higher component of soft tissue was visible beneath the collagen membrane as compared with the PGA : TMC membrane. The control sites exhibited noticeable deformation of the regenerated bone secondary to collapse of the overlying periosteum. The authors conclude that the PGA : TMC membrane protected the DFDB-filled defect and allowed a greater amount of bone regeneration than the defect protected by the collagen membrane or the control.

The use of guided bone regeneration (GBR) has proven, both experimentally and clinically, to promote osseous regeneration and to preserve a large percent of grafted material (Dahlin et al. 1990; Becker et al. 1994; Buser et al. 1995; Mellonig et al. 1998).

Tissue separation by the membrane at a deficient site is only one factor necessary for the regeneration of bone. Hardwick et al (1994) proposed several design criteria necessary for GBR, such as biocompatibility of the material, adaptability and space maintenance. Nonresorbable barriers were the first devices approved for clinical use. Because of their inherent structural integrity, the desired qualities of a barrier membrane are exhibited throughout their time *in situ*. However, this type of membrane requires removal at a second surgical procedure and has been described as technique-sensitive, possibly requiring premature removal due to membrane exposure, all of which are disadvantages to its successful clinical use (Simion et al. 1994).

Resorbable membranes with characteristics similar to nonresorbable membranes have been developed and are popular clinically, primarily due to the fact that a second surgical procedure is unnecessary. However, these membranes may elicit tissue reactions that could influence wound healing as well as their overall effectiveness (Moore & Brekke 1990; Schmitz et al. 2000).

The aim of this study was to compare a newly developed, resorbable membrane composed of 67% glycolide (PGA) and 33% trimethylene carbonate (TMC) to a resorbable collagen membrane, with assayed demineralized freeze-dried bone (DFDB) serving as GM, in an experimental bone defect.

Material and methods

The experimental protocol was approved by the Institutional Animal Care and Use Committee at W. L. Gore & Associates, Inc., an Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) accredited facility, and conducted in accordance with the Institute of Laboratory Animal Resources Guide for the Care and Use of Laboratory Animals.

Preoperative care

Five adult male foxhound dogs, obtained by USDA methods, weighing more than 30 kg were utilized for this study. Animals were identified by implanted microchip and cage card. During the acclimation period, all animals were fed a standard diet, exercised daily and had access to water *ad lib*. Approximately 13 weeks prior to initiation of the surgical protocol, edentulous areas in the mandibular premolar region were prepared by extracting the mandibular first, second, third and fourth premolars. After 7 weeks, the first mandibular molar was extracted bilaterally to ensure adequate space. Oral prophylaxis consisting of supragingival scaling and an antimicrobial rinse (0.1% chlorhexidine acetate, Nolvadent®, Fort Dodge Animal Health, Overland Park, KS, USA) was performed prior to tooth extraction.

Surgical procedures

Prophylactic antibiotic therapy, consisting of cephazolin 22–44 mg/kg i.v., was administered within 1 h prior to surgery and redosed every 3 h during surgery. One dose of flunixin meglumine 0.5 mg/kg i.v. was administered within 1 h prior to surgery. Each animal also received dexamethasone 1 mg i.v. immediately prior to surgery to reduce postoperative edema. All surgical procedures were performed under general anesthesia using either Diazepam 10 mg i.v. and Propofol i.v. or Diazepam 15 mg i.v. and Ketamine to effect for induction, followed by endotracheal intubation and maintenance with isoflurane gas. Local infiltration with 1% lidocaine 1 : 100,000 epinephrine was given for hemostasis and to reduce postoperative pain. Full thickness mid-crestal incisions were utilized after which full-thickness mucoperiosteal flaps were elevated buccally and lingually to expose the edentulous alveolar ridge. Three osseous saddle-type defects, measuring approximately 8 mm (apicocoronal) × 10 mm (mesiodistal), were prepared in the edentulous alveolar mandibular premolar area by removing the buccal and lingual plates and associated cancellous bone utilizing rotary and hand instruments and chilled saline irrigation. (Fig. 1) An attempt was made to make the defects uniform; however, due to variations in the basal width of the ridge, exact standardization (volume and geometry) was not possible. The actual dimensions of each osseous defect were measured with a periodontal probe and recorded. Each site was then thoroughly irrigated with sterile saline to remove any residual debris.

Each surgical defect site was filled with canine, DFDB in a thermoplastic gelatin matrix (Regeneration Technologies Inc., Alachua, FL, USA). Five membranes were evaluated in the study. Four membranes were composed of 67%PGA : 33%TMC (GORE RESOLUT ADAPT Regenerative Membrane, W. L. Gore & Associates, Inc., Flagstaff, AZ, USA), each with a different porosity, and a fifth membrane was composed of porcine collagen (Bio-Gide®, Geistlich AG, Switzerland). Using a randomization table, test sites were selected to receive one of five membranes (Table 1). One site in each animal did not receive a membrane and served as a control. Each membrane was secured with a single titanium 1.5 mm × 5 mm bone screw (Walter Lorenz Surgical Inc., Jacksonville, FL, USA) placed 2 mm below the inferior bone

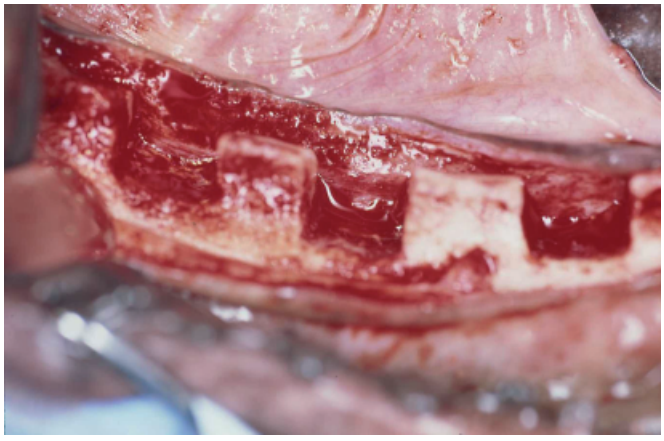

Fig. 1. Surgical defects, 8 mm apicocoronal × 10 mm mesiodistal, created in a canine mandible.

***Table 1*. Selected test sites**

Animal number	Right			Left		
	P2	P3	P4	P2	P3	P4
1	A	F	B	E	C	D
2	E	B	F	C	D	A
3	B	E	D	A	C	F
4	F	B	E	A	C	D
5	D	B	A	F	E	C

A–D: 67% PGA : 33%TMC (A: highest porosity; B: moderate porosity; C: minimal porosity; D: lowest porosity); E: collagen (BioGide®); F: control, no membrane.

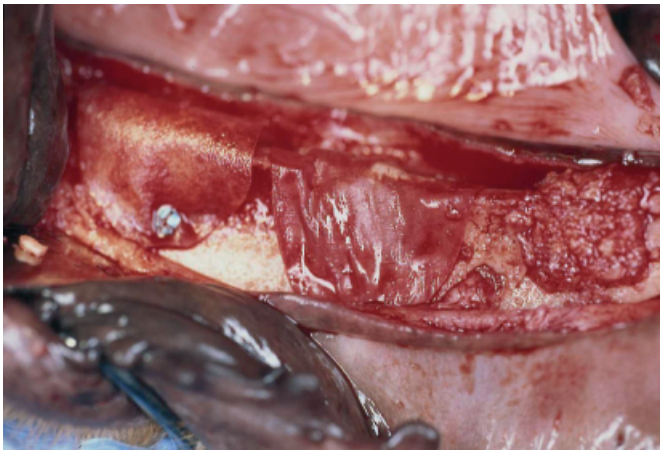

Fig. 2. Surgical defects filled with demineralized freeze-dried bone and test sites covered with membranes. Mid-portion of specimen marked by titanium screw. The control site remains uncovered.

cut to mark the mid-point of the defect (Fig. 2).

Postoperative procedures

During the entire postoperative period, the animals were fed a soft diet consisting of dry dog food soaked in warm water until completely soft. Postoperative medications included either Buprenorphine 0.01–0.04 mg/kg i.m./s.q. or Oxymorphone 0.05–1.0 mg/kg i.m./s.q./i.v. for pain, Oramorph® SR 30 mg orally (Roxane Laboratories, Columbus, OH, USA) and 1 mg dexamethasone on the first postoperative day, and amoxicillin 500–750 mg BID for 10 days. All sutures were removed 7 days following surgery. Oral hygiene was maintained with chlorhexidine gluconate wipes twice per week and a complete oral prophylaxis was performed once per month. Observations of the operative sites with respect to gingival health, maintenance of suture line, and evidence of tissue necrosis or infection were performed daily for 7 days following surgery and at least twice per week thereafter.

At 3 months, the animals were euthanized by induction of deep anesthesia with a subsequent intravenous sodium pentobarbital overdose. The surgical sites were then removed *en bloc* and placed in 4% formalin/1% $CaCl_2$ solution for at least 2 weeks.

Sample preparation

Undecalcified cut and ground sections

Following trimming and dissection, specimens were X-rayed on dental film and again immersed in 4% neutral buffered formaldehyde. Briefly, the specimens were dehydrated in graded series of ethanol (70% up to absolute ethanol), preinfiltrated in diluted resins, infiltrated in pure resin and finally embedded in light curing resin (Technovit 7200 VLC, Kültzer & Co., Wehrheim, Germany). Undecalcified cut and ground sections were prepared by using the Exakt® (Exakt Vertriebs GmbH, Norderstedt, Germany) sawing and grinding equipment as described by Donath & Breuner (1982) and Donath (1988). Each defect was divided at the central part. Altogether, three sections were prepared from each defect: one central, one proximal and one distal to the central one.

First, a section of about 100 µm thickness was prepared and microradiographed (see below). This section was then further ground to about 10 µm followed by routine histological staining in a solution of 1% toulidine blue in 1% borax solution mixed with 1% pyronin G (Johansson 1991; Johansson & Morberg 1995) followed by air drying and cover slipping.

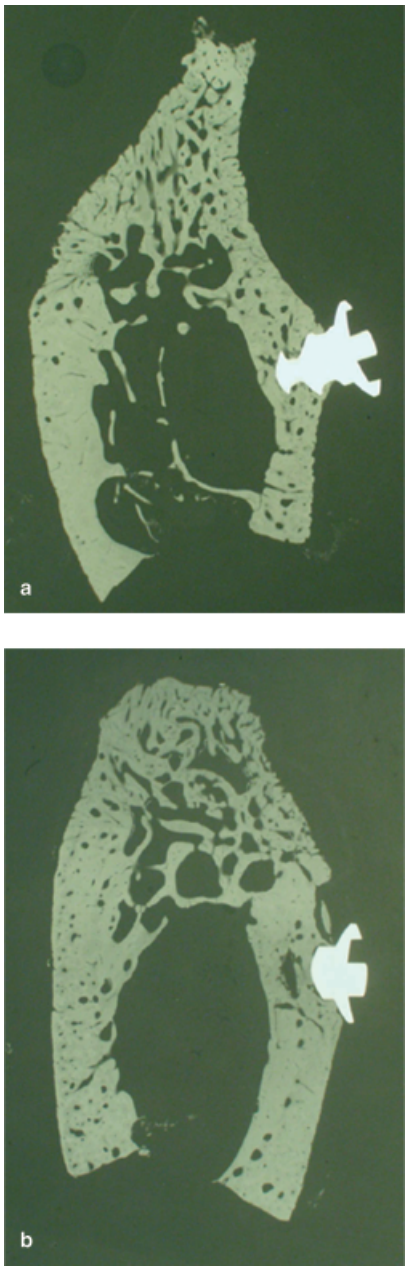

Fig. 3. (a) Microradiograph of control specimen. Section taken through mid-portion of specimen as marked by titanium screw. (b) Microradiograph of membrane-protected specimen. Section taken through mid-portion of specimen as marked by titanium screw.

Image access analysis

The ground sections with a thickness of about 100 µm were microradiographed (Fig. 3a, b) and the image was read into a PC-based image analysis system (Micro Macro Bildanalys AB, Stockholm, Sweden). The image was digitized by division into 512×756 pixels with gray values between 0 and 250. The area of interest was outlined by selecting a region of interest (ROI) and the proper intensity threshold was selected by the operator based on clinical measurements of the initial bone defects with regard to buccolingual and apicocoronal measurements (in mm). From these instructions, the system could calculate the area of bone and nonbone in the ROI. The percentage of bone area in the ROI was calculated directly through the computer for each measured area. The measurement procedure was

repeated three times for each section and expressed as a percentage mean value for each site. For details, see Kalebo et al. (1987) and Klinge et al. (1995).

Light microscopy and histomorphometry

Light microscopic investigations were performed in a Leitz Aristoplan light microscope (Leitz, Wetzlar, Germany). The histomorphometry was performed using Leitz Microvid equipment connected to the microscope and a PC computer (Johansson 1991).

With the aid of a grid placed in the eyepiece, the horizontal base line was drawn at the level of the original defect. Five longitudinal reference lines were made equidistant from each other and at right angles to the horizontal base line (Fig. 4a, b). On each reference line, a calculation of the percentage of bone, soft tissue and remnants of the DFDB graft material (GM) was carried out. A mean percentage for each individual section as well as a mean for each individual defect utilizing the three sections taken from each defect were then calculated. In all specimens, the following estimators were examined:

1. new bone,
2. soft tissue,
3. DFDB (GM),
4. bone + DFDB (GM).

The barrier membrane and bony walls of the defects determined the margins for the morphometric evaluation. In the defects without membrane protection, the evaluation was restricted to the field occupied by bone tissue. Soft tissue was defined as all fibrous tissue (including blood vessels) in the intertrabecular space and underneath the membrane material.

Statistical analysis

The data were analyzed for statistical significance using the Newman–Keuls test. The statistical significance level was set at $P<0.05$.

Results

Clinical observations

Four of the five animals healed without apparent complications. One animal experienced a dehiscence along the suture line, which exposed a portion of the PGA : TMC membrane. The site was irrigated with saline, sutured and subsequently healed without further complication. A moderate amount of swelling and post-operative edema was present during the first few days following surgery. Except as noted above, no GM or barrier membrane material was visible in any surgical site throughout the entire duration of the study.

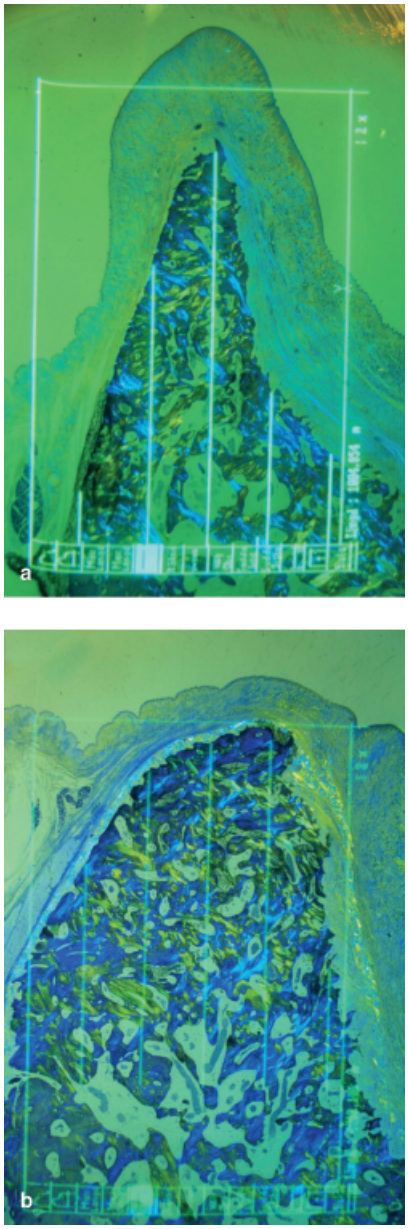

Fig. 4. (a) Survey picture of undecalcified cut and ground section (10 μm) from a control site as visualized in the light microscope using a polarizing filter in combination with a lambda filter. The reference lines used for histomorphometric quantification of the ratio of 'bone : filling material : soft tissue' are superimposed and indicate where the evaluations were performed. Original magnification × 10. (b) Survey picture of an undecalcified cut and ground section (10 μm) from a membrane-protected section as visualized in the light microscope using a polarizing filter in combination with a lambda filter. The reference lines used for histomorphometric quantification of the ratio of 'bone : filling material : soft tissue' are superimposed and indicate where the evaluations were performed. Original magnification × 10.

Histological and histomorphometric evaluation

In general, all the surgical sites demonstrated uncomplicated healing. The inflammatory and foreign body giant cell response to the respective barrier membranes and matrix material was mild. Overall, the DFDB material demonstrated a high turnover and incorporated within the newly regenerated bone.

Sites with DFDB GM only (control) exhibited noticeable deformation in the profiles of the regenerated bone. Generally, a knife-edge ridge was created via a partial collapse of the buccal and lingual walls (Fig. 5). In the collagen membrane group, a thicker soft tissue layer could be seen compared with the PGA : TMC-type membranes. In sites protected by the different types of biodegradable barrier membranes, substantial bone regeneration was generally seen within the proximity of the defects. New bone extended to the very near surface of the barrier membranes (Fig. 6).

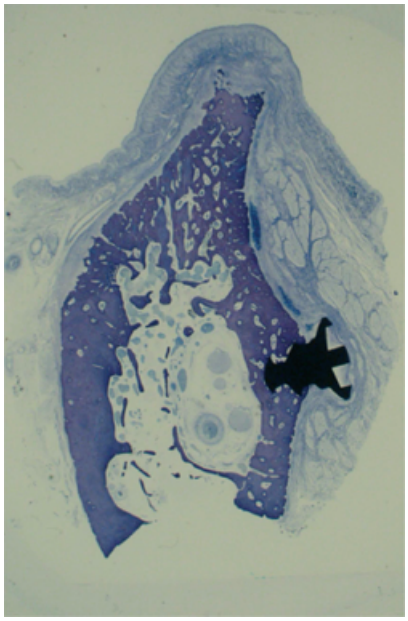

Fig. 5. Survey picture of an undecalcified cut and ground section (10 μm) from a control site as visualized in the light microscope with a knife-edge ridge due to partial collapse of buccal and lingual walls. Toluidine blue with pyronin G was used for staining. Original magnification × 10.

Histomorphometric analysis

The calculations of total bone fill in percent of the initial defect area, based on the microradiographic evaluation, are listed in Fig. 7. The results demonstrated a significantly ($P<0.05$) lower bone fill of the initial bone defect in group F (DFDB only) compared with all membrane-protected groups. Furthermore, groups A–D (PGA : TMC) demonstrated significantly ($P<0.05$) more bone content compared with group E (collagen membrane).

The quantitative histomorphometric analysis showed a statistically significant ($P<0.01$) higher percentage of total bone fill (new bone + GM) compared with the membrane-protected groups within the regenerate. The relative increase in total bone fill appeared to be at the expense of the soft tissue component. Groups A–D demonstrated a statistically significant higher percentage of new bone within the regenerate compared with group E ($P<0.05$). Group E demonstrated a statistically significant ($P<0.001$) higher soft tissue component within the regenerated tissue compared with all the other barrier groups (A–D). Generally, all groups demonstrated a low percentage of remaining DFDB GM within the regenerate (Table 2).

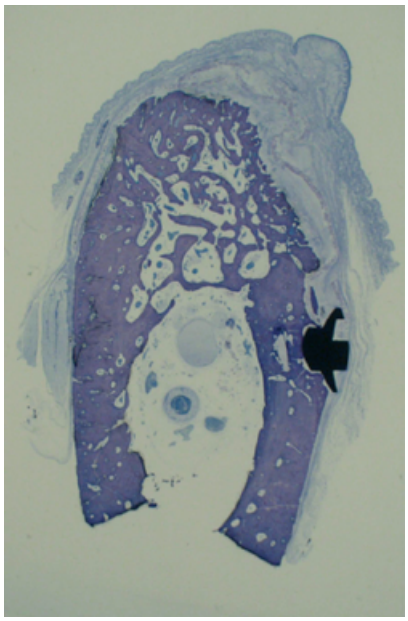

Fig. 6. Survey picture of an undecalcified cut and ground section (10 μm) from a membrane-protected section as visualized in the light microscope with new bone extending to the inner surface of the membrane. Toluidine blue with pyronin G was used for staining. Original magnification × 10.

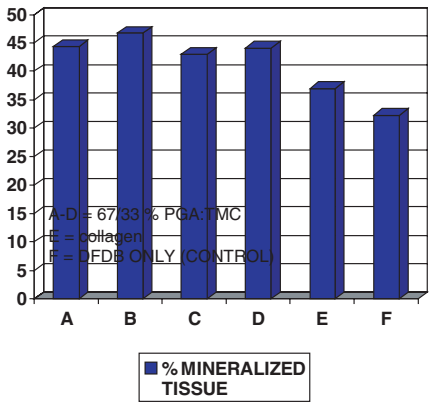

Fig. 7. Microradiographic results for bone fill.

Discussion

The present study evaluated a novel biodegradable membrane in combination with a DFDB matrix for the treatment of localized bone defects in the canine model. This experimental model in the dog mandible is well described in previous experimental studies on GBR (Schenk et al. 1994; Simion et al. 1999; Ruskin et al. 2000). In order to reduce the number of animals in the present study, control defects without GM and membranes were eliminated based on the substantial experience as mentioned above.

Over the past 15 years, the literature has been replete with experimental and clinical studies supporting the use of GBR for the reconstruction of osseous defects (Dahlin et al. 1988; Lang et al. 1994; Hammerle et al. 1995; Stetzer et al. 2002). Moreover, several studies, both experimental and clinical, have clearly demonstrated the synergistic effect when combining barrier membranes and different types of GM (Dahlin et al. 1991; Smukler et al. 1995; Buser et al. 1998; Salata et al. 1998). The most predictable results from a clinical, histologic and experimental perspective thus far seem to be the combination of autograft material and nonresorbable barrier membranes (Buser et al. 1996; Buser et al. 1998; von Arx et al. 2001). However, the donor site morbidity of harvesting autogenous bone in the clinical setting must not be neglected. Therefore, there is a constant need to develop and explore alternative techniques regarding GMs. In the present study, specially manufactured canine DFDB in a thermoplastic matrix, which was assayed for osteoinductive activity (Urist & Strates 1970), was tested as a GM. The GM was covered either with a biodegradable membrane comprised of a 67% : 33% ratio of PGA : TMC (GORE RESOLUT ADAPT Regenerative Membrane) with four different porosities or a collagen membrane (Bio-Gide®).

A critical issue associated with GBR procedures is the problem associated with barrier exposure during the healing phase. The e-PTFE membrane demonstrates a superior outcome with regard to bone regeneration in the case of uneventful healing. However, several authors describe a less favorable outcome (Becker et al. 1990; Simion et al. 1994) due to barrier exposure during healing. A clinical study by Zitzmann et al. in 1997 utilized a split-mouth setup comparing a biodegradable membrane (Bio-Gide®) with a nonresorbable membrane (e-PTFE) in combination with BioOss® (Geistlich AG, Wolhusen, Switzerland) as a filler material. Although the e-PTFE membranes demonstrated superior bone formation when uneventful healing occurred, the outcome for the sites covered with biodegradable barriers also demonstrated a successful outcome in the clinical perspective. Interestingly, the frequency of barrier exposure was less in the sites using biodegradable membranes. Furthermore, the treatment of the exposure was easier and the final outcome, with regard to new bone formation, was significantly better in exposed sites with biodegradable membranes compared with exposed sites with e-PTFE membranes. These findings are also confirmed in a recent case report by Rosen & Reynolds (2001).

A similar outcome was found in the present study. Generally, both the GM and the barrier membranes were very compatible with the tissue. The GM was well integrated into the bone turnover, as evidenced by an average of only 10% residual GM within the newly formed tissue after 3 months of healing. Material exposures or infections were not seen clinically during the healing phase. Also, all materials were well accepted as demonstrated by no significant histologic inflammatory or foreign body reactions. Quantitatively, the study clearly showed that synergistic effects are achieved when a GM is protected by means of a barrier membrane. In the present study, group F

***Table 2.* Percent distribution of tissue types for groups**

Groups	Soft tissue	New bone	Graft material
A	26.2 c	61.8 c	12 b
B	31.6 c	61.4 c	7.0 b
C	25.2 c	70.2 a	4.6 a
D	26.2 c	60.2 c	13.4 b
E	34.9 b	54.3 b	10.8 b
F	20.6 a	69.7 a	9.7 b

Groups with different letters (a–c) are statistically significantly different from each other ($P < 0.05$) using the null hypothesis (Newman–Keuls test).

(GM only) demonstrated significantly less new bone formation compared with all the other groups (A–E) using barrier protection. Another notable finding was that group E (collagen membrane), which demonstrated significantly more bone formation quantitatively than the control group (F), showed a significantly higher content of soft tissue within the regenerate compared with the PGA : TMC membranes, regardless of the level of porosity of those membranes. Quantitatively, the amount of newly formed bone within the regenerated tissue was also significantly higher within the groups utilizing the PGA : TMC membranes compared with the collagen membrane. The reason for this is as yet unknown. However, it has been proposed that differences in mechanical properties, degradation time and lack of integrated biologic components could be factors influencing the regenerative outcome (Schantz et al. 2002).

Conclusion

This experimental study clearly demonstrated that the combination of DFDB and a biodegradable barrier membrane represents a method for predictable bone regeneration in localized bone defects. Virtually no inflammatory reaction was seen against the GM or the barrier membranes tested in this study. Also, a wound dehiscence was seen in only one of 30 experimental sites and healed in an uneventful manner. The PGA : TMC membrane (GORE RESOLUT ADAPT Regenerative Membrane) + DFDB demonstrated a significantly higher bone fill quantitatively compared with collagen (Bio-Gide®) + DFDB or DFDB alone. The PGA : TMC membrane + DFDB also demonstrated a significantly lower content of soft tissue within the regenerate compared with the collagen membrane + DFDB.

This study provides evidence that the combination of a PGA : TMC biodegradable membrane (GORE RESOLUT ADAPT Regenerative Membrane) + DFDB offers a viable alternative in the treatment of localized bone defects in the clinical setting.

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Résumé

La régénération osseuse guidée est une approche chirurgicale bien documentée et prévisible pour le traitement de rebords alvéolaires insuffisants avant le placement d'implants dentaires. Le but de cette étude a été de comparer une nouvelle membrane résorbable, la membrane régénérative GORE RESOLUT ADAPT : 67% glycolide (PGA) : 33% carbonate de triméthyline (TMC) avec la Bio-Gide®, une membrane collagène résorbable. Cinq chiens ont été utilisés dans cette étude. Trois lésions osseuses en forme de selle ont été créées bilatéralement dans les zones édentées de la mandibule. Les lésions ont ensuite été comblées d'os déminéralisé congelé sec canin (DFDB) dans une matrice gélatine-thermoplastique. En utilisant un modèle de blocage randomisé, quatre sites ont été couverts avec les membranes PGA : TMC de quatre degrés de porosité différents, un site a été couvert avec une membrane collagène et un n'avait reçu que DFDB et servait donc de contrôle. Après trois mois, les animaux ont été euthanasiés et les mandibules ont été enlevées en bloc pour l'analyse de laboratoire. Trente sites ont été analysés microradiographiquement et subis une analyse histomorphométrique pour la régénération osseuse, la présence de tissu mou et de matériel de greffe restant. Tous les sites examinés ont guéri sans problème. Un pourcentage significativement plus important de régénération osseuse a été aperçu dans les sites protégés par la membrane PGA : TMC. Davantage de tissu mou était visible sous la membrane collagène comparé à la membrane PGA: TMC. Les sites contrôles exhibaient une déformation notable de l'os régénéré suite à l'affaissement du périoste les recouvrant. La membrane PGA : TMC protège la lésion remplie de DFDB et permet donc une plus importante quantité de régénération osseuse que la lésion protégée par une membrane collagène ou sans recouvrement.

Zusammenfassung

Die gesteuerte Knochenregeneration ist eine voraussagbare und gut dokumentierte chirurgische Technik zum Wiederaufbau eines ungünstigen Knochenkamms vor der Implantation von enossalen Implantaten. Das Ziel dieser Arbeit war, eine neue resorbierbare Membran, die Regenerative Membran GORE RESOLUTE ADAPT 67% Glycolide (PGA)/ 33% Trimethyline Karbonate (TMC) zu vergleichen mit Bio-Gide®, einer resorbierbaren Kollagenmembran. Man benötigte für diese Arbeit 5 Kaninchen. In der zahnlosen Region des Unterkiefers präparierte man drei sattelförmige Knochendefekte. Die Defekte wurden anschliessend mit gesammeltem, demineralisiertem und gefriergetrocknetem Kaninchenknochen (DFDB), eingebettet in eine thermoplastische Gelatinematrix aufgefüllt. Nach dem Zufallsprinzip bedeckte man vier Stellen mit PGA/ TMC-Membranen von vier verschiedenen Porositäten, eine Stelle bedeckte man mit einer Kollagenmembran, und eine Stelle enthielt nur DFDB (Kontrolle). Nach drei Monaten wurden die Tiere eingeschläft
und die Unterkiefer für die weiteren Schritte im Labor an einem Stück entfernt. Insgesamt konnte man 30 Stellen mikroradiographisch untersuchen und die histomorphometrischen Analysen lieferten Daten zur Knochenregeneration, zu den vorhandenen Weichgeweben und dem verbliebenen Transplantationsmaterial. Alle Stellen zeigten eine ereignislose Heilung. Man stellte bei den mit einer PGA/TMC-Membran bedeckten Stellen eine prozentual signifikant bessere Knochenregeneration fest. Unter der Kollagenmembran kam es zu einer sichtbar grössere Anlage von Weichgewebsanteilen als unter der PGA/TMC-Membran. Die Kontrollseiten zeigten beachtliche Verformungen des regenerierten Knochens. Sie sind die Folge eines Kollapses vom Augmentat wegen dem Druck des darüberliegenden Periosts. Die Autoren schliessen daraus, dass die PGA/TMC-Membran die mit DFDB aufgefüllten Defekte schützte, und somit eine Knochenregeneration grösseren Ausmasses zuliess, als bei den mit einer Kollagenmembran bedeckten Defekten od er der Kontrolle.

Resumen

La regeneración ósea guiada es un enfoque quirúrgico predecible y bien documentado para el tratamiento de crestas alveolares deficientes previo a la colocación de implantes endooseos. La intención de este estudio fue comparar una nueva membrana reabsorbible, la GORE RESOLUT ADAPT Regenerative Membrane 67% glicolide (PGA) : 33% carbonato de trimetiline (TMC) con la Bio-Guide®, una membra-

na reabsorbible de colágeno. Se usaron cinco canes en este estudio. Se crearon tres defectos óseos tipo silla de montar bilateralmente en áreas edéntulas de la mandíbula. Los defectos se rellenaron con hueso canino desmineralizado secado al frió (DFDB) probado, en una matriz de gelatina termoplástica. Usando un diseño aleatorio de bloque, se cubrieron cuatro lugares con membranas PGA : TMC de cuatro porosidades diferentes, un lugar se cubrió con una membrana de colágeno, y otro lugar consistió de DFDB solo (Control). A los 3 meses, los animales se eutanizaron y las mandíbulas se removieron en bloque para procesamiento de laboratorio. Se revisaron un total de 30 lugares microrradiograficamente y se sometieron a análisis histomorfométrico para regeneración ósea, presencia de tejido blando y material de injerto remanente. Todos los lugares exhibieron cicatrización libre de incidentes. Se observó un porcentaje mayor de regeneración ósea en los lugares protegidos por la membrana PGA : TMC. Un componente mayor de tejido blando fue visible bajo la membrana de colágeno comparada con la membrana PGA : TMC. Los lugares de control exhibieron una deformación noticiable del hueso regenerado secundario al colapso de la cubierta de periostio. Los autores concluyen que la membrana PGA : TMC protegió el defecto rellenado con DFDB y permitió una mayor cantidad de regeneración ósea que el defecto protegido por la membrana de colágeno o el control.

要旨

ＧＢＲは骨内インプラント埋入に先立つ歯槽堤欠損の治療として予知性の高い、十分に研究されてきた外科的術式である。本研究は、６７％のグリコリド（ＰＧＡ）、３３％のトリメチリン・カーボネート（ＴＭＣ）からなる新規の吸収性メンブレン Gore Resolut Adapt Regenerative Membrane と、吸収性コラーゲン・メンブレン Bio-Gide®を比較することを目的に行った。５頭の犬を本研究に用いた。下顎無歯顎部両側に３箇所の鞍状骨欠損を形成した。欠損には、熱可塑性ゼラチン・マトリクスに効力検定済みの、犬の脱灰凍結乾燥骨（ＤＦＤＢ）を入れたものを埋めた。無作為化ブロック・デザインを用いて、４箇所は４つの異なる多孔性を備えたＰＧＡ：ＴＭＣメンブレンで被覆し、１箇所はコラーゲン・メンブレンで被覆し、もう１箇所はＤＦＤＢのみの使用（対照）とした。３ヶ月後に動物を安楽死させ、下顎を一塊として切除し、組織学的処理をした。合計３０箇所をマイクロ・レントゲンで検査し、組織形態計測による分析を行い、骨再生、軟組織の存在、残存する移植材料を調べた。全ての部位は、問題なく治癒していた。ＰＧＡ：ＴＭＣメンブレンで保護した部位は、有意に高い比率の骨再生を示した。ＰＧＡ：ＴＭＣメンブレンに比べて、コラーゲン・メンブレン下ではより高い含有率の軟組織が認められた。対照部位では骨膜の圧壊による再生骨の変形が目立った。結論として、コラーゲン・メンブレンで保護した部位や対照部位に比べて、ＰＧＡ：ＴＭＣメンブレンはＤＦＤＢを移植した欠損部を保護し、より多くの骨再生を達成したと結論した。

References

von Arx, T., Cochran, D.L., Hermann J, S., Schenk, R.K. & Buser, D. (2001) Lateral ridge augmentation using different bone fillers and barrier membrane application. A histologic and histomorphometric pilot study in the canine mandible. *Clinical Oral Implants Research* **12**: 260–269.

Becker, W. & Becker, B. (1990) Guided tissue regeneration for implants placed into extraction sockets and for implant dehiscences: surgical techniques and case reports. *International Journal of Periodontics and Restorative Dentistry* **10**: 377–391.

Becker, W., Dahlin, C., Becker, B., Lekholm, U., van Steenberghe, D., Higuchi, K. & Kultje, C. (1994) The use of e-PTFE barrier membranes for bone promotion around titanium implants placed into extraction sockets: a prospective multicenter study. *International Journal of Oral & Maxillofacial Implants* **9**: 31–40.

Buser, D., Dula, K., Lang, N.P. & Nyman, S. (1996) Long-term stability of osseointegrated implants in bone regenerated with the membrane technique. 5-year results of a prospective study with 12 im]plants. *Clinical Oral Implants Research* **7**: 175–183.

Buser, D., Hoffman, B., Bernard, J.P., Lussi, A., Mettler, D. & Schenk, R.K. (1998) Evaluation of filling materials in membrane protected bone defects. A comparative histomorphometric study in the mandible of miniature pigs. *Clinical Oral Implants Research* **9**: 137–150.

Buser, D., Ruskin, J., Higginbotton, F., Hardwick, R., Dahlin, C. & Schenk, R.K. (1995) Osseointegration of titanium implants in bone regenerated in membrane-protected defects: a histologic study in the canine mandible. *International Journal of Oral & Maxillofacial Implants* **10**: 666–681.

Dahlin, C., Alberius, P. & Linde, A. (1991) Osteopromotion for cranioplasty. *Journal of Neurosurgery* **74**: 487–491.

Dahlin, C., Gottlow, J., Linde, A. & Nyman, S. (1990) Healing of maxillary and mandibular defects using a membrane technique. An experimental study in monkeys. *Scandinavian Journal of Plastic and Reconstructive Surgery and Hand Surgery* **24**: 13–19.

Dahlin, C., Linde, A., Gottlow, J. & Nyman, S. (1988) Healing of bone defects by guided tissue regeneration. *Plastic and Reconstructive Surgery* **81**: 672–676.

Donath, K. (1988) Die Trenn-Dünnscliff-Technik zur Herstellung histologischer Präparaten von nicht schneidbaren Geweben und Materialen. *Der Präparator* **34**: 318–325.

Donath, K. & Breuner, G.A. (1982) A method for undecalcified bones and teeth with attached soft tissues. The Säge–Schliff technique. *Journal of Oral Pathology* **11**: 318–325.

Hämmerle, C.H., Fourmousis, I., Winkler, J.R., Weigel, C., Brägger, U. & Lang, N.P. (1995) Successful bone fill in late peri-implant defects using guided tissue regeneration. A short communication. *Journal of Periodontology* **66**: 303–308.

Hardwick, R., Scantlebury, T., Sanchez, R., Whitley, N. & Ambruster, J. (1994) Membrane design criteria for guided bone regeneration of the alveolar ridge. In: Buser, D., Dahlin, C. & Schenk, R.K., eds. *Guided bone regeneration in implant dentistry*. 1st edition, 101–136. Chicago, IL: Quintessence.

Johansson, C.B. (1991) On tissue reaction to metal implants. Thesis, Department of Biomaterials/ Handicap Research, Göteborg University, Sweden.

Johansson, C.B. & Morberg, P. (1995) Importance of ground section thickness for reliable histomorphometrical results. *Biomaterials* **16**: 91–95.

Kalebo, P., Jacobsson, M., Albrektsson, T. & Turesson, I. (1987) Bone healing following irradiation during tourniquet ischaemia. *Acta Oncologica* **26**: 63–68.

Klinge, B., Johansson, C., Hallström, H. & Engdal, T. (1995) A new method to obtain bone biopsies at implant sites peri-operatively: technique and bone structure. *Clinical Oral Implants Research* **6**: 91–95.

Lang, N.P., Hämmerle, C.H., Brägger, U., Lehmann, B. & Nyman, S.R. (1994) Guided tissue regeneration in jawbone defects prior to implant placement. *Clinical Oral Implants Research* **5**: 92–97.

Mellonig, J., Nevins, M. & Sanchez, R. (1998) Evaluation of a bioabsorbable physical barrier for guided bone regeneration. Part II. Material and a bone replacement graft. *International Journal of Periodontics and Restorative Dentistry* **18**: 139–149.

Moore, J.W. & Brekke, J.H. (1990) Foreign body giant cell reaction related to placement of tetracycline-treated polylactic acid: Report of 18 cases. *Journal of Oral and Maxillofacial Surgery* **48**: 808–812.

Rosen, P.S. & Reynolds, M.A. (2001) Guided bone regeneration for dehiscence and fenestration defects on implants using an absorbable polymer barrier. *Journal of Periodontology* **72**: 250–256.

Ruskin, J.D., Hardwick, R., Buser, D., Dahlin, C. & Schenk, R.K. (2000) Alveolar ridge repair in a canine model using rhTGF-B1 with barrier membranes. *Clinical Oral Implants Research* **11**: 107–115.

Salata, L.A., Craig, G.T. & Brook, I.M. (1998) Bone healing following the use of hydroxyapatite or ionomeric bone substitutes alone or combined with guided bone generation technique: an animal study. *International Journal of Oral & Maxillofacial Implants* **13**: 44–51.

Schantz, J.T., Hutmacher, D.W., Ng, K.W., Khor, H.L., Lim, M.T. & Teoh, S.H. (2002) Evaluation of a tissue-engineered membrane cell construct for guided bone regeneration. *International Journal of Oral & Maxillofacial Implants* **17**: 161–174.

Schenk, R.K., Buser, D., Hardwick, W.R. & Dahlin, C. (1994) Healing pattern of bone regeneration in membrane-protected defects: a histologic study in canine mandible. *International Journal of Oral & Maxillofacial Implants* **9**: 13–29.

Schmitz, J.P., Lemke, R.R., Zardeneta, G., Hollinger, J.O. & Milam, S.B. (2000) Isolation of particulate degradation debris 1 year after implantation of Guidor membrane for guided bone regeneration: case report. *Journal of Oral and Maxillofacial Surgery* **58**: 888–893.

Simion, M., Dahlin, C., Blair, K. & Schenk, R.K. (1999) Effect of different microstructures of e-PTFE membranes on bone regeneration and soft tissue response: a histologic study in canine mandible. *Clinical Oral Implants Research* **10**: 73–84.

Simion, M., Trisi, P., Maglione, M. & Piattelli, A. (1994) A preliminary report on a method for studying the permeability of expanded polytetrafluoroethylene membrane to bacteria *in vitro*: A scanning electron microscopic and histological study. *Journal of Periodontology* **65**: 755–761.

Smukler, H., Barboza, E.P. & Burliss, C. (1995) A new approach to regeneration of surgically reduced alveolar ridges in dogs: a clinical and histologic study. *International Journal of Oral & Maxillofacial Implants* **10**: 537–531.

Stetzer, K., Cooper, G., Gassner, R., Kapucu, R., Mundell, R. & Mooney, M. (2002) Effects of fixation type and guided tissue regeneration on maxillary osteotomy healing in rabbits. *Journal of Oral and Maxillofacial Surgery* **60**: 427–436.

Urist, M.R. & Strates, B.S. (1970) Bone formation in implants of partially and wholly demineralized bone matrix. *Clinical Orthopaedics and Related Research* **7**: 271–278.

Zitzmann, N.U., Naef, R. & Scharer, P. (1997) Resorbable versus nonresorbable membranes in combination with Bio-Oss for guided bone regeneration. *International Journal of Oral & Maxillofacial Implants* **12**: 844–852.