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# Lateral ridge augmentation using different bone fillers and barrier membrane application

A histologic and histomorphometric pilot study in the canine mandible

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**Key words:** lateral ridge augmentation, bone grafting materials, barrier membrane, guided bone regeneration, histology, histomorphometry, experimental animal study, pilot study

**Abstract:** Lateral ridge augmentation has become a standard treatment option to enhance the bone volume of deficient recipient sites prior to implant placement. In order to avoid harvesting an autograft and thereby eliminating additional surgical procedures and risks, bone grafting materials and substitutes are alternative filler materials to be used for ridge augmentation. Before clinical recommendations can be made, such materials must be extensively studied in experimental models simulating relevant clinical situations. The present pilot study was conducted in three dogs. Different grafting procedures were evaluated for augmentation of lateral, extended (8×10×14 mm) and chronic bone defects in the mandibular alveolar ridge. Experimental sites received tricalcium phosphate (TCP) granules or demineralized freeze-dried bone allograft (DFDBA) particles. Barrier membranes (ePTFE) were placed for graft protection. These approaches were compared to ridge augmentation using autogenous cortico-cancellous block grafts, either with or without ePTFE-membrane application. After a healing period of six months, the sites were analyzed histologically and histomorphometrically. Autografted sites with membrane protection showed excellent healing results with a well-preserved ridge profile, whereas non-protected block grafts underwent bucco-crestal resorption, clearly limiting the treatment outcome. The tested alloplastic (TCP) and allogenic (DFDBA) filler materials presented inconsistent findings with sometimes encapsulation of particles in connective tissue, thereby reducing the crestal bone width. The present pilot study supports the use of autografts with barrier membranes for lateral ridge augmentation of extended alveolar bone defects.

Implant-borne tooth restorations have become a standard of care in modern dentistry. Ridge augmentation procedures have clearly widened the scope of implant treatment. Among the various techniques to reconstruct or enlarge a deficient alveolar ridge, guided bone regeneration (GBR) has become a predictable and well-documented surgical approach (Buser et al. 1999). Although autogenous bone grafts (autografts) are unequivocally accepted as the standard of care, bone allografts, xenografts and

alloplasts (substitutes) are being extensively studied in order to avoid the harvesting procedure of autogenous bone (Misch & Dietsch 1993; Gross 1997). The reasons most frequently cited for using an alternative bone grafting material are donor site morbidity and insufficient volume of (intraorally) harvested autogenous bone. However, these apparent shortcomings of autografts are outweighed by their safety in terms of disease transmission and immunologic aspects. New surgical techniques and in-

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struments, i.e. bone collectors, trephines, chisels, bone mills, and so on, have optimized the harvesting procedure of autogenous bone. However, ridge augmentation of extended or non-contained bone defects frequently requires larger amounts of bone than can be procured intraorally. To avoid complex and expensive extraoral bone harvesting procedures, research activities focus more and more on using bone substitutes. Apart from requirements such as clinical manageability and safety, these materials should undergo complete remodeling and substitution by newly formed bone in view of placing dental implants in such augmented sites.

In a recent experimental study, Buser et al. (1998) analyzed bone regeneration using different grafting materials protected by an ePTFE-membrane. After an extraoral incision, acute standardized defects were created in the mandibular angle of 12 miniature pigs. The defect fillers tested included a collagen sponge, a demineralized freeze-dried bone allograft (DFDBA; source: tibia of miniature pig), tricalcium phosphate (TCP) granules and coral-derived hydroxyapatite (HA) granules. These grafting materials were compared to the blood clot as the negative control and to particulate autogenous cortical bone as the positive control. Histomorphometric analysis after 4, 12 and 24 weeks of healing revealed the best results for autografts in the early phase of healing, whereas TCP demonstrated 70% new bone formation at the completion of the study compared to 54% in autografted sites. Less bone formation was observed for HA (49%) and DFDBA (44%). Since the negative control sites (blood clot) also showed a high percentage of bone regeneration (55%) at the completion of the study, it was assumed that the chosen model, i.e. a five-wall defect in an animal with an excellent osteogenic potential, led to an overall favorable response. Therefore, it was decided to test these promising TCP granules in a more demanding and clinically more relevant experimental model. Although DFDBA yielded disappointing results in the aforementioned study, this material was also included in the present evaluation since it is widely used in GTR (guided tissue regeneration) and GBR procedures (Meloni & Nevins 1995).

Hence, the objective of this pilot study was to evaluate lateral ridge augmentation using TCP and DFDBA particles with ePTFE-membrane protection, compared to autogenous bone with or without membrane application.

## Material and methods

### Study design and time schedule

The experimental study was designed as a pilot study employing three dogs. Initially, all premolars and first molars were removed bilaterally to create edentulous ridges. Simultaneously, two lateral bone defects were made on each side in the mandible by removing the buccal cortex. Two months later, the defect sites were reentered for lateral ridge augmentation using various grafting materials and procedures. All animals were sacrificed 6 months following ridge augmentation.

### Animals

Three lab-bred American foxhounds were used in this study. At the beginning, these animals were about 2 years old and weighed approximately 30 kg. The study was conducted according to the guidelines of the Department of Laboratory Animal Resources at UTHSCSA and the protocol was approved by the Institutional Animal Care and Use Committee at UTHSCSA.

### Pre- and postoperative medication

All surgical procedures were performed under general anesthesia in an operating room. For premedication, the following agents were used: Acepromazine (0.25 mg/kg, Aceproject<sup>®</sup>, Vetus Animal Health, Burns Vet Supply, Rockville Center, NY, USA) and Atropine (0.04 mg/kg, Atroject S.A.<sup>®</sup>, Vetus Animal Health) s.c., and a 4% solution of Thiopental-Na (25–30 mg/kg, Pentothal<sup>®</sup>, Abbott Laboratories, North Chicago, IL, USA). Subsequently, the dogs were intubated and were administered an inhalation of 1–3% isoflurane (AErane<sup>®</sup>, Ohmeda Carbide Inc., Liberty Corner, NJ, USA) in O<sub>2</sub>-maintenance. After disinfection of the surgical site with 10% povidone-iodine solution (Clinidine<sup>®</sup>,

Clinipad Co., Guilford, CT, USA), local anesthetic (Lidocaine HCl 2% with epinephrine 1:100,000, Henry Schein Inc., Port Washington, NY, USA) was administered by infiltration at the respective buccal and lingual sites.

Postoperatively, the dogs received 20 mg Nalbuphine s.c. *b.i.d.* (Nubain<sup>®</sup>, Astra Pharmaceutical Products Inc., Westborough, MA, USA) as an analgesic. Three ml of Benzathine-Penicillin 150,000 + Procaine-Penicillin G 150,000 (Pen-B<sup>®</sup>, Pfizer Inc., Lee's Summit, MO, USA) were administered s.c. *s.i.d.* every 48 hours for 7–10 days. In addition, 100 mg of the antibiotic Gentamicin (Gentocin<sup>®</sup>, Schering-Plough Animal Health Corp., Kenilworth, NJ, USA) were given s.c. on day 1 *b.i.d.*, and the same dosage *s.i.d.* from days 2–10. To reduce swelling, the dogs received 4 mg Dexamethasone i.m. (Dexaject<sup>®</sup>, Burns Veterinary Supply, Oakland, CA) *s.i.d.* on days 1 and 4.

For suture removal, an i.v. sedation with a combination-agent of RAAK = Rompun-Xylazine (7.1 mg/ml, X-Ject E<sup>®</sup>, Vetus Animal Health)/Acepromazine (2.1 mg/ml) /Atropine (0.1 mg/ml) /Ketamine (50 mg/ml, Ketaset<sup>®</sup>, Fort Dodge Laboratories Inc., Fort Dodge, IA, USA) was administered (1.1 ml/15 kg bw).

Oral hygiene procedures were carried out two times a week using 0.2% chlorhexidine gel (Plak-Out<sup>®</sup> Gel, Hawe Neos Dental, Biaggio, Switzerland). A soft diet was maintained throughout the study.

### Surgery 1 (Extraction and defect creation)

Sulcular incisions were made with subsequent reflection of full mucoperiosteal flaps. In the mandible, all premolars (P1–P4) and the first molar (M1) were removed, whereas in the maxilla P2 and P3 were extracted. Prior to removal, all two-rooted teeth were sectioned employing a separating disk to ease root extraction. Subsequently, two “chronic-type” bone defects (length 14 mm, height 10 mm, depth 8 mm) were created in the mandible by removing the buccal bone plate (Fig. 1). The two defects encompassed approximately the extraction sites of P2 and P4. A small round bur was used to outline the defect margins on the buccal bone plate. Subsequently, the bur holes were connected

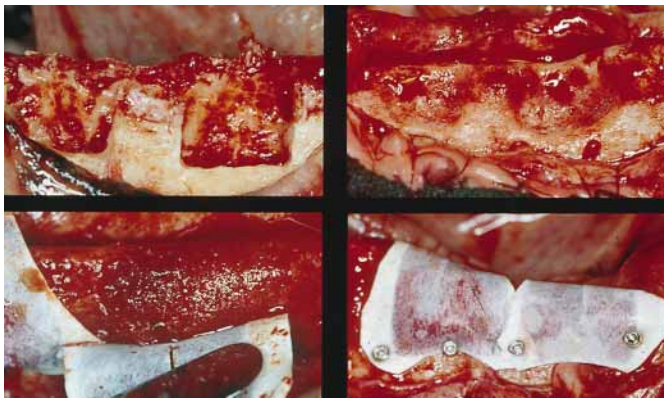


Fig. 1. Sequence of surgical treatment: (top left) outlining of lateral bone defects in surgery 1; (top right) reentry at surgery 2 demonstrating chronic bone defects; (bottom left) placement of grafting material around "tent-pole" screw; (bottom right) ePTFE-membranes draped over augmentation sites, note membrane fixation screws.

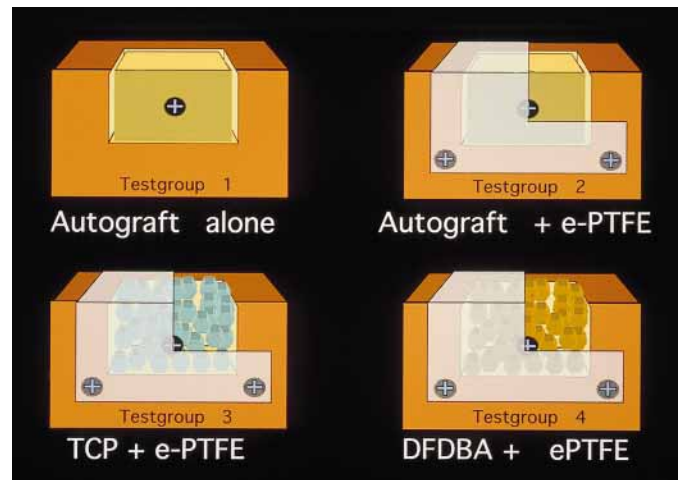


Fig. 2. Schematic illustrations of the four tested grafting procedures.

employing a fissure bur, and the buccal bone plate was removed with a chisel placed in the cut groove. In order to accentuate the defect, a pear-shaped bur was utilized. Caution was exercised to retain the lingual cortex and the height of the crest. All drilling was done with sterile saline irrigation. Finally, the flaps were reapproximated with interrupted sutures. These were removed two weeks postoperatively.

**Surgery 2 (Ridge augmentation)**

Two months later, the defect sites in the mandible were reopened using a mid-crestal incision from P1 to M1 (Fig. 1). Vertical releasing incisions enabled full access to the area. All granulation tissue was carefully removed from the formerly created ridge defects. To open up the bone marrow space around the chronic-type bone defect, small holes were drilled into the surrounding cancellous compartment. The four bone defects were then augmented in four different ways with random assignment of each grafting treatment (Table 1, Fig. 2).

- Site 1: *Autogenous bone (Autograft) alone*
- Site 2: *Autogenous bone (Autograft) with ePTFE-membrane*
- Site 3: *Tricalcium phosphate (TCP) with ePTFE-membrane*
- Site 4: *Canine demineralized freeze-dried bone allograft (DFDBA) with ePTFE-membrane*

The autografts were harvested from the site of the formerly extracted M1. Cortico-cancellous block grafts were procured from the buccal aspect using a small round bur to outline the grafts with a series of perforations. These were then connected with a side-cutting fissure bur and the fragments relieved with a chisel placed in the cut groove. In addition, cancellous bone was harvested with a surgical spoon. The block grafts were immediately transplanted to their assigned defect sites and secured with a stabilization screw (Memfix®, Institut Straumann AG, Waldenburg, Switzerland). Cancellous bone chips were placed on all sides around and on top of the monocortical block graft. Per dog, one autografted site was subsequently

covered with an ePTFE-membrane (GTAM®, W.L. Gore & Associates, Flagstaff, AZ, USA). The membrane was individually trimmed to overlap the defect margins by about 2 mm. The membrane was stabilized with two Memfix® fixation screws at the base on the buccal aspect. Subsequently, it was draped over the augmented site and tucked underneath the mobilized lingual flap. The third defect was grafted with DFDBA particles processed from canine tibia (Osteotech Inc., Shrewsbury, NJ, USA). The graft particles measured 250–500 µm. The remaining defect was augmented with TCP granules (Ceros®TCP, Robert Mathys AG, Bettlach, Switzerland) for ridge augmentation. The granules had a particle size of 0.7–1.4 mm, a porosity of 60% and a pore size of 100–400 µm. Both DFDBA- and TCP-sites received membranes. In order to prevent membrane collapse, a supporting Memfix® screw was inserted into the lingual cortex in the middle of the defect. The defects were then densely packed with the bone grafting material which was mixed with blood obtained from the sur-

**Table 1. Randomization of treatment options per dog and mandibular bone defect**

| Dog       | Mesial defect in right mandible (R1) | Distal defect in right mandible (R2) | Mesial defect in left mandible (L1) | Distal defect in left mandible (L2) |
|-----------|--------------------------------------|--------------------------------------|-------------------------------------|-------------------------------------|
| Dog #2583 | Autograft+M                          | DFDBA+M                              | Autograft alone                     | TCP+M                               |
| Dog #2584 | DFDBA+M                              | Autograft+M                          | TCP+M                               | Autograft alone                     |
| Dog #2586 | DFDBA+M                              | Autograft+M                          | TCP+M                               | Autograft alone                     |

M=membrane DFDBA=demineralized, freeze-dried bone allograft TCP=tricalcium phosphate

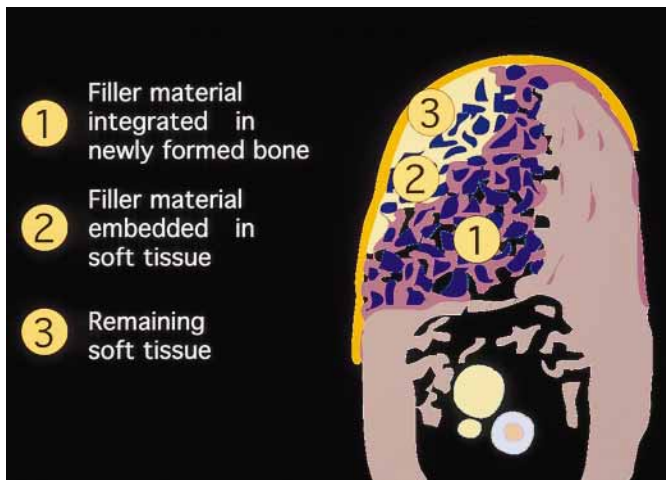


Fig. 3. Definitions of the evaluated tissue compartments within the bone defect delineated by the membrane.

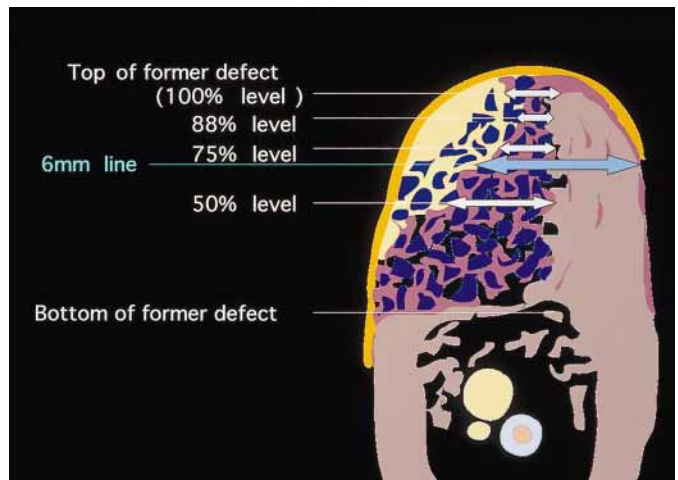


Fig. 4. Horizontal measurements of actual bone gain at different defect levels; determination of level of 6 mm ridge width.

gical site following bone marrow perforation. Membrane adaptation and fixation were carried out similarly to the technique specified above. To facilitate a fluid-tight and tension-free wound closure, the periosteum was released at its base. Wound margins were then reapproximated and closed with horizontal mattress and interrupted sutures. Sutures were removed two weeks postoperatively.

**Sacrifice**

All animals were sacrificed six months after lateral ridge augmentation. Euthanasia was performed with an overdose of pentobarbital sodium 0.2 ml i.v. (=65 mg/kg, Euthanasia-5®, Henry Schein Inc.). Subsequently, the mandibles were block-resected using an oscillating autopsy saw and the recovered segments were immediately immersed in a solution of formaldehyde 4% combined with CaCl<sub>2</sub> 1% prior to histologic preparation.

**Histologic and histomorphometric analysis**

The specimens were prepared for histology as described by Schenk et al. (1984). Non-decalcified specimens were embedded in methyl-methacrylate and stained with toluidine blue and basic fuchsin. Orofacial step sections with a thickness of approximately 80 µm, spaced at intervals of about 1 mm, were obtained for descriptive histology and hi-

stomorphometric analysis. For the latter evaluation, all sections were photographed and prints were made at exactly ×10 magnification of the original sections. Tissue compartments within the bone defect area were delineated and measured using a superimposed grid for point counting. Percentages of each compartment were subsequently calculated for areas showing new bone tissue with integrated filler particles, soft tissue encapsulating non-integrated filler particles, and the rest (soft tissue without filler particles) (Fig. 3). Since percentage values are only relative, absolute measurements were obtained for the actual bone gain, i.e. the width of bone regeneration. Distances were measured from the inside of the residual lingual cortex to the most buccal aspect of new bone formation at levels 50%, 75%, 88% and 100% of the height of the former bone defect (Fig. 4). In view of subsequent placement of a root-form dental implant with an outer diameter of 4 mm, the crest level was identified where it measured at least 6 mm. In addition, the distance from the top of the original crest to this 6 mm line was determined.

**Statistical analysis**

Although 5 to 7 sections were obtained per site, these were only used to increase the precision of measures per site. Therefore, the section values were averaged per site with a statistical test performed using only one value per site.

One-way analysis of variance was employed to determine if any significant differences were present across the four treatments for a given parameter. If the resulting F-test was significant ( $P < 0.05$ ), then Bonferroni-adjusted Student's *t*-tests were run to identify treatments that were significantly different from each other ( $P < 0.05$ ).

**Results**

**Clinical findings**

The overall postoperative wound healing was excellent. Only two minor soft tissue dehiscences were noted in the right mandible of one dog, without further healing disturbances.

**Descriptive histology**

**Autograft alone (Fig. 5)**

Two sites augmented with an autogenous block graft without membrane protection showed resorption at the buccal-crestal aspect of the autograft. Bone formation could not completely keep up, thus resulting in a partial, and therefore inadequate, bony fill of the created defect. In both of these sites it was obvious that the cortical portion of the block graft had undergone remodeling only to a small extent, but the osteoconductivity, i.e. deposition of new bone onto the block surface, was deemed to be excellent. The gaps around the head and the shaft of the stabilization screw might have resulted from initial micromotion

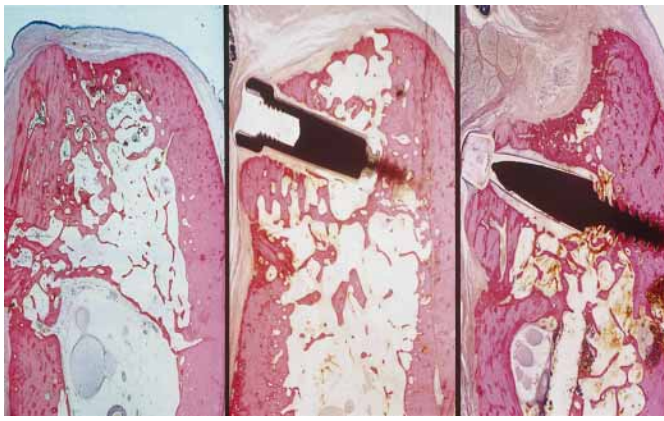


Fig. 5. Histology of the three sites treated by autogenous block grafts alone.

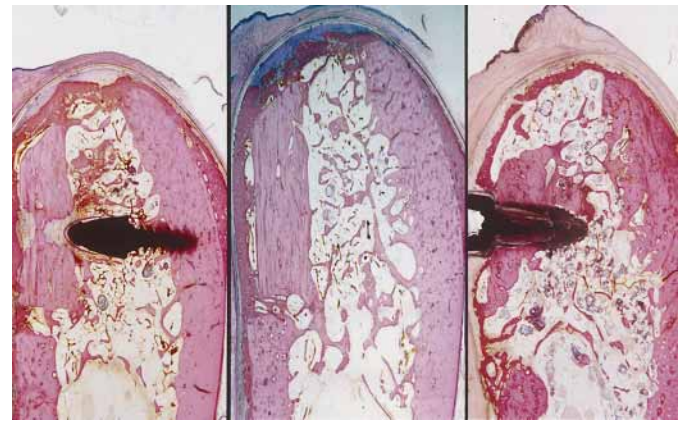


Fig. 6. Histology of the three sites augmented with autogenous block grafts covered with an ePTFE-membrane.

of the graft-screw-complex prior to osseous integration of the block graft. In comparison, the thread portion tapped into the lingual cortex always showed intimate bone contact.

**Autograft+ePTFE-membrane (Fig. 6)**

Sites augmented with an autogenous block graft and ePTFE-membrane coverage demonstrated the most favorable and consistent results in terms of ridge expansion and new bone formation. However, the use of a barrier membrane did not seem to accelerate the remodeling of the cortical portion of the autograft. With regard to preserving the contour of the alveolar ridge, this treatment option showed excellent ridge profiles for the accommodation of a root-form dental implant. Another finding was the formation of a neo-cortex immediately beneath the ePTFE-

membrane. However, direct bone-to-membrane contact was seen less often than anticipated from previous experimental studies. In contrast to the other grafting procedures, more bone apposition was noted on the shaft or head of the fixation screw.

**TCP+ePTFE-membrane (Fig. 7)**

Sites augmented with TCP granules and ePTFE-membrane coverage exhibited very inconsistent findings with regard to ridge contour and amount of new bone formation. One TCP-site had an excellent outcome, whereas the other two TCP-sites showed poor results. On the other hand, regenerated bone in TCP-sites had more bone-to-membrane contact than all other treatment modes. Independent of the quantity of new bone formation, all TCP-sites showed re-

sidual graft particles. TCP granules were also found embedded in connective tissue beneath the membrane and around the stabilization screw. The membrane also had a tendency to collapse toward the bone defect.

**DFDBA+ePTFE-membrane (Fig. 8)**

Sites augmented with DFDBA particles and ePTFE-membrane application also showed great variability in contour maintenance and new bone formation. One site demonstrated a well-preserved ridge with excellent new bone formation. However, the other DFDBA-sites presented with poor osseous regeneration. Large areas of DFDBA particles embedded in connective tissue were present adjacent to the barrier membrane. As for TCP-treated sites, areas around the "tent-pole" screw demon-

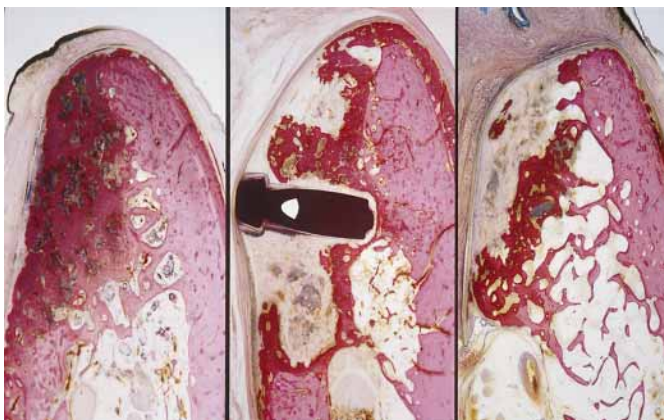


Fig. 7. Histology of the three sites receiving TCP granules covered with an ePTFE-membrane.

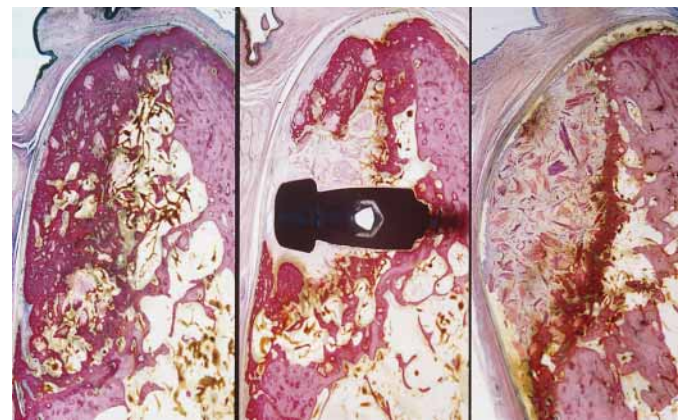


Fig. 8. Histology of the three sites treated with DFDBA particles protected by an ePTFE-membrane.

**Table 2. Area of tissue compartments (in percent) within membrane-protected bone defect (mean±SD)**

| Tissue compartment                                    | Autograft+ Membrane | TCP+ Membrane | DFDBA+ Membrane |
|---|---------------------|---------------|-----------------|
| New bone tissue including integrated filler particles | 91.1±7.9            | 76.6±14.4     | 74.3±15.8       |
| Soft tissue with encapsulated filler particles        | 0.8±2.3             | 11.4±10.9     | 18.8±17.8       |
| Rest (soft tissue without filler particles)           | 8.1±6.3             | 12.0±6.4      | 6.8±5.2         |

TCP=tricalcium phosphate      DFDBA=demineralized, freeze-dried bone allograft

**Table 3. Measurements (in mm) of horizontal bone gain at different defect levels (mean±SD)**

| Defect level      | Autograft alone | Autograft+ Membrane | TCP+ Membrane | DFDBA+ Membrane |
|-------------------|-----------------|---------------------|---------------|-----------------|
| Bone gain at 50%  | 7.3±1.2         | 7.2±1.7             | 4.8±1.3       | 3.8±2.0         |
| Bone gain at 75%  | 4.2±2.3         | 6.0±1.2             | 3.7±1.4       | 3.4±1.3         |
| Bone gain at 88%  | 2.9±1.9         | 4.9±0.9             | 2.8±1.4       | 2.9±1.1         |
| Bone gain at 100% | 1.5±1.6         | 3.5±1.1             | 1.9±0.9       | 1.7±1.0         |

TCP=tricalcium phosphate      DFDBA=demineralized, freeze-dried bone allograft

**Table 4. Distance (in mm) from top of alveolar crest to 6 mm ridge width (mean±SD)**

| Autograft alone | Autograft+Membrane | TCP+Membrane | DFDBA+Membrane |
|-----------------|--------------------|--------------|----------------|
| 1.6±1.2         | 0.9±0.7            | 2.2±1.6      | 2.3±1.5        |

TCP=tricalcium phosphate      DFDBA=demineralized, freeze-dried bone allograft

strated the least amount of bone formation.

**Histomorphometry**

Tissue compartments were only analyzed for three treatment options. Autografted sites without membrane application were excluded from this analysis since the defect area was not confined by a membrane. Among the evaluated treatment options, autografts with membrane protection (autograft+M) showed the highest percentage of new bone tissue with integrated graft particles (91.1±7.9%) compared to 76.6±14.4% for TCP+membrane-treated sites and 74.3±15.8% for DFDBA+membrane (Table 2). However, the differences between the three treatment options ( $P>0.3$ ) were statistically not significant. With regard to horizontal measurements of ridge enlargement, autograft+M sites showed the highest values (i.e. the largest bone gain) at all defect levels compared to the other experimental treatments. For example, bone gain at

the crestal level for autograft+membrane-treated sites measured 3.5±1.1 mm compared to only 1.5±1.6 mm for autografts alone or 1.7±1.0 mm for DFDBA+membrane (Table 3). At the 75% defect level, autograft+membrane-treated sites showed 6.0±1.2 mm bone gain compared to 3.4±1.3 mm for DFDBA+membrane or 3.7±1.4 mm for TCP+membrane. However, differences were not statistically significant ( $P>0.1$ ). The distance from the top of the crest to the 6 mm line measured only 0.9±0.7 mm in autograft+M sites, indicating a well-preserved ridge profile (Table 4). The worst value was recorded for DFDBA+membrane-treated sites with 2.3±1.5 mm. Again, no significant differences were observed across the treatment options ( $P>0.1$ ).

**Discussion**

The present pilot study has evaluated different bone grafting materials for lateral ridge augmentation in an experi-

mental dog model. A clinically frequent situation with mandibular bone atrophy was simulated by creating chronic bone defects on the buccal aspect of the alveolar ridge. Although no statistically significant differences were found in this pilot study of 3 animals across the tested treatment options, defect sites augmented with autografts and barrier membranes showed the most promising results from a clinical, histologic as well as histomorphometric perspective. The present study corroborates data from other clinical and experimental studies demonstrating the benefit of combining autografts and barrier membranes for localized ridge augmentation using the GBR principle (Becker et al. 1995, Buser et al. 1996).

A large number of experimental animal studies have evaluated the GBR technique using a barrier membrane. However, the majority of these experimental studies have reported osteopromotion techniques in extraoral bone defects or bone regeneration around simultaneously inserted implants. The present experimental study has evaluated regeneration of jawbone. Similar experimental studies evaluating regeneration of jawbone using barrier membranes with or without a filler material are listed in Table 5. The great variability of study parameters such as test animals (rats, rabbits, minipigs, dogs, monkeys), surgical access (intraoral, extraoral), type and size of bone defect (acute, chronic; transosseous, contained) and defect location (ramus, alveolar ridge) make a comparison of the studies difficult.

A number of studies were conducted in rats, a low phylogenetic animal characterized by a high osteogenic potential (Dahlin et al. 1988; Sandberg et al. 1993; Dahlin et al. 1994; Zellin et al. 1995; Furusawa et al. 1998; Salata et al. 1998; Zahedi et al. 1998). In addition, most of these studies analyzed bone regeneration of acute, small and transosseous bone defects in the mandibular ramus. These models, therefore, do not represent the typical clinical situation encountered in patients where a chronic and large bone defect is often present on the buccal aspect of the alveolar ridge.

The first experimental study utilizing the membrane technique for ridge augmentation of such defects was published

**Table 5. Summary of experimental animal studies evaluating the GBR principle for jawbone promotion without concomitant or subsequent implant insertion**

| Author               | Animal  | Access    | Site                                    | Defect size  | Defect type | Tested membranes  | Fillers  |
|----------------------|---------|-----------|---|--|-------------|---|--|
| Dahlin et al. 1988   | Rat     | Intraoral | Mandibular angle                        | Ø 5 mm transosseous                                      | Acute       | ePTFE   | None   |
| Dahlin et al. 1990   | Monkey  | Intraoral | Mandibular alveolar ridge               | 12×8 mm; apical through-and-through                      | Acute       | ePTFE   | None   |
| Seibert & Nyman 1990 | Dog     | Intraoral | Maxillary and mandibular alveolar ridge | 13×7×3.5 mm contained, buccal                            | Chronic     | ePTFE   | Porous HA blocks; tissue growth matrix (porous PTFE) |
| Sandberg et al. 1993 | Rat     | Extraoral | Mandibular angle                        | Ø 5 mm transosseous                                      | Acute       | ePTFE; 3 bioabsorbable PLA/PLG prototypes with different resorption times (8, 20, 40 weeks) | None   |
| Dahlin et al. 1994   | Rat     | Extraoral | Mandibular angle                        | Ø 5 mm transosseous                                      | Chronic     | ePTFE   | None   |
| Fritz et al. 1994    | Monkey  | Intraoral | Mandibular alveolar ridge               | 10×8 mm and 16×8 mm; Chronic crestal through-and-through | Chronic     | ePTFE reinforced with a polypropylene mesh  | None   |
| Schenk et al. 1994   | Dog     | Intraoral | Mandibular alveolar ridge               | 12×10×8 mm crestal through-and-through                   | Acute       | ePTFE; prototype reinforced ePTFE   | None   |
| Bartee & Carr 1995   | Rat     | Extraoral | Mandibular angle                        | Ø 4 mm transosseous                                      | Acute       | High-density nPTFE (TefGen-FD)  | None   |
| Smukler et al. 1995  | Dog     | Intraoral | Maxillary and mandibular alveolar ridge | Vertical and buccal deficiencies (size N/A)              | Chronic     | ePTFE; allogenic bone membrane  | Cortical columns of DFDBA (canine source)            |
| Zellin et al. 1995   | Rat     | Extraoral | Mandibular angle                        | Ø 5 mm transosseous                                      | Acute       | 10 different non- and bioabsorbable membranes   | None   |
| Buser et al. 1998    | Minipig | Extraoral | Mandibular angle                        | 12×12×5 mm contained, buccal                             | Acute       | ePTFE   | Collagen, autograft, DFDBA, TCP, HA                  |
| Furusawa et al. 1998 | Rat     | N/A       | Mandibular alveolar ridge               | Ø 2 mm (1–1.5 mm deep) contained, buccal                 | Acute       | Collagen  | Bioactive glass particles                            |
| Lundgren et al. 1998 | Rabbit  | Intraoral | Maxillary alveolar ridge                | 11×5×3 mm contained, buccal                              | Acute       | ePTFE; occlusive or perforated titanium foils   | None   |
| Salata et al. 1998   | Rat     | Extraoral | Mandibular ramus                        | Ø 3 mm transosseous                                      | Chronic     | ePTFE   | HA granules, glass ionomer granules                  |
| Zahedi et al. 1998   | Rat     | Extraoral | Mandibular ramus                        | Ø 5 mm transosseous                                      | Acute       | Collagen (bovine Type I)  | None   |
| Simion et al. 1999   | Dog     | Intraoral | Mandibular alveolar ridge               | 10×8×10 mm crestal through-and-through                   | Acute       | Titanium-reinforced ePTFE, two prototypes of titanium-reinforced ePTFE                      | None   |

ePTFE=expanded polytetrafluoroethylene  
DFDBA=demineralized freeze-dried bone allograft  
HA=hydroxyapatite  
TCP=tricalcium phosphate  
N/A=not available

by Seibert & Nyman in 1990. In fact, similar to the present study, chronic and buccal bone defects were created in the premolar area in the maxilla and mandible of two beagle dogs. Three months later, ridge augmentation was performed. A filler material (HA) was used for space maintenance, with or without ePTFE-membrane coverage. In addition, some sites received only membranes or were

sham-operated. Evaluation included comparison of photographs taken at different time intervals and histologic assessment at the completion of the study after 2–3 months. Histologically, spaces provided by membrane coverage were filled with bone matrix which had not yet matured. Sites without filler material showed membrane collapse towards the defect, reducing the amount of newly

formed bone. No new bone formation was observed in the sham-operated control sites without membrane application.

The use of GBR to fill even larger bone voids was reported by Fritz et al. (1994). Extended chronic, mandibular bone defects created through *en bloc* resection were examined in three primates. Since no bone fillers were utilized, the ePTFE-membranes were reinforced with a poly-

propylene mesh lamination for space maintenance. Within 4 weeks, two out of six membrane sites experienced soft tissue dehiscence with subsequent infection. The remaining sites healed uneventfully. Histologically, substantial new bone formation was found after 12 months and the regenerated bone exhibited normal maturation dynamics. These findings were corroborated in a similar experimental model conducted in dogs (Schenk et al. 1994). Standard and prototype reinforced ePTFE-membranes without a filler material were used to evaluate the pattern of bone regeneration of acute and transosseous bone defects located in the mandibular alveolar ridge. The histologic evaluation showed a sequence of maturation steps closely resembling the pattern of bone development and growth. Control sites without barrier membranes clearly resulted in less bone formation. The benefit of using a barrier membrane was also shown in the present study comparing the two autograft treatment options with or without membrane coverage. Block grafts with membrane application maintained their contour, whereas non-protected block grafts underwent crestal and buccal bone resorption.

Only one other experimental study has evaluated DFDBA filler materials for lateral ridge augmentation of non-periimplant bone defects in dogs using the membrane technique (Smukler et al. 1995). Similar to the present study, chronic and buccal bone defects of the alveolar ridge were treated with different surgical methods. Experimental sites received barrier membranes (ePTFE or allogenic bone membranes), and allogenic cortical bone struts were inserted for membrane support. In some sites, the voids were filled with DFDBA particles. Control sites were not covered with membranes. At the completion of the study after 3 months, osseous regeneration was histologically observed only in membrane-protected defects. The added DFDBA particles were usually embedded in connective tissue and, apparently, did not contribute to bone regeneration. A similar conclusion was drawn from the present study in which the application of DFDBA particles + membrane did not enhance bone for-

mation in lateral ridge augmentation of large bony defects. Similarly, clinical and experimental studies have questioned the use of DFDBA around dental implants since DFDBA particles were often found enmeshed in minimally inflamed connective tissue (Becker et al. 1995; Becker et al. 1996).

With regard to the TCP filler material, apart from the minipig study by Buser et al. (1998) mentioned in the introduction, no other experimental study has been published evaluating this material in conjunction with membrane coverage for osseous regeneration of large bone defects. The promising results obtained in the cited minipig study or in studies conducted in other extraoral sites (Nagahara et al. 1992; Breitbart et al. 1995; Hamson et al. 1995) could not be confirmed in the present study. The particulate texture of the TCP filler material in combination with the geometry of the bone defect might have led to graft instability. As a consequence, large areas of the filler material were encapsulated by connective tissue, suggesting initial micromotion. Apparently, the "tent-pole" screw did not enhance the stability of the grafting material, since it was also encapsulated by soft tissue. Therefore, this treatment option of using an alloplastic filler material protected by a barrier membrane but without the addition of autogenous bone appears to be least predictable for lateral augmentation of large bone defects of the alveolar ridge. In general, a particulate grafting material irrespective of its source might be more susceptible to initial micromotion compared to a block graft stabilized with a fixation screw. The present study has clearly demonstrated such an association, suggesting less favorable terms for the tested DFDBA and TCP granules for lateral ridge augmentation of large bone defects compared to autogenous bone blocks.

## Conclusions

1) Within the limits of this pilot study, cortico-cancellous block grafts and bone chips covered with an ePTFE-membrane were found to be superior

to the other grafting procedures in terms of ridge enlargement and amount of new bone formation.

- 2) Autografts with membrane protection also yielded the best crestal contour in view of subsequent placement of a root-form dental implant.
- 3) In contrast, autografts without membrane protection showed considerable crestal bone resorption.
- 4) Both DFDBA and TCP filler materials, although protected with an ePTFE-membrane, yielded inconsistent results with a large variability of treatment outcome.
- 5) Although significant differences among the four treatment conditions were not found, likely due to the limited number of animals, autogenous bone covered by an ePTFE-membrane showed the most consistent and predictable results.

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## Résumé

L'épaulement latéral de crête osseuse est devenu une option de traitement standard pour augmenter le volume osseux de sites trop peu importants et devant recevoir des implants. Afin d'éviter une autogreffe et ainsi éliminer les procédures chirurgicales additionnelles et les risques qui y sont associés, des matériaux de greffage osseux et des substituts ont été proposés. Avant que les recommandations cliniques puissent être faites, ces matériaux doivent être extrêmement bien analysés lors d'études expérimentales simulant les situations cliniques. L'étude pilote suivante a été effectuée sur trois chiens. Différents processus de greffage ont été comparés pour l'épaulement de lésions latérales, étendues (8×10×14 mm) et chroniques dans la crête alvéolaire mandibulaire. Les sites

expérimentaux ont reçu des granules de phosphate tricalcique (TCP) ou des particules allogènes osseuses congelées, séchées et déminéralisées (DFDBA). Des membranes barrières en téflon (ePTFE) ont été placées pour protéger ces greffons. Ces approches chirurgicales ont été comparées à l'épaissement de la crête utilisant des greffons en bloc d'os autogène cortical et spongieux avec ou sans utilisation de membranes ePTFE. Après six mois de guérison les sites ont été analysés histologiquement et histomorphométriquement. Les sites autogreffés avec protection membranaire montraient d'excellents résultats de guérison avec un profil de la crête bien constitué tandis que les greffons en bloc non-protégés subissaient une résorption vestibulo-crestale limitant clairement la suite du traitement. Les matériaux testés alloplastiques (TCP) et allogéniques (DFDBA) apportaient des résultats inconsistants avec parfois une mise en capsule de particules dans le tissu conjonctif réduisant ainsi la largeur osseuse crestale. Cette étude pilote propose donc l'utilisation des autogreffes avec des membranes barrières pour l'augmentation latérale des crêtes osseuses de lésions alvéolaires étendues.

## Zusammenfassung

Der seitliche Alveolarknochenkammaufbau ist zur Standardbehandlung beim Aufbau von fehlendem Knochen an den für Implanationen vorgesehenen Stellen geworden. Um die Entnahme von autogenen Transplantaten und den somit zusätzlichen operativen Eingriff mit all seinen Risiken zu vermeiden, können Knochentransplantate und Ersatzmaterialien alternative Füllstoffe für den Knochenkammaufbau sein. Bevor jedoch klinische Empfehlungen abgegeben werden können, müssen solche Materialien in experimentellen Modellen, die klinisch relevante Situationen nachstellen, gründlich studiert werden. Diese Pilotstudie wurde mit drei Hunden durchgeführt. Man untersuchte verschiedene Transplantationsverfahren zum Aufbau ausgedehnter (8×10×14 mm), seitlicher und chronischer Knochendefekte am Unterkieferalveolarkamm. Die experimentellen Stellen wurden aufgebaut mit Tricalciumphosphatkörnern (TCP) oder entmineralisierten, gefriergetrockneten Knochentransplantatkörnern (DFDBA). Zum Schutz der Transplantate

wurden Membranen (ePTFE) darübergespannt. Diese Verfahren verglich man mit dem Einsatz von autogenen korticospongiösen Transplantatblöcken, sowohl mit und ohne ePTFE-Membranabdeckung. Nach einer Heilphase von sechs Monaten wurde die Stellen histologisch und histomorphometrisch analysiert. Membrangeschützte und mit allogenen Material gefüllte Stellen zeigten hervorragende Heilungsergebnisse und ein gut erhaltenes Alveolarkammprofil. Die nicht geschützten Blöcke waren einer bucco-crestalen Resorption unterworfen, die ganz klar das klinische Resultat einschränkte. Die getesteten alloplastischen (TCP) und allogenen (DFDBA) Füllmaterialien zeigten sehr variable Ergebnisse, teils mit Bindegewebeinkapselung von Partikeln. Dies schränkte den Erfolg der Knochenkammverbreiterung ein. Diese Pilotstudie unterstreicht die Bedeutung des Einsatzes von Autotransplantaten mit Membranen beim seitlichen Alveolarknochenkammaufbau von ausgedehnten Alveolarknochendefekten.

## Resumen

El aumento de la cresta lateral se ha convertido en una opción de tratamiento estándar para incrementar el volumen óseo de lugares de recepción deficientes antes de la colocación del implante. En orden a evitar la recolección de un autoinjerto y por lo tanto eliminar procedimientos quirúrgicos y riesgos, los materiales de injerto óseo y los sustitutos son unos materiales de relleno alternativos para ser usados en aumentos de la cresta. Antes de poder hacer recomendaciones clínicas, dichos materiales deben ser estudiados extensivamente en modelos experimentales que simulen las situaciones clínicas relevantes. En presente estudio piloto fue conducido en tres perros. Se evaluaron diferentes procedimientos de injertos para el aumento de defectos óseos laterales, extensos (8×10×14 mm) y crónicos en la cresta alveolar mandibular. Los lugares experimentales recibieron gránulos de fosfato tricálcico (TCP) o partículas de aloinjerto óseo desmineralizado congelado seco (DFDBA). Se colocaron membranas de barrera (ePTFE) para la protección del injerto. Estos enfoques se compararon con aumentos de la cresta usando injertos autógenos en bloques corticales, tanto con como sin aplicación de membranas- ePTFE. Des-

pués de un periodo de cicatrización de 6 meses, los lugares se analizaron histológicamente e histomórfometricamente. Los lugares con autoinjertos y protección de membranas mostraron unos excelentes resultados de cicatrización con un perfil de cresta bien preservado, mientras los bloques de injertos no protegidos sufrieron reabsorción buccocrestal limitando claramente los resultados del tratamiento. Los materiales de relleno aloplásticos (TCP) y alogénicos (DFDBA) presentaron hallazgos inconsistentes con encapsulación en ocasiones de partículas de tejido conectivo, por lo tanto reduciendo la anchura de la cresta ósea. El presente estudio piloto apoya el uso de autoinjerto con membrana de barrera para aumento de la cresta lateral de defectos óseos alveolares extensos.

## 要旨

側方顎堤増多術はインプラント埋入にインプラント床の先立ち骨量不足を補うための標準的な治療選択肢法になっている。顎堤増多術において自家骨採取のための追加手術やリスクを避けるために、骨移植材料や代替材料がフィラー材料として用いられている。このような材料は臨床応用の前に、妥当な臨床条件を模擬再現した実験モデルにおいて、徹底的に検討すべきである。本パイロット研究は、3匹の犬において下顎堤の側方に広範な(8×10×14mm)慢性骨欠損を作成し、顎堤増多に幾つかの異なる移植手順を用いて評価した。実験部位は、燐酸3カルシウム(TCP)の顆粒あるいは脱灰乾燥凍結同種骨(DFDBA)の顆粒を入れ、バリアー・メンブレン(ePTFE)を用いて移植片を保護した。自家皮質骨-海綿骨ブロック移植にePTFEメンブレンの有無を組み合わせた、これらの術式による顎堤増多術を比較した。治療6ヶ月後これら部位を組織学及び組織形態測定学によって分析した。メンブレンで保護した自家骨移植部位は優れた治療結果を示し、顎堤の輪郭は良好に保存されていた。他方保護しなかったブロック移植片は明らかに頰側一係線部の吸収を起しており、治療結果に限界があった。試験部位の人工フィラー材料(TCP)および同種骨材料(DFDBA)は、時として結合組織に顆粒が取りこまれていることがあり、歯槽頂線の幅が減少していた。本パイロット研究の結果は、広範な歯槽骨欠損の側方顎堤増多のために、バリアー・メンブレンと併用する自家骨の使用を支持するものである。

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