

## Augmentation of osseous-implant dehiscence with membrane alone or with a combination of bone graft and membrane

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هدف هذا البحث لمقارنة محيط العظم والقابلية لنمو عظم جديد في عيوب الغرسات العظمية المطعمة بجزيرات عظم مغاير منسزوعة المعدن والمغطى بغشاء تجدد النسيج الموجه، مع عيوب تمت تغطيتها بغشاء تجدد النسيج الموجه فقط. شملت الدراسة سبع من الماعز غرست في كل واحدة منها أربع غرسات في الصفيحة الخدية للحزء الأسفل من جسم الفك السفلي، واستعملت أربعة أنواع من الأغشية وهي: NP-BioBarrier®، P-BioBarrier®، Biomend®، Capset® ومادة التطعيم المستعملة هي Laddec®. شملت مجموعة الدراسة أربعة وعشرون عيباً للغرسات العظمية، اثنا عشرة منها للتطعيم مع التغطية بأحد أنواع الأغشية، وبذلك يكون كل نوع من الأغشية قد استعمل لتغطية ثلاثة عيوب مطعمة. أما بقية الاثنا عشر عيباً فقد جرى تغطيتها بأحد أنواع الأغشية فقط، وكما سبق فكل نوع من الأغشية استعمل لتغطية ثلاثة عيوب. دلت النتائج على تزايد كمية العظم في العيوب باستعمال الأغشية. تراوح محيط العظم في العيوب غير المطعمة بين 550 مايكرومتر و 1135 مايكرومتر. لوحظت أكثر نخانة للعظم في العيوب غير المطعمة التي تمت تغطيتها بغشاء 1135 (Capset® مايكرومتر). ازدادت نخانة العظم في العيوب العظمية المطعمة إذ تراوحت الزيادة ما بين 512 و 950 مايكرومتر عن ماهو عليه في العيوب غير المطعمة. ومن بين الأغشية المستعملة يمكن القول بأن غشاء NP-BioBarrier® قد أدى إلى أكثر نخانة في العظم في العيوب المطعمة (1800 مايكرومتر). لم يلاحظ حدوث أية زيادة في العظم في عيوب مجموعة المقارنة.

This investigation compared bone contour and the potential for new bone growth in osseous-implant defects grafted with demineralized xerographic bone particles (DXBP) and covered with guided tissue regeneration membrane (GTRM), with defects covered with GTRM alone. In the study, each of seven goats received four implants. The implants were fixed in the buccal cortex of the left body of the mandible. Four types of GTRM were used. These were Capset®, Biomend®, P-BioBarrier®, and NP-BioBarrier®. The grafting material used was Laddec®. Twenty-four osseous-implant defects were used as the test group. Twelve of these defects were grafted and covered with one of the GTRMs used, so that each GTRM covered 3 grafted defects. The remaining 12 test defects were covered with one of the GTRMs alone; again, each membrane was used for 3 defects. It was found that both resorbable and non-resorbable GTRMs augmented implant-osseous defects. The range of bone contour in the ungrafted defects was between 550 and 1135 µm. Capset membrane produced the thickest bone in the ungrafted defects (1135 µm). Grafting osseous-implant defects increased the bone thickness. The increase ranged from 512 to 950 µm. Of the membranes tested, NP-BioBarrier produced the thickest bone in the grafted defects (1800 µm). Control osseous-implant defects were not augmented with new bone.

### Introduction

Different grafting materials have been used to augment the bone in deficient implant sites. These materials include filling materials that serve as a scaffold for new bone growth (osteoconduction),<sup>1,2</sup> growth factors that transform undifferentiated mesenchymal cells into osteoblasts (osteoinduction),<sup>2-4</sup> autogenous bone grafts in the form of particles or blocks that have both osteoinduction and osteoconduction properties,<sup>5,6</sup> and guided bone regeneration membrane (GTRM) based on the concept of using a barrier to separate bone from soft tissues and at the same time creating a space into which new bone can grow.<sup>7,8</sup>

Demineralized xerographic bone particles (DXBP) have been used to fill various bone defects successfully and in conjunction with implant-bone dehiscence.<sup>6, 9,18,22-24</sup>

Laddec is a resorbable natural hydroxyapatite (HA) material derived from trabecular bone matrix

taken from the femoral condyles of 6-month-old calves. It is a demineralized and deproteinized porous bone graft consisting of cancellous bone granules with a diameter of around 600 µm. Since all raw materials and organic components are removed during processing, this bone is essentially cancellous bone matrix made of purified mineralized type I collagen that retains the trabecular bone microstructure.<sup>13, 16</sup>

This study compared bone thickness and the potential for new bone growth in bone-implant defects grafted with DXBP (Laddec) and covered with GTRM to defects covered with GTRM alone.

### Material and Methods

Seven goats each 8 months old and weighing approximately 20 kg were used. Each animal received four dental implants 3.75 mm in diameter and 8 mm long (Osteo® Implant Corp., New Castle, PA, USA). The implants were fixed in the buccal cortex of the left side of the body of the mandible.

Four types of GTRM were used to cover the

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bone-implant defects. Each was derived from a different source (collagen-based, polymers, or synthetic). Two membranes were resorbable and two were non-resorbable. The resorbable GTRMs were bovine collagen-based Biomend® (Calcitek Inc., Carlsbad, CA, USA) and calcium sulfate hemihydrate (Capset®, Lifecore Biomedical Inc., Chaska, MN, USA). The non-resorbable GTRMs were non-porous polytetrafluoroethylene (PTFE) 0.185 mm thick (NP-BioBarrier®, IMTEC Corp., Ardmore, OK, USA) and porous PTFE with 5-micron pores, 0.125 mm thick (P-BioBarrier®, IMTEC Corp. Ardmore, OK, USA).

The grafting material used to augment the implant-bone defects was bovine DXBP (Laddec®, Transphyto S.A., Clermont, Ferrand, France). The test group consisted of 24 osseous-implant defects. Each GTRM was used to cover 3 grafted defects and 3 ungrafted test defects. Different combinations of GTRMs, with and without bone graft, were used in different animals. Four osseous-implant defects were left ungrafted and uncovered by membrane to act as controls.

All the goats were given a presurgical intramuscular injection of inactivated vaccination against toxic anaerobic bacterial infections (Imotoxan®, Rhone Merieux, Lyon, France). An initial 2-ml dose was given 2 weeks before the start of the experiment and another dose was given 4 weeks later. The animals were also given inactivated adjuvanted vaccine against pasteurellosis (Aysopast®, Rhone Merieux, Lyon, France). An initial 1-ml dose was given 2 weeks before surgery and another dose was given 4 weeks later.

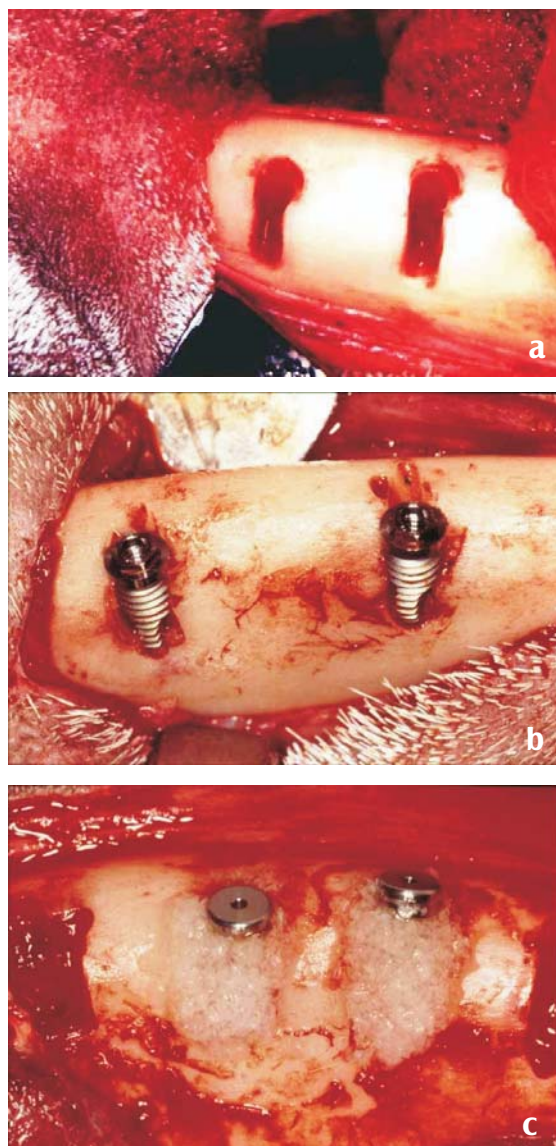
Post-surgically, the animals were medicated with an analgesic dose of analgin 0.5 ml i.m. twice daily for 3 days (Pharalgin®, Arab Drug Co., Cairo, Egypt). The animals were also given an intramuscular injection of long acting antibiotics at a dose of 0.2 ml/kg containing 12,500,000 IU benzyl penicillin benzathine and 5 g streptomycin per 100 ml (Duphopen Strap® B.P., Solvay, Italy).

The goats were sedated with an intramuscular injection of xylazine 0.15 g/kg (Seton® 2% Laboratorios Calier, S.A. Barcelona, Spain). The animals were given an intramuscular injection of atropine sulfate pre-surgically (1% 50 (g/kg Arab Drug Co., Cairo, Egypt). Animals were anaesthetized with 0.2% halothane general anesthesia via an endotracheal tube for the duration of the surgical procedure.

An intravenous line was maintained with 5% dextrose, 0.45% sodium chloride solution at 50 ml/hr (Abbot, North Chicago, IL, USA) during

surgery and for 2 hours afterwards.

### Surgical Procedures (Fig. 1)



**Fig. 1.** Surgical procedure used in implant placement.  
 a) Exposure of the buccal side of the body of the mandible; preparation of implant sockets and creation of a buccal cortical defect in each implant socket.  
 b) Placement of the implants.  
 c) Grafting osseous defects with Laddec particles.

The facial hair was shaved on the left side of the mandibular and in the mental region. The skin was washed with chlorohexidine. Lidocaine 2% with 1/100,000 epinephrine (Astra, Sodertalje, Sweden) was injected subperiosteally through the skin at the lower border of the left side of the

mandible.

An extra-oral incision was made at the lower border of the left mandible starting from the angle of the mandible and extending 5 cm anteriorly. Skin and periosteal flaps were elevated to expose the underlying lower border of the mandible. Bony defects were prepared in the buccal cortex of the mandible 1.5 cm. apart. Soft tissue in the mental region was carefully reflected and the mental foramen was located visually.

Standard surgical procedures for bone receiving an implant were used to prepare the implant socket. The bone defects for implant insertion measured approximately 8 mm high and 3 mm wide. A fissure bur 2.5 mm wide and 8 mm long was used to prepare a 3-mm wide dehiscence in the buccal cortical bone in each implant socket, under a continuous stream of saline. One standard Osteo implant 3.75 mm wide and 8.0 mm long was placed into each bony socket. Emphasis was placed on minimizing surgical trauma during preparation of the implant sockets and on achieving primary bone-implant stability.

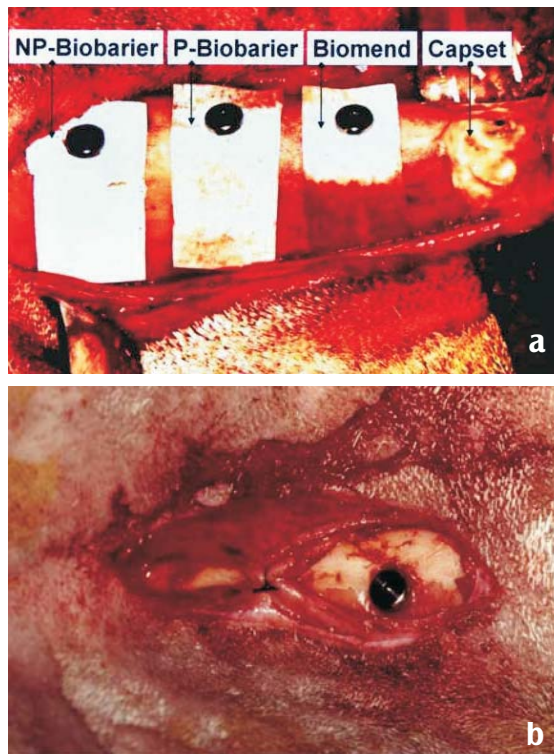
Photographs of the surgical area were taken after preparation of the bony defects, after implant insertion, after membrane fixation, and after sacrificing the animals.

#### Membrane Fixation (Fig. 2)

Each membrane was laid on top of the exposed implant surface. At least 5 mm of membrane extended beyond the fixture-healing cap and the margins of the osseous defect. The calcium sulfate membrane (Capset) was mixed with sterile saline and placed on the osseous defects when it had a dough-like consistency without fixation. The other membranes were fixed with the healing cap for the respective fixture. All membranes at the bottom of the defects were carefully secured in place by tucking underneath the reflected periosteal flaps. Additional stability of these membranes was obtained by suturing periosteal flaps between the membranes and on top of the membrane with 3-0 resorbable sutures (Vicryl® Ethicon, Johnson & Johnson International, Brussels, Belgium) (Fig. 2b). The calcium sulfate barrier was applied on top of bone-implant defects without fixation or tucking underneath the periosteum. The periosteal layers and skin flaps were shaped and sutured before the Capset hardened completely to prevent it from cracking.

The periosteal flaps covering all the test and control defects were incised and several horizontal cuts were made on top of the bone defects in order to open the periosteal tissue

barrier and allow soft tissue cells to re-adapt and heal again.



**Fig. 2.** Fixation of different membranes.  
a) Capset, Biomend, P-Barrier, NP-BioBarrier.  
b) Suturing a periosteal flap between and over each implant.

All animals were sacrificed 4 months after surgery. The surgical sites were re-opened. The skin and periosteum were incised and a full thickness flap elevated. The surgical sites were photographed and then the sections of bone containing the implants were cut out *en bloc*.

Radiographs of each implant-bone specimen were taken after cutting out the specimens *en bloc* to show a bucco-lingual view of the implant-bone defect (Fig. 5). All bone blocks were placed on top of the x-ray film and were positioned 1 cm from the x-ray cone after establishing a 1:1 magnification ratio with a reference metallic ball.

Each bone bloc was then labeled and fixed in 10% formalin solution for histologic processing.

#### Histologic Preparation

Undecalcified block samples were fixed in 10% formalin solution for one month and dehydrated through a graded series of ethanol (70 - 90%). The infiltrating and embedding resin used for undecalcified specimens was JB-4 Plus®

embedding kit (Polysciences Inc., Washington, PA, USA).

Infiltration resin was prepared by mixing 1 gram of JB-4 Plus Catalyst powder with 100 ml of JB-4 Plus Solution A. Bone samples were immersed in the infiltration solution for 10 days at 4°C in a dark bottle.

An electric diamond cutting wheel (Leitz, Germany) was used to cut 50- $\mu$ m sections from the specimens. A longitudinal cut from the top of the healing screw to the bottom of the implant was made in the bucco-lingual direction in the middle of the implant and the investing bone. A vacuum adhesive system was used to mount the polymerized tissue sections on Plexiglas slides using photo-polymerizing glue. The surface of the final specimen tissue was treated with 30% hydrogen peroxide for 1 minute and then stained with toluidine blue stain to evaluate osseointegration between the exposed implant surface and the newly regenerated bone in the augmented osseous defects. Additional bone specimens were cut in similar manner from the grafted defects and stained with Goldner's trichrome stain to evaluate the maturity and quality of the newly formed bone near the augmented implant surface. The stained sections were washed with alcohol, then with water, and finally dried. A precision adhesive press was used to affix the stained sections on plane parallel Plexiglas slides with photo polymerizing glue.

The sections of the grafted sites were viewed also under polarized light to evaluate the status of the bone remodeling in conjunction with the implant surface and remnants of the graft material.

#### Measurement of the new bone thickness

The thickness of new bone from the deepest point on the implant threads in the middle of the implant to the external surface of the augmented cortical bone was measured. Each radiograph was imaged using the image analysis system (IAS) and evaluated by one examiner. The IAS consists of (1) viewer optics (Polyvar<sup>®</sup>, Richert-Jung; Austria), (2) an image-analysis device (Leica<sup>®</sup>, Cambridge, UK), (3) a video camera (Donphisha<sup>®</sup>, Sony; Japan), and (4) a computer-based image processor based on the Qwin<sup>®</sup> software program. Qwin is a Leica Windows<sup>®</sup>-based image analysis tool for measurements in a fully automated system.

All the radiographs (active and control) were compared in the same manner.

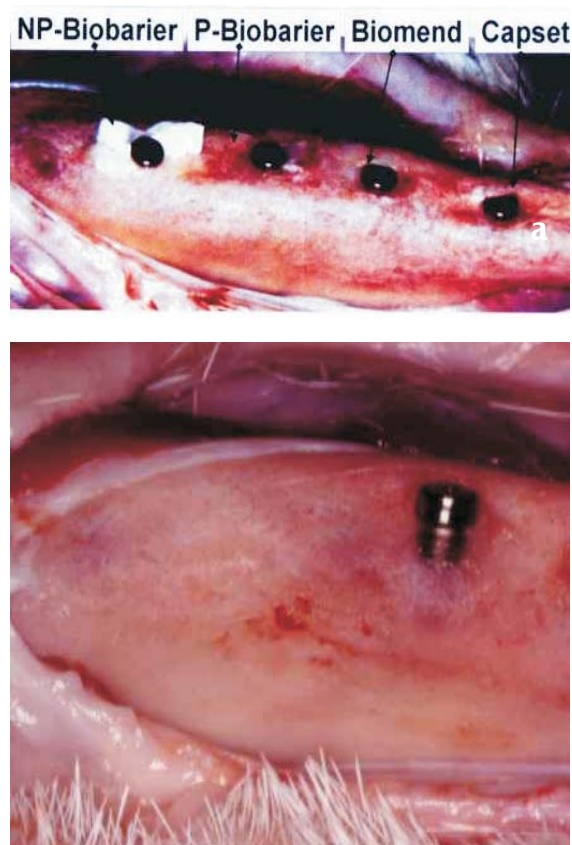
The mean bone thickness was determined for

each GTRM with and without bone grafting. The bone thickness in the control defects was evaluated in the same manner.

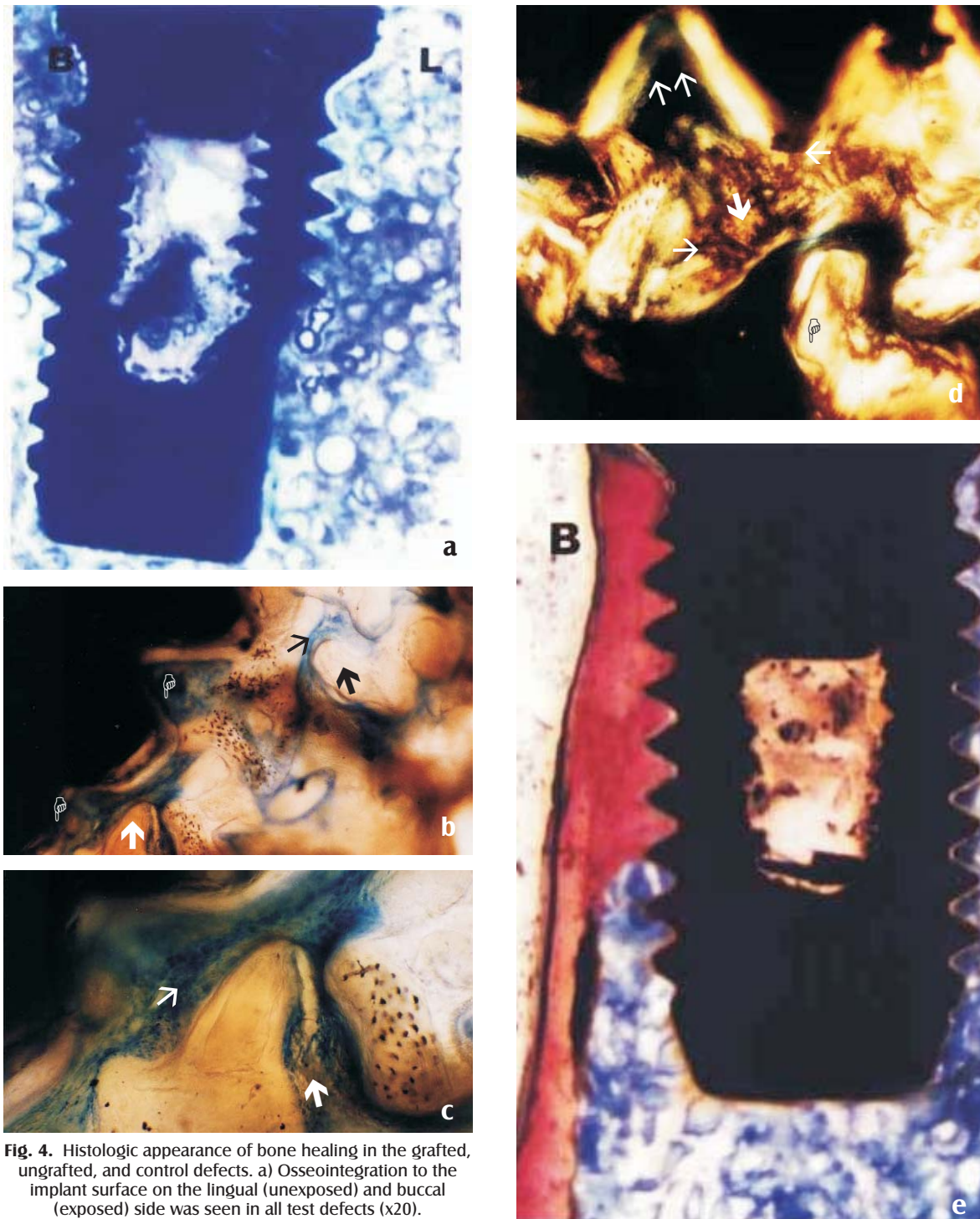
## Results

### Clinical observations

All the animals remained healthy until the day of sacrifice. The osseous defects healed uneventfully without signs of inflammation and all the implants appeared very stable in their bony sockets. After a 4-month healing period, the Biomend had degraded and the Capset was resorbed completely. P-BioBarrier and NP-BioBarrier retained the proper positions (Fig. 3a). Bone healing in the control osseous-implant defects failed to cover the exposed implant surfaces. Only a few threads near the bottoms of the defects were covered with new bone ingrowth (Fig. 3b).



**Fig. 3.** Clinical observations of bone healing in all osseous-implant defects. a) Capset, Biomend, P-BioBarrier and NP-BioBarrier. Note that the osseous-implant defects are fully augmented with new bone. b) Control defects. Note incomplete bone augmentation in the buccal implant surface.



**Fig. 4.** Histologic appearance of bone healing in the grafted, ungrafted, and control defects. a) Osseointegration to the implant surface on the lingual (unexposed) and buccal (exposed) side was seen in all test defects (x20). b) New bone formation (←) surrounds Laddec particles (◄). Contact between newly formed bone and the implant surface (⊞) (x40). c) Higher magnification of b (shows viable new bone capping Laddec (◄). Osteoclastic bays are evident adjacent to Laddec particles (◄) (x100).

d) Under polarized light of b) a mixture of woven bone (←), lamellar bone (◄), and remnants of the Laddec (⊞) are seen. Note bone-implant contact (◄◄) (x 30). e) View of a control osseous-implant defect showing failure of augmentation on the osseous-implant defect side (x20).

### Histologic Analysis

All the membrane-protected defects were augmented with new bone without evidence of connective tissue growing between the implant threads and the newly deposited bone (Fig. 4a). Most of the Laddec granules had been resorbed and the space was occupied by active stroma or newly formed bone. Resorption of the material was observed with active bone remodeling as demonstrated by the appearance of active osteogenesis between the partially resorbed Laddec particles. None of the bone defects covered with GTRM showed signs of inflammation. Bone-implant thread contact confirmed osseointegration of the newly formed bone to the surface of the implant (Figs. 4b & c). The polarized light view of the same section showed a mixture of woven and lamellar bone capping the remnants of the Laddec granules. In addition, new growing bone was in contact with the implant threads (Fig. 4d).

In the control defects, only a few implant threads were covered with new bone and the remaining threads were exposed. The entire length of the lingual side of the implant was covered with bony matrix extending from the host bone (Fig. 4e).

### Radiographic Examination (Fig. 5, Table1)

Radiographically, all the defects covered with GTRM alone or with graft showed bone in contact with the implant surfaces. The bone thickness near the implant-bone defect border varied within the membrane alone and membrane plus grafting groups. However, the bone was thicker in the grafted defects compared to the ungrafted one. The thickness in the ungrafted defects ranged from 550 to 1135  $\mu\text{m}$ , while the bone increase in the grafted defects was from 512 to 950  $\mu\text{m}$  greater. The greatest thickness in the non-grafted defects was seen in the Capset-covered defects (1135  $\mu\text{m}$ ), followed by NP-BioBarrier, P-BioBarrier, and Biomend, in order. In the grafted defects, the greatest thickness was seen with NP-BioBarrier (1800  $\mu\text{m}$ ), followed by P-BioBarrier, Capset, and Biomend, in order.

In control defects, the entire lingual length of the implant was lined with bony matrix growing from the host bone, while on the buccal side, the implant surface was exposed and only a few threads at the bottom of the implant were covered with new bone.

**Table 1.** Bone thickness in osseous-implant defects covered with GTRM + Laddec and GTRM alone.

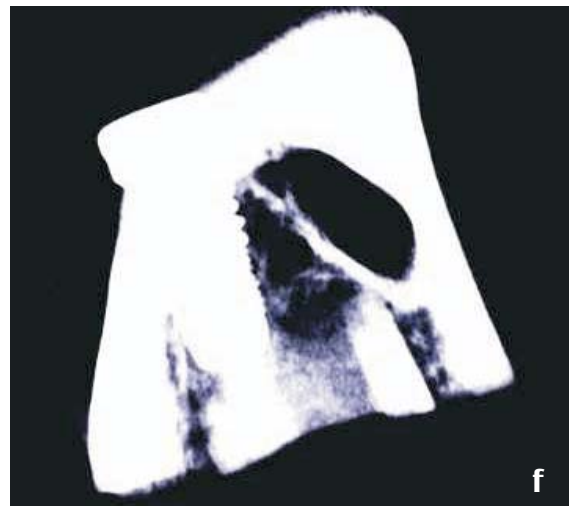
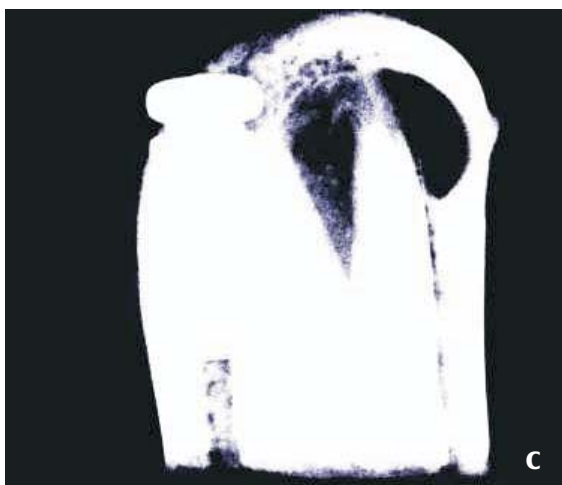
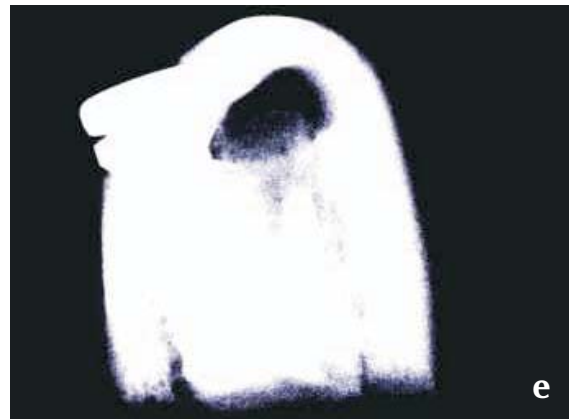
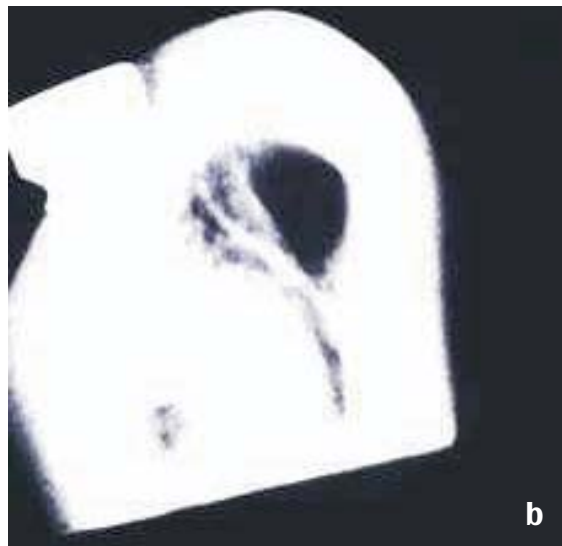
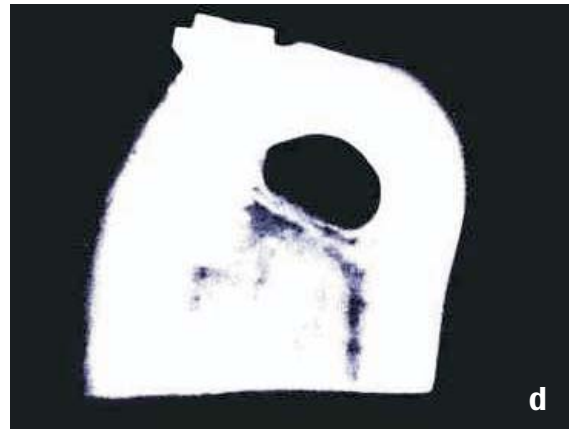
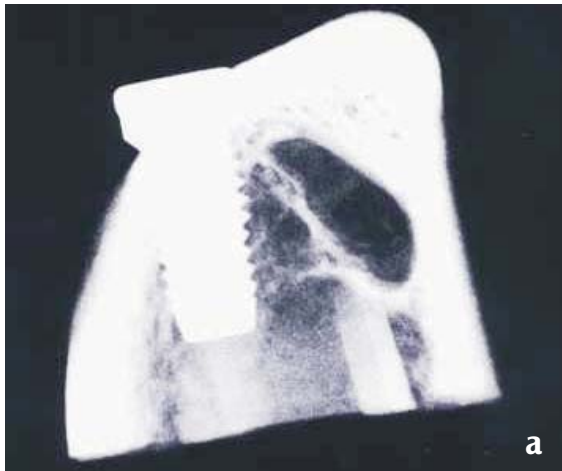
GTRM type	Ungrafted defects $\mu\text{m}$	Grafted defects $\mu\text{m}$	Difference $\mu\text{m}$
Biomend	550	1235	685
Capset	1135	1647	512
NP-BioBarrier	850	1800	950
P-BioBarrier	830	1680	850

### Discussion

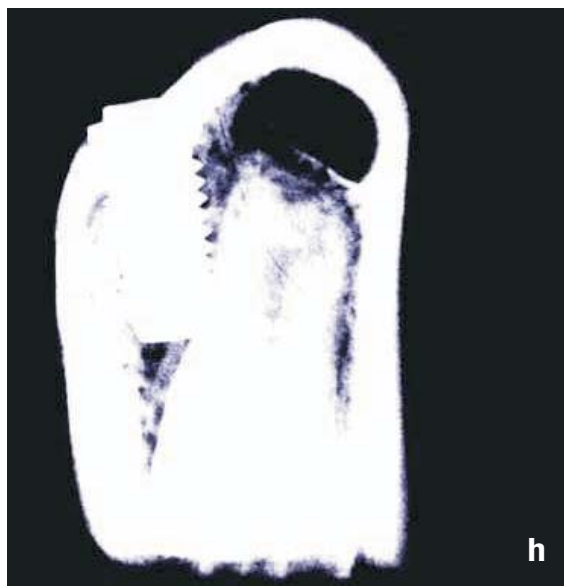
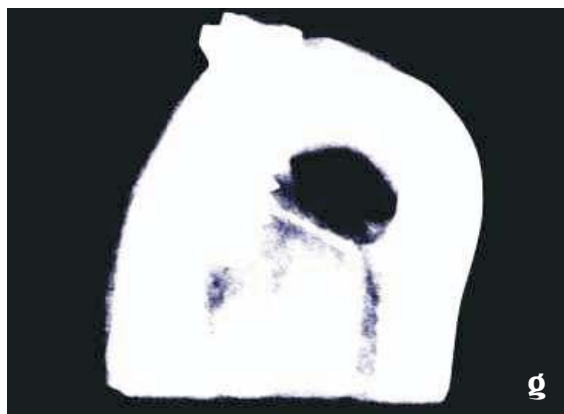
Bone grafting is used in osseous-implant defects to maintain a space between the implant and the overlying GTRM, and to promote bone growth over the exposed implant threads. This study showed that placing grafting material underneath GTRM helped to prevent the membranes from collapsing towards the exposed implant surface, and resulted in increased bone thickness.

DXBP (Laddec) has the same trabecular structure as natural bone and acts as a scaffold for physiologic remodeling. Remodeling is activated by osteoclasts that resorb the material and the subsequent deposition of new bone by osteoblasts.<sup>1</sup> In the manufacture of Laddec, all antigenic proteins and cellular elements contained in the intra-trabecular spaces are eliminated. Animal and human histologic studies have proven its biocompatibility, safety, and potency as an osteoconductive bone substitute.<sup>13,16</sup>

In an animal investigation, Becker et al<sup>19,20</sup> compared implant-bone defects filled with demineralized freeze-dried bone allograft (DFDBA) and covered with expanded polytetrafluoroethylene (ePTFE), defects filled with autogenous bone graft and covered with the same membrane, and defects covered with ePTFE membrane alone. They found regeneration was least favorable when DFDBA was covered with ePTFE, and concluded that DFDBA did not increase bone thickness on exposed implant surfaces. They observed no osteoblastic or osteoclastic activity in the grafted field. The purity of the demineralized bone grafting material with respect to fatty debris or residual protein is very important in determining a successful outcome.<sup>21</sup> Their laboratory produced the DFDBA material used in their experiments, and this might be why the material that Becker et al. used failed to induce physiologic bone remodeling. However, it is



**Fig. 5.** Radiographic appearance of test and control defects.  
 a) Capset without grafting.  
 b) Capset with grafting.  
 c) Biomend without grafting.  
 d) Biomend with grafting.  
 e) P-BioBarrier without grafting.  
 f) P-BioBarrier with grafting.



g) NP-BioBarrier without grafting.  
 h) NP-BioBarrier with grafting. In all cases, note the osseointegration on the bucco-lingual sides of the implants and the relative amount of bone gained between the grafted and ungrafted osseous-implant defects.  
 i) Control defect. Note the exposed implant threads on the buccal side.

difficult to conclude that all DFDBA materials on the market would have the same results.

Our findings disagree with those of Becker et al. In the grafted site, evidence of new bone growth and active osteogenesis between the Laddec particles undergoing resorption and the exposed implant surface were observed. Lorenzoni et al<sup>12</sup> found that the application of ePTFE membrane in combination with bovine DXBP (Bio-Oss<sup>®</sup>) appeared to enhance new bone formation on exposed implant threads, in agreement with our results. Landsberg et al<sup>22</sup> also evaluated augmentation procedures on implants using human DFDBA in clinical cases. Their implants were covered with ePTFE membrane for 6 months. Bone biopsies of the augmented bone examined histologically revealed osteogenic activity and the presence of osteoblastic and osteoclastic reactions in between the DFDBA

particles. Resorption of DXBP material and continuous deposition of new bone have also been documented in earlier studies.<sup>1, 2, 13, 16-18</sup>

This author<sup>32</sup> compared the osteogenic potential of six osteoconductive materials derived from human, animal, and synthetic sources. The study examined osseous cavities in the tibial condyles of rabbits and concluded that DXBP (Laddec) possessed the optimal criteria for an osteoconductive grafting material.

The present study observed an increase in bone thickness when DXBP material was applied in combination with GTRM. Obviously, the use of grafting materials prevented collapse of the GTRM against the exposed implant surfaces. The thickest bone in the grafted defects was seen with NP-BioBarrier (Table 1).

Shanaman<sup>24</sup> reported a clinical evaluation of 237 implant sites treated with GTRM alone or in combination with DFDBA. He noticed enhanced bone ingrowth when DFDBA was used. However, the study did not observe a statistically significant difference in bone thickness between implants that were grafted with allografts and those that were not grafted. Gher et al<sup>15</sup> conducted a clinical study to analyze the efficacy of bone allograft and Gore Tex<sup>®</sup> membranes in osseous-implant dehiscence. They noticed that the use of membrane in combination with allograft resulted in complete bone fill compared to defects that had not been grafted.

Hammerle et al<sup>9</sup> evaluated the application of ePTFE membrane to osseous-implant defects

alone and in conjunction with DXBP (Bio-Oss®). They observed 90 and 100% bone fill in the defects, respectively. Furthermore, the direct bone-to-implant contact fractions were 55 and 65%, respectively.

Hockers et al<sup>6</sup> evaluated the effect of the combined use of resorbable collagen membrane (BioGuide®) with bovine DXBP (Bio-Oss®) and autogenous bone particles in the treatment of bone defects around implants in dogs. They concluded that collagen membrane enhanced bone regeneration. DXBP and autogenous grafts were equally well integrated into the regenerated bone and autogenous bone and DXBP had no additional effect on bone growth. The comprehensive review of literature by Tolman<sup>5</sup> concluded that autogenous bone is optimal for grafting bone-implant defects. Block and onlay autogenous bone grafts were the optimal materials for augmenting a resorbed ridge in conjunction with implants.

The different GTRMs used in our experiment all promoted bone regeneration around the exposed implant surfaces. Calcium sulfate (Capset) barrier resulted in the thickest bone contour in ungrafted defects (1135 µmm) (Table 1). This author<sup>33</sup> found in another animal investigation that adding calcium sulfate to various grafting materials used to fill osseous defects resulted in increased bone deposition and increased mineralization. The increase of bone contour may be due to the direct calcium supply to the newly regenerated bone and avoidance of the collapse of the material to the underlying exposed implant surface that can happen with other membranes.

One major problem that has been reported as associated with the use of non-resorbable GTRM is a high rate of complications if the membrane is exposed to the oral environment and a subsequent infection develops. This is in addition to the disadvantage of needing a second procedure to remove the membrane.<sup>25-29</sup> On the other hand, the use of bioabsorbable GTRM could result in the use of limited gingival flap reflection in a one-step procedure and, consequently, better adaptation of the gingival tissues to the titanium abutments.<sup>30</sup>

Soft tissue pressure can lead to collapse of the GTRM and consequent reduced bone regeneration. A Gore-Tex® GTRM with a titanium net (TR-GTAM®) was introduced to help prevent collapse of the membrane towards the exposed implant surface. The reinforcement in this membrane stabilizes the position of the membrane after adaptation, and provides more

space for bone ingrowth for the duration of the healing period. Jovanovic and Spiekermann<sup>31</sup> reported increased bone formation with TR-GTAM compared to standard Gore-Tex membrane. Lorenzoni et al<sup>12</sup> also reported relatively increased bone gain with TR-GTAM membrane compared to standard ePTFE. However, the need for a second time surgery to remove it, and the possible complications that can appear with the use of non-resorbable membranes if they are exposed to the oral cavity, remain major disadvantages for the use of this kind of membrane.

This study concluded that resorbable and non-resorbable GTRM successfully augmented implant-osseous defects. Laddec (DXBP) increased bone thickness in defects covered with GTRMs and was well integrated into the regenerated bone. A calcium sulfate (Capset) barrier resulted in the thickest bone among the ungrafted osseous-implant defects, while NP-BioBarrier had the best result for the grafted defects.

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