

Bicon, Inc.
Reclassification Petition for Beta-Tricalcium Phosphate

November 12, 2002

**PETITION FOR RECLASSIFICATION
FOR
BETA-TRICALCIUM PHOSPATE**

**SUBMITTED BY:
BICON, INC.**

Beta-Tricalcium Phosphate Reclassification Petition

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I. Specification

The device for which reclassification is requested is Beta-Tricalcium Phosphate Bone Substitute. Tricalcium Phosphate (beta phase) can be made in a distinctive crystalline form to the exclusion of other phases of calcium phosphate that conform to various other chemical formulations. Beta-TCP exhibits a unique X-ray diffraction powder pattern that must conform to the standard powder pattern on file with the JCPDS (Joint Committee on Powder Diffraction Standards).

FORMULA FOR TRI-CALCIUM PHOSPHATE – $\text{Ca}_3(\text{PO}_4)_2$

Three calcium ions arranged around two phosphate ions in a well-defined three dimensional array of repeating units. The chemical is an inorganic compound having ionic character caused by the presence of Ca^{2+} and $[\text{PO}_4]^{3-}$ ions. Phosphate ions tend toward tetrahedral configurations; the calcium ions would be packed around these configurations in as efficient a manner as possible. This is in contrast to a molecular compound, which would exist as discrete, relatively unassociated molecules.

The compound's formula weight is 310.20, and in theory contains 38.76% Ca, 41.26% O, and 19.97% P. It is an odorless, tasteless granular powder having a melting point of approximately 1670 degrees Celsius and a density of approximately 3.15 grams per cubic centimeter.

Beta-TCP is essentially insoluble in water, alcohol, or acetic acid. It does react or show solubility in mineral acids. It is non-toxic and not flammable. The Merck Index cites its use in various ceramic and dental applications. The synthetic form of single-phase (beta) TCP is difficult to make, and requires evaluation by X-ray powder diffraction to ensure proper phase purity. Material that conforms to these specifications and character has been assigned the unique CAS (Chemical Abstract Service) Registry Number 7758-87-4, which completely defines the material as beta phase tricalcium phosphate, and which can be applied to no other chemical entity.

II. Statement of Action

Tri-calcium phosphate is presently a Class III device and it is requested that beta-tricalcium phosphate be reclassified from a transitional Class III device to a Class Unclassified.

III. Supplemental Data Sheet

Please refer to Appendix I

IV. Classification Questionnaire

Please refer to Appendix II

V. Basis for Disagreement

Our petition for reclassification is based on the fact that the identical material is currently only in Class III for dental purposes and not when it is used for orthopaedic purposes. In addition, it has successfully been marketed and used for dental purposes for over twenty years by Miter, Inc. under a 510(k) approval.

VI. Reasons for Reclassification

Our petition for reclassification is based on the fact that the identical material is currently only in Class III for dental purposes and not when it is used for orthopaedic purposes. In addition, it has successfully been marketed and used for dental purposes for over twenty years by Miter, Inc. under a 510(k) approval.

Please refer to Appendix III to review copies of literature from a search of PubMed MedLine and an Analysis and Evaluation for each piece of literature that supports the claim that reclassification will result in a device that remains safe and effective for its intended use.

VII. Unfavorable Data

There is no unfavorable data known to us.

VIII. Summary of New Information

Please refer to Appendix IV to review copies of literature from a search of PubMed MedLine and an Analysis and Evaluation for each piece of new literature (less than 3 years old).

IX. Source Documents

There are no source documents to be submitted relevant to this product.

X. Financial Certification/Disclosure Statement

Vincent J. Morgan, D.M.D. does not own any equity position in Bicon, Inc. and has not received any compensation for any clinical studies associated with this product, nor will he have an equity interest in the product.

XI. Appendices

Bicon, Inc.
Reclassification Petition for Beta-Tricalcium Phosphate

APPENDIX I

SUPPLEMENTAL DATA SHEET

Panel Recommendation

1. GENERIC TYPE OF DEVICE

Beta Tricalcium Phosphate Bone Substitute

2. ADVISORY PANEL

3. IS DEVICE AN IMPLANT (21 CFR 860.3)?

Yes No

4. INDICATIONS FOR USE IN THE DEVICE'S LABELING

Bone substitute material for dental/alveolar procedures.

5. IDENTIFICATION OF ANY RISKS TO HEALTH PRESENTED BY DEVICE

General

Infection, pyrogenic response

6. RECOMMENDED ADVISORY PANEL CLASSIFICATION AND PRIORITY

Classification

Unclassified

Priority (Class II or III Only)

7. IF DEVICE IS AN IMPLANT, OR IS LIFE-SUSTAINING OR LIFE-SUPPORTING AND HAS BEEN CLASSIFIED IN A CATEGORY OTHER THAN CLASS III, EXPLAIN FULLY, THE REASONS FOR THE LOWER CLASSIFICATION WITH SUPPORTING DOCUMENTATION AND DATA

Beta tricalcium phosphate is in Class III only when used for dental purposes and yet the identical material is not a Class III device when used in orthopedics, which is not a scientifically sound distinction.

8. SUMMARY OF INFORMATION, INCLUDING CLINICAL EXPERIENCE OR JUDGMENT, UPON WHICH CLASSIFICATION RECOMMENDATION IS BASED

Beta tricalcium phosphate has been used widely in medicine and dentistry for over twenty years and its properties are known to be beneficial when used as a bone substitute material.

9. IDENTIFICATION OF ANY NEEDED RESTRICTIONS ON THE USE OF THE DEVICE (e.g., special labeling, banning, or prescription use)

Use restricted to those licensed to practice medicine or dentistry.

10 IF DEVICE IS RECOMMENDED FOR CLASS I, RECOMMEND WHETHER FDA SHOULD EXEMPT IT FROM

Justification / Comments

- a. Registration / Device Listing
- b. Premarket Notification
- c. Records and Reports
- d. Good Manufacturing Practice

11 IF DEVICE IS RECOMMENDED FOR CLASS II, RECOMMEND WHETHER FDA SHOULD EXEMPT IT FROM PREMARKET NOTIFICATION

- a. Exempt
- b. Not Exempt

Justifications/Comments

12. EXISTING STANDARDS APPLICABLE TO THE DEVICE, DEVICE SUBASSEMBLIES (*Components*) OR DEVICE MATERIALS (*Parts and Accessories*)

13. COMPLETE THIS FORM PURSUANT TO 21 CFR PART 860 AND SUBMIT TO:

Food and Drug Administration
Center for Devices and Radiological Health
Office of Health and Industry Programs (HFZ-215)
1350 Piccard Drive
Rockville, MD 20850

OMB STATEMENT

Public reporting burden for this collection of information is estimated to average 1-2 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration, (HFZ-215)
2094 Gaither Road
Rockville, MD 20850

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Bicon, Inc.
Reclassification Petition for Beta-Tricalcium Phosphate

APPENDIX II

Bicon, Inc.
Reclassification Petition for Beta-Tricalcium Phosphate

December 9, 2002

Food and Drug Administration
Center for Devices and Radiological Health
Regulations Staff (HFZ-215)
1350 Piccard Drive
Rockville, MD 20857

RE: Reclassification Petition-Beta-Tricalcium Phosphate

Dear Sir/Madam:

The enclosed documents are a Petition for Reclassification of Beta-Tricalcium Phosphate, and devices found equivalent to it, from Class III to Class II.

Upon reclassification this material should conform to the requirements in the proposed document for guidance for dental bone grafting materials.

The petition is being submitted under Sections 513(e) and (f), 514 (b) and 520(l) of the act which allows for reclassification of a device and outlines the procedures to be followed. The information presented is submitted according to the reclassification procedure 21 CFR 860.123.

Your prompt attention to this submission is very much appreciated. Please contact me with any questions you may have.

Sincerely,


Vincent J. Morgan, D.M.D.
President

02P.0520



CCP1

PANEL MEMBER / PETITIONER

Bicon, Inc.

DATE

11/12/02

GENERIC TYPE OF DEVICE

Beta tricalcium phosphate

CLASSIFICATION RECOMMENDATION

Unclassified

1. IS THE DEVICE LIFE-SUSTAINING OR LIFE-SUPPORTING ?

YES NO

Go to Item 2.

2. IS THE DEVICE FOR A USE WHICH IS OF SUBSTANTIAL IMPORTANCE IN PREVENTING IMPAIRMENT OF HUMAN HEALTH ?

YES NO

Go to Item 3.

3. DOES THE DEVICE PRESENT A POTENTIAL UNREASONABLE RISK OF ILLNESS OR INJURY ?

YES NO

Go to Item 4.

4. DID YOU ANSWER "YES" TO ANY OF THE ABOVE 3 QUESTIONS ?

YES NO

If "Yes," go to Item 7.
If "No," go to Item 5.

5. IS THERE SUFFICIENT INFORMATION TO DETERMINE THAT GENERAL CONTROLS ARE SUFFICIENT TO PROVIDE REASONABLE ASSURANCE OF SAFETY AND EFFECTIVENESS ?

YES NO

If "Yes," Classify in Class I.
If "No," go to Item 6.

6. IS THERE SUFFICIENT INFORMATION TO ESTABLISH SPECIAL CONTROLS IN ADDITION TO GENERAL CONTROLS TO PROVIDE REASONABLE ASSURANCE OF SAFETY AND EFFECTIVENESS ?

YES NO

If "Yes," Classify in Class II and go to Item 7.
If "No," Classify in Class III.

7. IF THERE IS SUFFICIENT INFORMATION TO ESTABLISH SPECIAL CONTROLS TO PROVIDE REASONABLE ASSURANCE OF SAFETY AND EFFECTIVENESS IDENTIFY BELOW THE SPECIAL CONTROL(S) NEEDED TO PROVIDE SUCH REASONABLE ASSURANCE. FOR CLASS II.

- Guidance Document
- Performance Standard(s)
- Device Tracking
- Testing Guidelines
- Other (Specify) _____

8. IF A REGULATORY PERFORMANCE STANDARD IS NEEDED TO PROVIDE REASONABLE ASSURANCE OF THE SAFETY AND EFFECTIVENESS OF A CLASS II OR III DEVICE, IDENTIFY THE PRIORITY FOR ESTABLISHING SUCH A STANDARD.

- Low Priority _____
- Medium Priority _____
- High Priority _____
- Not Applicable _____

9. FOR A DEVICE RECOMMENDED FOR RECLASSIFICATION INTO CLASS II, SHOULD THE RECOMMENDED REGULATORY PERFORMANCE STANDARD BE IN PLACE BEFORE THE RECLASSIFICATION TAKES EFFECT ?

YES NO
 NOT Applicable

10. FOR A DEVICE RECOMMENDED FOR CLASSIFICATION / RECLASSIFICATION INTO CLASS III, IDENTIFY THE PRIORITY FOR REQUIRING PREMARKET APPROVAL APPLICATION (PMA) SUBMISSIONS.

- Low Priority _____
- Medium Priority _____
- High Priority _____
- Not Applicable _____

11 IDENTIFY THE NEEDED RESTRICTION(S)

Only upon the written or oral authorization of a practitioner licensed by law to

administer or use the device

Use only by persons with specific training or experience in its use

Use only in certain facilities

Other (Specify)

12. COMPLETE THIS FORM PURSUANT TO 21 CFR PART 860 AND SUBMIT TO:

Food and Drug Administration
Center for Devices and Radiological Health
Office of Health and Industry Programs (HFZ-215)
1350 Piccard Drive
Rockville, MD 20850

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APPENDIX III

Article Analysis and Evaluation

ARTICLE TITLE AND BIBLIOGRAPHIC INFORMATION:

The use of tricalcium (Synthograft). Part I: Its use in extensive periodontal defects.
Hoexter DL.
J Oral Implantol 1983;10: 599-610.

PURPOSE/QUESTION:

This purpose of this study was to report the experience of tricalcium phosphate in treating three patients with unusually extensive periodontal pathology.

SOURCE OF FUNDING:

Not mentioned

TYPE OF STUDY/DESIGN:

Case reports

SUMMARY FROM AUTHORS' MANUSCRIPT

Subjects (Patients):

Three patients were investigated in the study.

Exposure:

The main exposure was extensive periodontal pathology.

Main Outcome Measure:

Main outcome measure was to determine the pocket depth, stability of the teeth, and function at 9 months.

Main Results:

The authors' results reported that in three cases with unusually large osseous defects were filled with tricalcium phosphate, a new synthetic osseous graft material. Clinical impression, patients reports, and radiographs show that in each case the material was biocompatible and was retained, providing good support, virtually eliminating mobility, and preserving function at least as long as six months.

Conclusions:

This material would suggest a hopeful prognosis with teeth of extensive periodontal pathology in view of this author's experience.

in beide. Erprobung von Hohlzylinder-
Titanspritzschicht-Oberfläche. Der
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n knochenähnlicher Biowerkstoff.

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orous Titanium Surgical Implant

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aterials to obtain direct skeletal at-
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zahnärztl. Z., 34, 907-911 (1979).

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Zylinderimplantat. Jahrestagung

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. 1974, AAID.

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80), John Wiley & Sons, Inc.

he ultrastructure of the interface
Res., Vol. 15, 291-305 (1981), John

othetik und Werkstoffkunde, Carl

an einem belasteten intramobilien
chts-Chir. 6, 129-133 (1982).

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he Implantologie e.v.

THE USE OF TRICALCIUM (SYNTHOGRAFT*) PART I: ITS USE IN EXTENSIVE PERIODONTAL DEFECTS

David L. Hoexter, D.M.D.

Sintered tricalcium phosphate, a crushed biodegradable ceramic, is one of the new materials recently used to aid bone regeneration. This article is one of a series showing the use of T.C.P. in clinical studies. One of the articles to follow in this series will show its use in aiding oral implants. This paper presents three clinical patients with unusually large periodontal defects. Increased radio-opacity, reduced mobility, and improved function survived nine months and provides the basis for positive clinical prognosis. The most likely alternative in each case was loss of teeth with extensive resplinting. The size of the lesions made uncertain the value of seeking autogenous bone graft sites. A second wound site would be necessary for the donor site and the unpredictability of the results led us to the use of the new T.C.P. Techniques of handling the new medium are discussed. Re-exposure of the periodontium after a year, agreed to by all patients, will help determine if bone regeneration with resorption of ceramic has taken place.

In trying to regenerate periodontium, researchers have tried a variety of calcareous materials. The quest has been for a substance that could immediately substitute for lost bone as structural support, provide access and scaffolding for blood-borne osteogenic components, and eventually become resorbed after engulfment by new native bone.

Such a material must meet rather strenuous physical and biological specifications. It must submit to packing and shaping, set rigidly enough to stabilize the tooth without too great delay, yet be porous, manifest no toxicity, set off no rejection, and yield only to new bone. An additional feature to be hoped for might be a biochemical characteristic that would actively encourage osteoblastic transformation and activity.

The earliest candidate for this substance was plaster of paris, which reportedly achieved mixed successes in some small defects.⁽¹⁻⁴⁾ However, in larger defects and in most moderate and small ones, plaster of paris either resorbed or flushed out too quickly to accomplish its restorative assignment. Ground bovine bone was also tried but in humans it failed to fulfill the regenerative promise of its trails in experimental animals.⁽⁹⁾

In the past decade and a half autogenous grafts have become the materials of choice but their use has been somewhat restricted by unpredictability as well as by the clinical difficulties related to their availability and procurement. For small defects, Robinson's method of using osseous coagulum harvested by burr from intraoral sites has met with important success.⁽⁶⁾ However, the intraoral body supply may be insufficient for larger defects or non-existent when there is a full complement of teeth.

Frequent but unpredictable successes have been achieved with iliac cancellous bone and hemopoietic marrow. Such autogenous materials have proved their worth for osseous induction and reconstruction in orthopedic surgery. However, their use in periodontics must be weighed against a somewhat different scale of values considering the procedure's discomfort, pain, unpredictability, doubled surgical insult, expense, and the healing complications associated with an open healing system.

The best solution for these problems would be a prepared graft material that can be kept on the shelf for use as needed, at short notice. Bone allografts, used successfully in nonperiodontal applications, would appear to meet these requirements. However, the periodontal use of allograft materials has so far been disappointing. Results have not been predictable, and further disadvantages stem from an uncertain supply, considerable expense and a slim but unavoidable potential for antigenicity and transfer of disease.⁽⁷⁾

For all these reasons periodontists have greeted with considerable eagerness the recent appearance of synthetic bone graft materials. One such is sintered tricalcium phosphate, a biodegradable ceramic supplied in crushed form. Relatively inexpensive, easily stored and readily available on the shelf, nonantigenic, nontoxic, and sterile, the synthetic graft promises to fill a great need if its performance in humans replicates its successful trials in experimental animals.⁽⁸⁾ It is of particular interest to find out whether or not the inert synthetic can accomplish its bridging and regenerative functions in the larger osseous defects, where organic materials, so dependent for survival on blood supply and proximity to bony walls, have been inconsistent.

Here we report our experience with this new material in treating three patients with unusually extensive periodontal pathology. In each case the use of the synthetic graft saved teeth, time and expense. At nine months follow-up there has been no repocketing, teeth have been stabilized, and function is maintained. Our experience, we believe, may help characterize some of the indications for using the new material and provide some helpful information concerning technique.

MATERIALS AND METHODS

Sintered beta-tricalcium phosphate vials, that may be packed into defect: sterile physiologic saline or the patient: our own experience has led to a prefer consistency, which in our hands produ opacity than did the dry packing meth we used the patient's blood early in processes of surgery reduced the suppl.

The defect is prepared as for other and provide access to the defect are incisions. The defect is thoroughly thoroughly planed and scaled. We use r a proper blood supply to the graft, and to decorticate one or more bony walls. I blood should be seen in the socket.

The depth of the defects described i by graduated probe from the crest of th pocket.

The tricalcium phosphate can then l with a spatula, periosteal elevator, or ar grainy, some of it may wash away durin; we have found it best to overfill the def shaped away later. After filling, firm sust by finger over sterile gauze. The compres firm mass, which will shortly become visi site has been properly prepared.

The flap is repositioned and tightly prevent the graft material from being wa with a periodontal dressing, and it is th change it in ten days, the new dressing th week. The repair site should not be pr several months we follow the patient every of home care. Radiographs are usually ta

I should add that it is our practice spectrum antibiotic for seven days after st

CASE 1

This patient was a 42-year-old male. mobile at presentation (Grade 2 mobilite swelling. The tooth, which had been tre:

substance was plaster of paris, which in some small defects.⁽¹⁻⁴⁾ However, in and small ones, plaster of paris either accomplish its restorative assignment. but in humans it failed to fulfill the experimental animals.⁽⁹⁾

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MATERIALS AND METHODS

Sintered beta-tricalcium phosphate is a dry granular material, supplied in vials, that may be packed into defects either dry or as a slurry mixed with sterile physiologic saline or the patient's blood or saliva. As will be related, our own experience has led to a preference for the slurry, used at a putty-like consistency, which in our hands produced greater and more consistent radiopacity than did the dry packing method. In order to reduce extra materials we used the patient's blood early in the procedure before vasoconstrictive processes of surgery reduced the supply.

The defect is prepared as for other bone grafts. Flaps sufficient to expose and provide access to the defect are incised and reflected, with relieving incisions. The defect is thoroughly curetted and the exposed root is thoroughly planed and scaled. We use no chemicals. It is important to assure a proper blood supply to the graft, and for this purpose it may be necessary to decorticate one or more bony walls. Before proceeding with packing, fresh blood should be seen in the socket.

The depth of the defects described in the cases that follow was measured by graduated probe from the crest of the gingival margin to the base of the pocket.

The tricalcium phosphate can then be packed and tapped into the defect with a spatula, periosteal elevator, or amalgam carrier. Since the material is grainy, some of it may wash away during the procedure, and for that reason we have found it best to overfill the defect — excess volume can always be shaped away later. After filling, firm sustained compression should be applied by finger over sterile gauze. The compression will compact the ceramic into a firm mass, which will shortly become visibly suffused with fresh blood if the site has been properly prepared.

The flap is repositioned and tightly sutured. A tight seal is essential to prevent the graft material from being washed away. The wound is covered with a periodontal dressing, and it is this author's practice to inspect and change it in ten days, the new dressing then to remain in place for at least a week. The repair site should not be probed during healing. For the first several months we follow the patient every two weeks with scaling and review of home care. Radiographs are usually taken every other visit.

I should add that it is our practice to cover the patient with a broad spectrum antibiotic for seven days after surgery.

CASE 1

This patient was a 42-year-old male. His first maxillary left molar was mobile at presentation (Grade 2 mobility) with accompanying pain and swelling. The tooth, which had been treated endodontically, supported a

crown. In the Radiographs (Case I, Figure 3) radiolucency could be seen at each of the apices and it appeared possible that there might be a fracture in the root where the post seemed deep. Clinically, the defect was seen to be extensive, more than 8 mm deep at mesial, distal, and palatal aspects (Case I, Figure 1). The surgical exposure showed no fracture but revealed no bone to the apex from the palatal aspect. Removal of granulomatous tissue further revealed a void far too large to be readily filled from autogenous sources.

The alternative to trying a synthetic graft involved loss of the tooth and crown or a root amputation and construction of a three unit splint. This was explained to the patient, who elected a trial of the new material.

In this early case we packed the void with dry tricalcium phosphate, which we found presented some difficulty and waste in handling. Once in place, however, the material rapidly flooded with blood and appeared firm. (Case I, Figure 2)

Radiographs taken immediately after the procedure and during the following nine months (Case I, Figure 4) showed some non-uniformity in radiopacity, which we felt might have been avoided by first wetting the material to a putty-like consistency instead of packing it dry. However, the lack of any change over the nine month period suggests satisfactory retention of the material and continuing structural support. After nine months the patient is functioning comfortably, the tooth remains stable, and there has been no recurrence of swelling or pocketing.



Case I, Figure 1: Palatal flap reveals bone loss extending beyond the apex, where the gutta percha point can be seen



Case I, Figure 2: Defect is filled with



Case I, Figure 3: Radiograph before s radiolucency

Figure 3) radiolucency could be seen at
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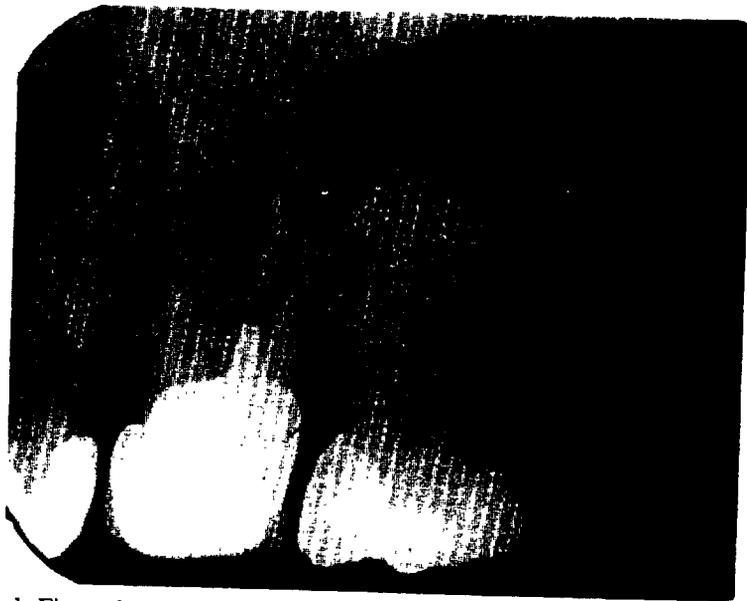
At the procedure and during the
 recovery showed some non-uniformity in
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 instead of packing it dry. However, the
 12 month period suggests satisfactory retention
 structural support. After nine months the
 the tooth remains stable, and there has
 been no settling.



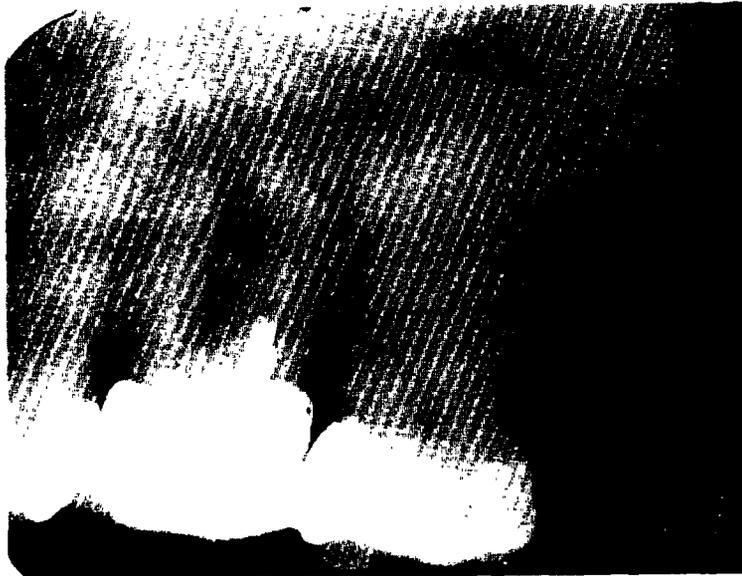
reveals bone loss extending beyond the
 the gutta percha point can be seen



Case I, Figure 2: Defect is filled with tricalcium phosphate material



Case I, Figure 3: Radiograph before surgery shows extensive periapical
 radiolucency



Case I, Figure 4: Radiolucency has been replaced by radiopacity in this radiograph taken 9 months after surgery

CASE 2

This patient was a 59-year-old female with an extensive periodontal pocket 8-9 mm in depth at the mesial aspect of the upper left second bicuspid and 6 mm at the mesial aspect of the first molar (Case II, Figure 1). The upper left second bicuspid was mobile to an extreme degree; it was splinted to the second molar, the first molar being absent.

The situation was complicated by deterioration of osseous support throughout the maxillary arch. The upper right quadrant lacked more than half its osseous support posteriorly and could not be expected to carry additional burdens shifted from the failing left side. The upper right first molar was missing and the first bicuspid was weak.

The weakness on the left side prejudiced the success of even a partial denture. The second molar was already too weak to provide much splint support to the second bicuspid, and the first bicuspid was not strong enough to be of much help in supporting a splint. In all probability the entire maxillary arch would have to be splinted and crowned, a laborious procedure involving 14 units and offering only a guarded prognosis at best.



Case II, Figure 1: Periodontal probe in this buccal view



Case II, Figure 2: Preoperative radiog at the mesial aspect



as been replaced by radiopacity in this
in 9 months after surgery

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ed and crowned, a laborious procedure
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Case II, Figure 1: Periodontal probes show pockets at least 9 mm deep
in this buccal view



Case II, Figure 2: Preoperative radiograph shows large radiolucent area
at the mesial aspect of upper left second bicuspid

When the alternatives were explained to the patient, she elected for a trial of synthetic graft material in the hope that this might save her teeth and at the same time forestall an expense her modest means could ill afford. The presence of some bone, both as support and as a source of blood supply for regeneration, on the distal aspect of the first bicuspid and the distal and buccal aspects of the principally involved tooth, justified some cautious speculation that the synthetic graft material had a chance to succeed although we had never employed it in defects so large.

In this procedure we used the patient's blood to make a slurry of putty-like consistency instead of using it dry.

At nine months, the x-rays (Case II, Figure 3) showed satisfactory radiopacity in the defect, with no signs of rejection or deterioration. The patient functions comfortably and the mobility of the tooth remains considerably reduced. Whether or not the tooth can continue to function as chief support for so basically weak an arch remains to be seen, even though the question of its osseous support seems to be satisfactorily answered for the time being.



Case II, Figure 3: Nine months after surgery, radiograph shows radiopacity where graft material has been placed

CASE 3

This patient is a 43-year-old female who presented with a highly mobile four-unit bridge from the lower left cuspid to first molar. She had been referred because of x-rays showing osseous defects around what appeared to the referring dentist to be a rare "three-root molar" supporting the bridge but which seemed to us to be a fractured root.

Exposure of the root by a flap technique revealed an extensive defect surrounding the molar which proved to have a fractured distal root. The tooth was removed, part of the tooth under the crown was splinted, root did not seem viable and it was now the only anchorage, had some lingual

Our initial recommendation was that the patient required a partial denture because removal of the tooth cantilever opposed to a full maxillary arch. A hygienist well informed in dentistry, plus the patient, we agreed on a trial of tricalcium phosphate. The chances for success were slim in view of

The root and defect were prepared in the manner already described, again using a patient's blood.

The results were beyond expectation. The root was nearly gone in two months. Six months later the patient was comfortable and the bridge remained rigid. Radiographs showed consistent radiopacity around the root. We plan eventually to replace the bridge, but avoid stress over more teeth, but avoided a re-



Case III, Figure 1: Preoperative LL are: pocket depth around

ned to the patient, she elected for a trial that this might save her teeth and at the modest means could ill afford. The port and as a source of blood supply for the first bicuspid and the distal and involved tooth, justified some cautious material had a chance to succeed although so large.

tient's blood to make a slurry of putty-y.

ase II, Figure 3) showed satisfactory signs of rejection or deterioration. The the mobility of the tooth remains t the tooth can continue to function as n arch remains to be seen, even though ms be satisfactorily answered for the



fter surgery, radiograph shows ere graft material has been placed

ale who presented with a highly mobile : c to first molar. She had been used defects around what appeared to e-root molar" supporting the bridge but l root.

Exposure of the root by a flap technique and degranulation revealed an extensive defect surrounding the molar (Case III, Figure 1 B), which indeed proved to have a fractured distal root. When the fractured portion was removed, part of the tooth under the crown also came away. The remaining splinted root did not seem viable and it too was removed. The mesial root, now the only anchorage, had some lingual but no buccal supporting bone.

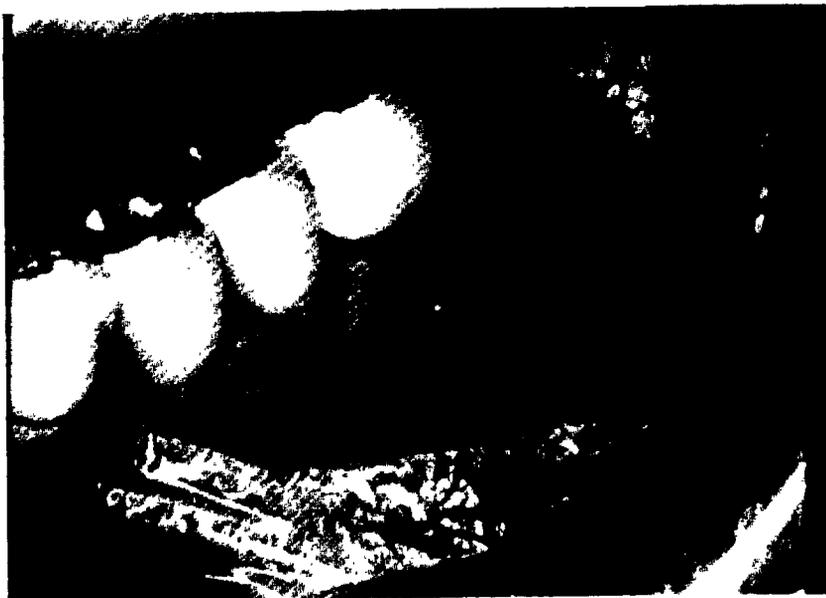
Our initial recommendation was for extraction, which would have required a partial denture because removing the molar would have left a one-tooth cantilever opposed to a full maxillary complement of teeth. The patient, a hygienist well informed in dentistry, pleaded for saving the tooth. Together we agreed on a trial of tricalcium phosphate with the understanding that the chances for success were slim in view of the extensive pathology.

The root and defect were prepared and the ceramic graft packed in the manner already described, again using a putty-like mix made by using the patient's blood.

The results were beyond expectations. The mobility of the bridge was nearly gone in two months. Six months later, the patient was still functioning comfortably and the bridge remained rigid. Radiographs (Case III, Figure 4) showed consistent radiopacity around the root and no loss of graft material. We plan eventually to replace the bridge, which is no longer sound under the area where the fractured portion was removed, with one correctly distributing stress over more teeth, but avoided a removable partial denture.



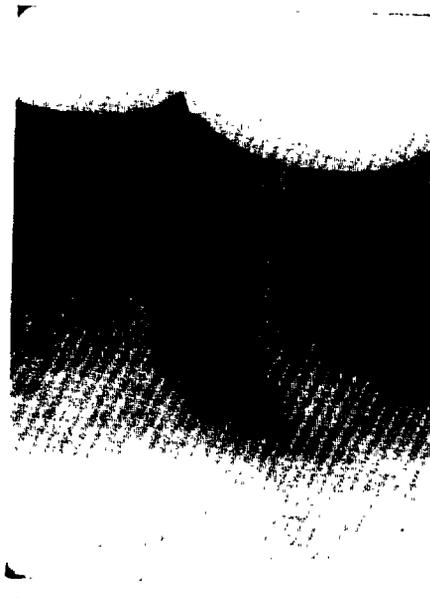
Case III, Figure 1: Preoperative LL area with extreme suppurating pocket depth around the molar and 3 mobility



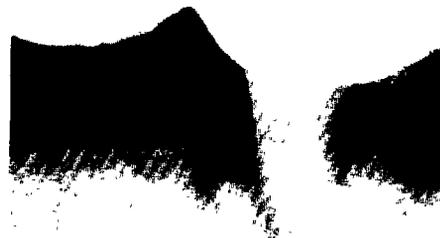
Case III, Figure 2: Area exposed by flap showing extensiveness of bone loss from buccal view



Case III, Figure 3: Buccal view showing tricalcium phosphate filling defect around mesial root and distal root amputated



Case III, Figure 4: Radiograph before radiolucencies are well as the fracture



Case III, Figure 5: Nine months post consistent radiopaque root of the now fir



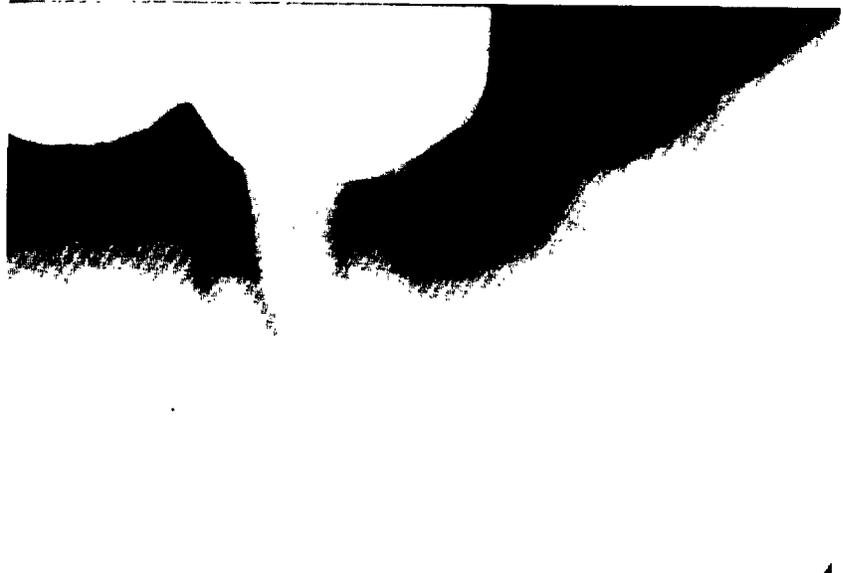
by flap showing extensiveness of bone
cal view



tetracalcium phosphate filling
mesial root and distal root amputated



Case III, Figure 4: Radiograph before treatment showing the
radiolucencies around both mesial and distal roots as
well as the fractured distal root



Case III, Figure 5: Nine months postoperative radiograph shows
consistent radiopacity around the remaining mesial
root of the now firm splinted tooth

CONCLUSIONS

We have reported three cases in which unusually large osseous defects were filled with tricalcium phosphate, a new synthetic osseous graft material. Clinical impression, patient reports, and radiographs show that in each case the material was biocompatible and was retained, providing good support, virtually eliminating mobility, and preserving function at least as long as six months. This would suggest a hopeful prognosis in view of the experience that a failure of such graft materials is usually apparent within a few months.

In each case the synthetic graft preserved natural teeth, time, discomfort, and considerable expense. Alternative approaches involved sacrifice of teeth and extensive splinting. In each case the discomfort and difficulties of preparing a second wound site and harvesting autogenous graft material seemed a poor exchange for the uncertain predictability of any graft materials in osseous defects as large as these. The attempt at salvage was made feasible, we felt, by the presence of the synthetic material on the shelf, its economy, and its availability within minutes of assessing the extent of the pathology.

In addition, an important indication was satisfied in that these were all cooperative patients who had participated in the decision to take a chance. While our experience here provides no guarantees, such decisions can now be better informed, we feel.

The ultimate question, of course, is whether or not the radio-opacities we now perceive reflect regeneration of bone throughout the ceramic scaffolding with final resorption of the synthetic material. We have acquired permission from all patients to flap and re-enter the site for inspection after a year, and at that time we expect to have more clinical facts pertaining to tricalcium phosphate resorption and bone formation capabilities to present answers to those questions since there have been no human histological studies, only histological animal studies and reports to date.

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THE USE OF SYNTHOGRAFT* IN PERIODONTAL DEFECTS

Thomson

The development of a totally resorbable repair of bone defects originated with the use of Synthograft* in 1970. This new material, Synthograft* specifically prepared and processed for use in periodontal defects, developed ceramic slowly dissolves as

In 1970, Tom Driskell proposed the use of Synthograft* at the Institute of Dental Research at Walter Reed Army Institute of Medicine. In 1970, Tom Driskell and a number of colleagues studied this material in animals and humans.

BACKGROUND

Today, autogenous transplants are used to repair bone defects. It does require additional cooperation to obtain the autogenous material. If the material is organic there is an inflammatory reaction which may affect the success of the repair. Due to the use of homografts and heterografts with altered properties to improve efficiency and reduce the pain of the procedure. Many studies using these materials and other attractive substances enjoy widespread acceptance and promise.¹

All of the above mentioned materials are made of tricalcium phosphate ceramic is inorganic and non-toxic. The material are:

1. It is inorganic and not organic. It does not react with subsequent inflammation.
2. This material is readily available and possesses a long shelf life.

Article Analysis and Evaluation

ARTICLE TITLE AND BIBLIOGRAPHIC INFORMATION:

An evaluation of tricalcium phosphate as a treatment for endodontic perforations.
Sinai IH, Romea DJ, Glassman G, Morse DR, Fantasia J, Furst ML.
J Endod 1989; 15: 399-403

PURPOSE/QUESTION:

This purpose of this study was to initiate a study using tricalcium phosphate to attempt to seal perforations in maxillary molars of rats.

SOURCE OF FUNDING:

Endowment and Memorial Foundation of the American Association of Endodontists or the Endowment and Memorial Foundation.

TYPE OF STUDY/DESIGN:

Animal Research Study

SUMMARY FROM AUTHORS' MANUSCRIPT

Animals:

In this study, the experimental animals were 35 Sprague-Dawley rats with healthy periodontal tissues.

Exposure:

In each rat, two main exposures were examined:

- (1) Maxillary molar on one side was treated with Cavit (Premier Dental Products Co., Norristown, PA)
- (2) Maxillary molar on the contralateral side was treated with tricalcium phosphate (Synthograft; Johnson & Johnson, East Windsor, NJ)

Main Outcome Measure:

Main outcome measures were the evaluation of four evaluative factors (inflammation, bone resorption, cementum and dentin resorption, and epithelial proliferation) were analyzed and compared for the two materials at the four time intervals (1 day, 1 wk, 2 wk, and 1 month).

Main Results:

The authors' results showed that for the individual time periods, there were no statistically significant differences between the two materials ($p > 0.05$).

However, when all four time periods were combined, there was a statistically significant better result for tricalcium phosphate than for Cavit with respect to decreased inflammation ($p < 0.05$).

Conclusions:

The authors' findings concluded that since tricalcium phosphate did result in significantly less inflammation in the combined time periods that did cavitate, a rationale could be presented for its clinical use and applications.

SCIENTIFIC ARTICLES

An Evaluation of Tricalcium Phosphate as a Treatment for Endodontic Perforations

Irving H. Sinai, DDS, David J. Romea, DMD, Gary Glassman, DDS, Donald R. Morse, DDS, MA (Biol), MA (Psychol), John Fantasia, DDS, and M. Lawrence Furst, PhD, MPH

In the rat, perforations of maxillary molars were created and treated with either tricalcium phosphate (Synthograft) or Cavit. At four time intervals (1 day, 1 wk, 2 wk, and 1 month), four evaluative factors (inflammation, bone resorption, cementum and dentin resorption, and epithelial proliferation) were analyzed and compared for the two materials. For the individual time periods, there were no statistically significant differences between the two materials. However, when all four time periods were combined, there was a statistically significant better result for tricalcium phosphate than for Cavit with respect to decreased inflammation ($p < 0.05$).

Perforations have been cited as the second greatest cause of endodontic failure (1). Seltzer et al. (2) found 3.5% of endodontic failures were related to perforations. Perforations of the furca region of molars are especially troublesome because they cause considerable damage and frequently lead to periodontal involvement of the furcation (3). This damage, therefore, results in a questionable prognosis for the tooth. Information on periodontal tissue reactions to endodontic perforations in dogs (3-8), monkeys (3), and humans (9-13) has been previously evaluated. In general, the most favorable prognosis for healing was found when the perforation was sealed immediately. In addition, the further the perforation was from the apex, the better was the prognosis (3, 4, 7, 8, 11).

Perforations have been sealed with a variety of materials with varying degrees of success. These materials include (a) plaster of paris; (b) zinc phosphate cement (14); (c) phosphate cement (4, 5); (d) copper plus amalgam (15); (e) gutta-percha alone (4, 5); (f) gutta-percha following surgical access (4, 16, 17); (g) amalgam alone (8); (h) amalgam after surgical access (4, 11, 16, 17); (i) combination of gutta-percha, platinum sheet, and lead disc (15); (j) indium foil and amalgam (9); (k) calcium hydroxide (8, 12, 18); and (l) Cavit¹ (8, 11, 13, 15).

¹ Cavit contains zinc oxide, calcium sulfate, zinc sulfate, glycol acetate, polyvinyl acetate, polyvinyl chloride acetate, triethanolamine, and red pigment (19)

Tricalcium phosphate has recently been used with some success in clinical and animal studies for endodontic and periodontal cases involving (a) pulp capping (20, 21); (b) osseous defect repair (14, 22, 23); (c) apical barrier formation (24-26); and (d) apical lesion repair (27). Recently, it has been used in an attempt to seal perforations (28). Since this material is absorbed, new tissue proliferates and calcification can occur (22). Considering that the stimulation of hard tissue formation is accomplished without causing severe inflammation (according to the reports), it was decided to initiate a study using tricalcium phosphate to attempt to seal perforations. In addition, since Cavit has recently been used with some degree of clinical success for sealing perforations, it was chosen as the positive control material. Since it is well known that *not* sealing perforations results in marked destruction, it was decided not to use a negative control.

MATERIALS AND METHODS

The experimental animals were 35 Sprague-Dawley rats with healthy periodontal tissues. The animals were anesthetized with an intraperitoneal injection of Nembutal sodium. They were secured on a small animal board. Access was gained into the maxillary first and second molars using a 1/4 round bur under high speed and water spray. Sterile spoon excavators were used to complete each pulpotomy. The furcation perforations were created with uniform penetrations by the use of a sterile #20 reamer and an endodontic explorer with a stop. There were a total of 140 perforations made in this way.

In each rat, the maxillary molar on one side was treated with Cavit (Premier Dental Products Co., Norristown, PA) and the maxillary molar on the contralateral side was treated with tricalcium phosphate (Synthograft; Johnson & Johnson, East Windsor, NJ). All treated teeth were sealed occlusally with Cavit. Both of the test materials were inserted with small spoon excavators and condensers. The tricalcium phosphate was made into a slurry with the pooled blood in the defect.

The animals were killed at four time intervals: (a) 1 day; (b) 1 wk; (c) 2 wk; and (d) 1 month. One-hundred blocks for

each time interval were rapidly obtained with the use of a bone rongeur. Each block was immersed in a separate bottle of 10% formalin solution and labeled.² All blocks were then decalcified in a 15% formic acid solution and processed for histological examination. From each block, twenty-five 5 μ m thick longitudinal serial sections were cut in a mesiodistal direction and stained with hematoxylin-eosin. Eight sections per time period (judged as being typical) were selected for further study. Four sections each were placed on a slide. With the use of an ordinary light microscope, all slides were thoroughly examined, graded, and rated by two evaluators (an oral pathologist and an uninvolved clinician trained in histopathological interpretation) who were blind to the materials used. Five high-power magnification fields were scanned from each of two representative slides for each time period. The responses were graded by counting the number of inflammatory, osteoblastic, or epithelial cells (dependent upon which sections were examined) within a grid per high-power field. An average was obtained for each of the slides.

The variables examined were (a) inflammation; (b) bone resorption; (c) cementum and dentin resorption; and (d) apical proliferation of crevicular epithelium (12). As in previous studies by our group (29-31), the criteria for evaluation of furcation changes were (a) none (0), no changes from the normal; (b) mild (1), less than 25 cells (inflammatory, osteoblastic, or epithelial) per high-power field; (c) moderate (2), 25 to 50 cells (inflammatory, osteoblastic, or epithelial) per high-power field; and (d) severe or extensive (3), greater than 50 cells (inflammatory, osteoblastic, or epithelial) per high-power field. In most cases with inflammation, the inflammatory exudate consisted of a mixture of neutrophils, lymphocytes, and occasional plasma cells. For statistical evaluation, chi-square was used with statistical significance set at the 0.05 level.

RESULTS

The discrepancy in the number of specimens, 81 versus 140, is related to the loss of animals as a result of untimely death or the loss of teeth from accidental mutilation during the operative procedures. In addition, the inequality of specimen totals in some of the investigative factors (e.g., cementum and dentin resorption) was related to interpretive difficulties (e.g., differentiation of bur cut versus resorption).

With all of the teeth, the temporary fillings were intact at the time of sacrifice. However, some debris was observed in the pulp chamber of most specimens. This debris did not appear to be related to coronal leakage.

For both Cavit and Synthograft, in most time periods, inflammation ranged from mild to severe. With individual time periods, there was no statistically significant differences between the two materials ($p > 0.05$). However, when all of the time periods were combined, a comparative analysis of inflammation showed a statistically significant better result with Synthograft ($p < 0.05$, Fig. 1). This significance, with respect to Synthograft specimens, was related to the absence of severe inflammation in the 1-month specimens and an apparent shift toward no and mild inflammation (Fig. 2).

² With small animals, perfusion is very difficult and time consuming. Block sectioning, as was used in this experiment, is effective for distribution of fixative. This has been demonstrated in previous studies by our group (29-31).

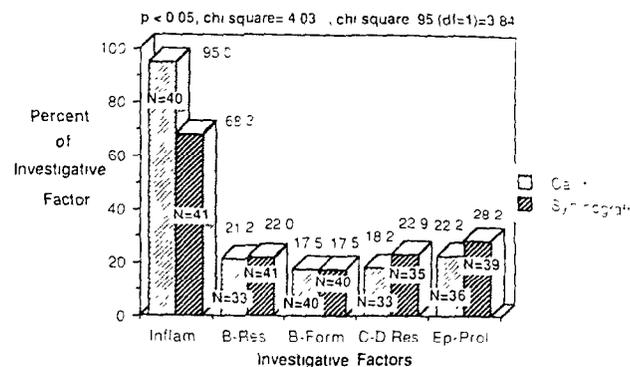


FIG 1. A comparative analysis of tricalcium phosphate and Cavit for the combined four time periods with respect to the evaluative factors: inflammation (*Inflam*), bone resorption (*B-Res*), bone formation (*B-Form*), cementum and dentin resorption (*C-D Res*), and epithelial proliferation (*Ep-Prol*). The statistically significant difference was with respect to inflammation.

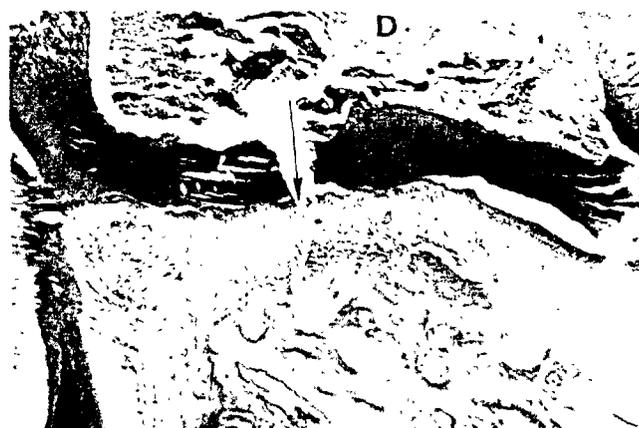


FIG 2. Minimal inflammation (arrow) from use of Synthograft in a 1-month specimen. Low-power photomicrograph of perforated furca region (hematoxylin and eosin; original magnification $\times 25$). D, debris in chamber.

This finding is consistent with the results of Himel et al. (28) which showed less inflammation with tricalcium phosphate as compared with calcium hydroxide. Cavit displayed an equal distribution from mild to severe inflammation during all the time intervals (Fig. 3).

Bone resorption became progressively worse with time. However, many teeth remained normal or showed only slight resorption in the 2-wk and 1-month specimens with both materials (Fig. 4). New bone formation was generally absent for both Cavit and Synthograft in the time periods examined in this study (Fig. 5). This was true in spite of the absence of inflammation in the 1-month Synthograft specimens.

Cementum and dentin resorption was generally absent, except for the 2-wk Synthograft specimens which demonstrated mild and some moderate cementum and dentin resorption (Fig. 6). Epithelial proliferation was generally absent, although mild proliferation was noted in the 1-month specimens of both materials (Fig. 7). When all of the time periods were combined, a comparative analysis of the investigative factors of the two materials (i.e., bone resorption, bone deposition, dentin and cementum resorption) showed no statistically significant differences. However, as previously men-

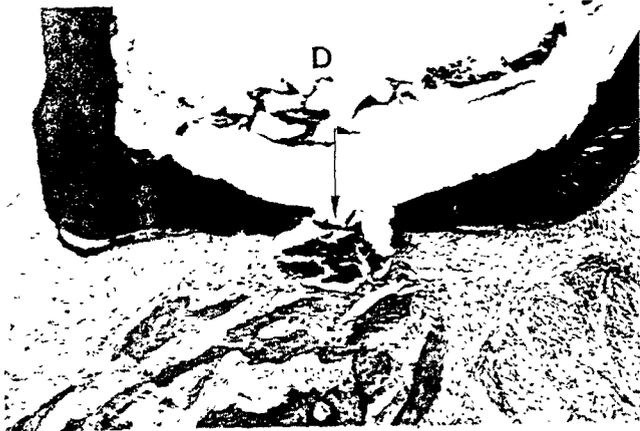


FIG 3. Moderate inflammation (arrow) from use of Cavit in a 1-month specimen. Low-power photomicrograph of perforated furca region (hematoxylin and eosin, original magnification $\times 25$). D, debris in chamber.



FIG 4. Slight bone resorption (arrows) following use of Cavit in a 1-month specimen. Low-power photomicrograph of perforated furca region (hematoxylin and eosin; original magnification $\times 25$). D, debris in chamber.

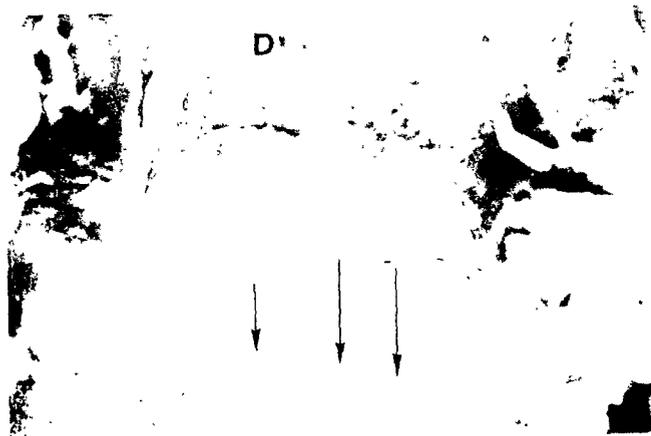


FIG 5. Absence of bone formation (arrows show slight resorption) following use of Synthograft in a 1-month specimen. Low power photomicrograph of perforated furca region (hematoxylin and eosin, original magnification $\times 40$). D, debris in chamber

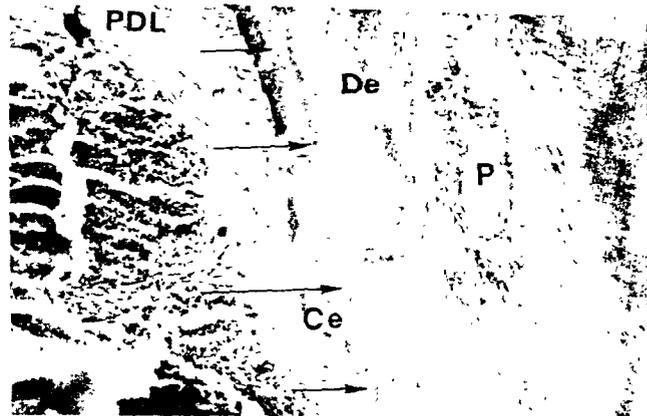


FIG 6. Moderate cementum and dentin resorption (arrows) from use of Synthograft in a 2-wk specimen. Low-power photomicrograph of perforated furca region (hematoxylin and eosin, original magnification $\times 50$). De, dentin; Ce, cementum; P, pulp; PDL, periodontal ligament



FIG 7. Mild epithelial proliferation (arrows) following use of Cavit in a 1-month specimen. Low-power photomicrograph of perforated furca region (hematoxylin and eosin, original magnification $\times 40$). D, debris in chamber.

tioned, with inflammation, there was a statistically significant advantage for Synthograft (Fig. 1).

DISCUSSION

In the search for effective management of perforations by the use of specific materials, one must not lose sight of factors which are beyond control in the traumatic event. This particular violation of the periodontal apparatus through tooth structure has serious dental implications. The perforation causes severe inflammation, a reorganization of the periodontal fiber; resorption of bone, cementum and dentin; and a downgrowth of epithelium from the sulcus. These changes may be sufficient to preclude tooth retention (3, 7, 28). This is especially true in instances of perforation into the furcation region of multirooted teeth or near the gingival sulcus in both single-rooted and multirooted teeth (32-35).

The quest, therefore, for a material to seal the perforation may be secondary in importance to the realization of the damage done by the mechanical event itself. All materials may prove to be of limited usefulness after the event has

occurred. The search must continue, nonetheless, in an attempt to salvage what is possible from a compromised situation.

Even though there is some indication in the literature that tricalcium phosphate can have some merit in sealing perforations, the evidence, as shown in this study, is that tricalcium phosphate is not an ideal solution. Since there were no statistically significant differences with all of the evaluative factors assessed in this study between Cavit and Synthograft, except for the combined time periods with inflammation, it may be that these findings are more a reflection of the response to the mechanical injury than to the properties of the sealing materials themselves. This has previously been shown with perforations induced without any material placed over them (3, 32).

Bone formation, which might better reflect the properties of the materials, also did not show any statistically significant difference between the two materials. In all time periods, there was little evidence of bone formation. This indicates, perhaps, the ongoing effect of the physical injury. However, it is possible that with longer time periods, more evidence of bone formation would have been observed.

In the 1-month comparisons, Synthograft appeared better in some respects than Cavit. With inflammation, Synthograft showed a tendency toward a milder response than did Cavit (although it was not statistically significant). The factor of bone resorption showed insignificant differences between the two materials and epithelial proliferation appeared to be more deleterious with Synthograft. Bone formation with Synthograft was no better than that of Cavit in spite of the apparent decreased incidence of inflammation.

With respect to the animal model used in this study, the rat is inexpensive, simple to maintain, and relatively easy to handle. However, because of the small size of the molars, extreme care is required to prevent mutilation of the teeth. Considering this, for future studies, if money and facilities are available, the use of monkeys (or other human-like species) are recommended for perforation studies.

CONCLUSIONS

Since Synthograft was not significantly better than Cavit for the sealing of perforations, it does not seem necessary to add this material to the endodontic armamentarium. Therefore, it would appear at this time, that the commonly used materials of Cavit, amalgam, and calcium hydroxide hold as much, or as little, promise in controlling the clinical situation as any material currently available. Nevertheless, since Synthograft did result in statistically significant less overall inflammation in the combined time periods than did Cavit (Fig. 1), a rationale could be presented for its clinical use. However, the statistically significant reduction in inflammation did not result in statistically significant reductions in the sequelae of inflammation, i.e., bone, cementum and dentin resorption, and epithelial proliferation. In addition, the decreased inflammation did not result in a statistically significant increase in the advantageous sequela, i.e. bone formation. Hence, further studies with larger samples are needed. In the meantime, great effort should be placed, in teaching and practice, on the avoidance of perforations. Perforations are so damaging an event to the attachment apparatus, and so poorly manageable

after the injury, as to be more consequential to the prognosis than the material used to seal the defect

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The opinions, assertions, materials and methodologies herein are private ones of the authors and are not to be construed as official or reflecting the views of the American Association of Endodontists or the Endowment and Memorial Foundation.

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Article Analysis and Evaluation

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Snyder AJ, Levin MP, Cutright DE.

J Periodontol 1984 55: 273-7

PURPOSE/QUESTION:

This purpose of this study was to further evaluate of using tricalcium phosphate ceramic (TPC) material was undertaken on 17 carefully selected patients with 1-wall, 2-wall, crestal and furcation defects using standardized preoperative and postoperative radiographs, clinical measurements and clinical photographs.. The motivation of the stated purpose was that initial pilot studies using tricalcium phosphate ceramic placed into human periodontal osseous defects demonstrated osseous repair

SOURCE OF FUNDING:

Not mentioned

TYPE OF STUDY/DESIGN:

Prospective cohort study with carefully selected patients

SUMMARY FROM AUTHORS' MANUSCRIPT

Subjects(Patients):

During the study period from April 1977 to January 1979, 17 carefully selected patients requiring periodontal surgery had TPC placed in crestal, furcation, 1-wall, and 2-wall defects.

Exposure:

The main exposure was patients who had been diagnosed as having advanced periodontitis were reevaluated after initial therapy.

Main Outcome Measure:

Main outcome measures included the measurements of pocket depth (from gingival margin to the base of the pocket), attachment level (from the cementoenamel junction to the base of the pocket).

Main Results:

The authors' results shown that eighteen-month reentry procedures and evaluations were completed on 10 of the 17 patients, at which time no residual ceramic material was found.

Of the 17 patients, two had been total failures. Both of these involved extensive defects and were originally recognized as having an exceptionally poor prognosis.

Conclusions:

Then placement of tricalcium phosphate ceramic in human periodontal defects resulted in average new osseous formation nearly equal to the 3mm.

The ideal graft material is still being sought, and perhaps the major determinant for such a material will be its predictability.

Commentary

Although TPC was not found to be totally predictable in this study, it nevertheless exhibited a potential for osseous repair in areas otherwise noted for poor or totally unsuccessful results.

TPC may become a useful graft material because of its potential for osseous repair in combination with its availability, host acceptability, ease of manipulation and storage advantages.

Alloplastic Implants of Tricalcium Phosphate Ceramic in Human Periodontal Osseous Defects*

Alvin J. Snyder,† Marvin P. Levin‡ and Duane E. Cutright§

Accepted for publication 9 October 1983

INITIAL PILOT STUDIES using tricalcium phosphate ceramic placed into human periodontal osseous defects demonstrated osseous repair. Therefore, further evaluation of this material was undertaken on 17 carefully selected patients with 1-wall, 2-wall, crestal and furcation defects using standardized preoperative and postoperative radiographs, clinical measurements and clinical photographs. Inverse bevel, full-thickness flaps were raised, the areas debrided, root surfaces planed with ultrasonic and hand instrumentation, osseous penetrations made with curet point and the flaps sutured after the defects were filled. Eighteen-month reentry surgical procedures were performed on 10 of the 17 patients, with a resultant average of 2.8 mm of new bone. Controls were not used in this study since a protocol describing a sham procedure with other than 3-wall osseous defects was not acceptable in 1973 to the Clinical Human Use Committee.

Although the tricalcium phosphate ceramic material was not found to be totally predictable in this study, it may nevertheless become a useful graft material because of its potential for osseous repair in combination with its availability, host acceptability, ease of manipulation and storage advantages.

Biodegradable tricalcium phosphate ceramic (TPC) has been associated with repair of lost periodontium.¹ There is also evidence that it possesses the potential to inhibit osseous resorption.² It is well tolerated by the tissues³ and, when placed in periodontal osseous defects, has been found to disappear in 12 to 18 months, depending upon particle size.⁴ Furthermore, TPC is easily obtainable and requires no processing to render it nonantigenic. It is easy to manipulate and can be kept on a shelf in the operatory and used as needed without additional preparation.

Considering the numerous possible uses of a material with such desirable properties, an evaluation was made to determine its potential for the treatment of periodontal osseous defects in humans. Interest was intensified after initial pilot studies were conducted in which

TPC was placed in periodontal defects of humans with subsequent osseous repair. One of the teeth treated in these pilot studies has been used as the distal abutment for a mandibular removable partial denture during the past 10 years and remains in excellent periodontal health today (Figs. 1A-1C).

MATERIALS AND METHODS

The tricalcium phosphate ceramic powder used in this study was supplied by Battelle Laboratories.¶ The powder was prepared by Battelle from a batch of calcined tricalcium phosphate which was die-pressed to form discs 2 inches in diameter × 1/8-inch thick and fired at 2000°F for 2 hours. The discs were then crushed in an alumina mortar and pestle, with the resulting powder being sieved to recover the -200/+325 mesh size fraction. To avoid contamination during secondary handling, the powder was packaged in small (1/6 dram) unit-dose size vials (Fig. 2). The vials and their FDA-approved polyethylene caps were washed and rinsed with ethyl alcohol and vacuum oven-dried. After the vials were filled with the powder, they were dry-heat sterilized at 500°F for 2 hours. The vials were then capped using the same sterile procedures (masks, gloves, gowns, etc.) used during vial preparation and filling.

*"The opinions expressed herein are those of the authors and are not to be construed as those of the Army Medical Department." The information in this report was gathered under Federal Drug Administration IND # 10-374.

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¶ Battelle Laboratories, Columbus, OH.



Figure 1. A, Preoperative radiograph. B, 1-year postoperative radiograph. C, 9-year posttreatment view of tooth treated with a ceramic graft. It serves as an abutment for a removable partial denture.

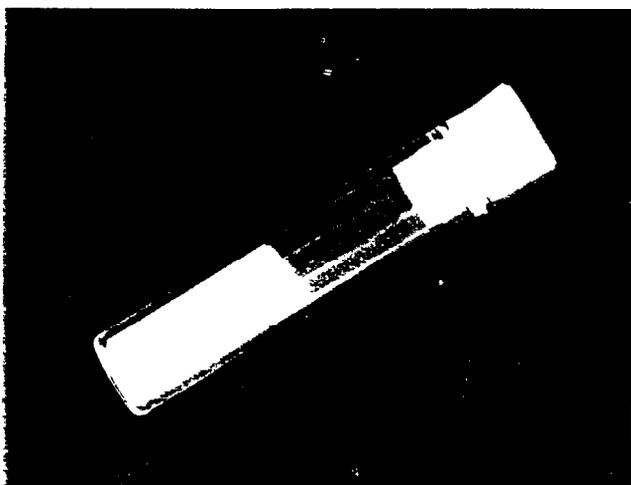


Figure 2. Vial containing tricalcium phosphate ceramic.

Patients who had been diagnosed as having advanced periodontitis were reevaluated after initial therapy. During the period from April, 1977, to January, 1979, 17 carefully selected patients requiring periodontal surgery had TPC placed in crestal, furcation, 1-wall and 2-wall defects. These defects were selected primarily because of their known association with results of low predictability in "reattachment procedures."¹² The following procedures were carried out:

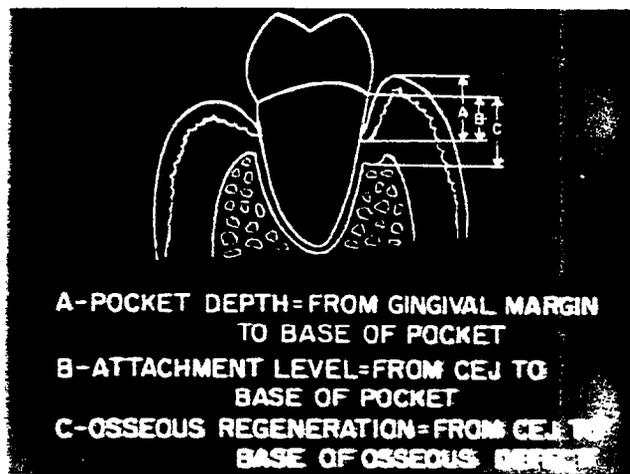


Figure 3. Measurements taken.

Preoperative measurements were made with a periodontal probe from the gingival margin to the base of the pocket (Fig. 3A) and from the cemento-enamel junction to the base of the pocket (Fig. 3B). Clinical photographs were also taken at this time, with the understanding that an attempt would be made to closely approximate angulation, magnification, color and composition with all subsequent clinical photographs for purposes of comparison and evaluation. Occlusal registrations were made on Rinn plastic x-ray tabs. Hirsch-

Table 1
Data on Ten Patients in Whom Reentry Procedures Were Performed

Patient	Defect	A	B	C
		Decrease in pocket depth (mm)	Increase in attachment (mm)	Osseous repair (mm)
1	1-Wall hemiseptal	2.7	1.0	1.7
2	2-Wall	3.0	2.0	2.0
3	2-Wall	3.3	2.6	1.3
4	Class II F Furcation	3.0	3.0	5.5
5	2-Wall (coronal) 3-Wall (base)	3.0	0.4	1.3
6	1-Wall (coronal) 2-Wall (base)	5.0	3.5	2.8
7	2-Wall (coronal) 3-Wall (base)	5.3	3.7	3.5
8	2-Wall	2.7	3.3	3.3
9	2-Wall	1.7	3.0	2.0
10	1-Wall F Furcation	6.3	4.3	5.0
Mean ± SEM		3.6 ± 1.4	2.7 ± 1.2	2.8 ± 1.5

feld points were placed to the depth of the defect and the tabs were used to take standardized preoperative periapical radiographs.⁷

After initial preparation and reevaluation, a surgical procedure was performed consisting of facial and lingual internally beveled full-thickness flaps designed to retain maximum gingival tissue. The defects were debrided, and definitive root planing was accomplished using ultrasonic followed by hand instrumentation. Measurements were made from the cemento-enamel junction to the base of the osseous defect (Fig. 3C), and clinical photographs of the exposed defect were taken. Intramarrow penetrations were made with the point of a curet, and TPC was placed in the defect and contoured. The TPC was carried to the defect with a sterile amalgam carrier used only with TPC and then lightly condensed into the defect with an amalgam condenser, also used only with TPC. Once the defect was filled with the TPC, the original contour of the area was achieved by gently placing the slightly moist facial and lingual flaps momentarily against the TPC build up and then contouring with an explorer. The flaps were approximated and sutured, with an effort being made to achieve complete coverage of the filled defect. Periodontal dressing* was placed, and systemic tetracycline (250 mg, 1 tablet q.i.d.) was prescribed for 10 days postoperatively.

RESULTS

Seventeen-month reentry procedures and evaluations were completed on 10 of the 17 patients, at which time no residual ceramic material was found.

*Coe-Pak.

Of the 17 patients, two have been total failures. Both of these involved extensive defects and were originally recognized as having an exceptionally poor prognosis; nevertheless, treatment was carried out within the criteria of the experimental design. Without consulting us, a third patient was treated by another dentist with flap curettage of the area 2 months prior to our reentry date. One patient developed a periodontal abscess 17 months posttreatment in an area that clinically and radiographically appeared successful until the abscess occurred. Another patient moved to a distant state; and, although radiographs and clinical measurements were requested and received from a dentist in that area, the material was of poor quality and could not be included in the study. All other patients are being followed in this continuing study.

Table 1 illustrates, in millimeters, the mean decrease in pocket depth (Column A), the mean increase in attachment level (Column B) and the mean amount of osseous repair (Column C) in those patients on whom 18-month reentry surgical procedures were performed. Illustrations of two of the cases completed appear in Figures 4 and 5. Use of the x-ray digital subtraction technique⁸ with standardized preoperative and postoperative radiographs made it possible to demonstrate definitive postoperative radiopaque changes in those areas originally exhibiting massive radiolucencies.

DISCUSSION

In this study, placement of tricalcium phosphate ceramic in human periodontal defects resulted in average new osseous formation nearly equal to the 3 mm recorded by Shallhorn et al.⁵ and Froum et al.⁶ and offers sufficient evidence that there is a potential for

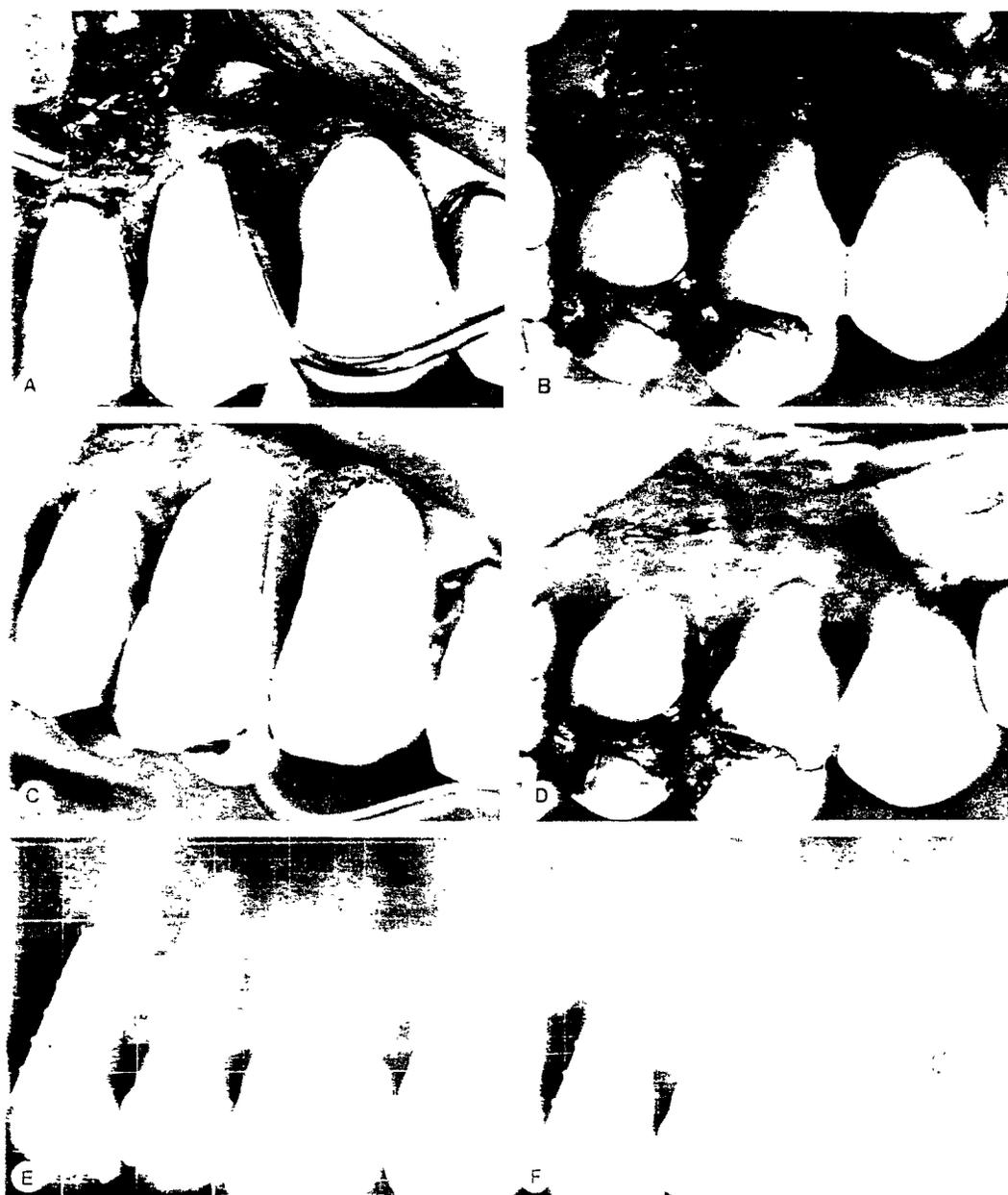


Figure 4. A, buccal view of periodontal defect; B, palatal view of defect; C, buccal view—18-month reentry; D, palatal view—18-month reentry; E, preoperative radiograph; F, eighteen-month postoperative radiograph.

osseous repair with this material and other ceramics.⁹⁻¹² In four of the 10 cases, osseous repair was greater than 3 mm, with two cases exhibiting 5 mm or more.

The authors recognize that the use of controls for comparisons and block sections for histologic information would have contributed greatly to this study. However, the protocol for the study was submitted in early 1973, a time when neither periodontal surgical procedures consisting of curettage only (of other than 3-wall osseous defects) nor block sections were acceptable to the Clinical Human Use Committee at Walter Reed Army Medical Center.

The ideal graft material is still being sought, and

perhaps the major determinant for such a material will be its predictability. Although TPC was not found to be totally predictable in this study, it nevertheless exhibited a potential for osseous repair in areas otherwise noted for poor or totally unsuccessful results. It is conceivable that TPC may become a most useful material for periodontal surgery due to this osseous potential in combination with its availability, host acceptability and ease of manipulation, along with the fact that it can be stored in the operatory for use as required.

ACKNOWLEDGMENT

The authors would like to acknowledge the assistance of Dons Cole for manuscript preparation.



Figure 5. A, preoperative photograph with silver point to depth of defect. B, defect exposed. C, eighteen-month reentry. D, preoperative radiograph. E, eighteen-month postoperative radiograph

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Article Analysis and Evaluation

ARTICLE TITLE AND BIBLIOGRAPHIC INFORMATION:

Tricalcium phosphate ceramic as immediate root implants for the maintenance of alveolar bone in partially edentulous mandibular jaws. A clinical study.

Mathai JK, Chandra S, Nair KV, Nambiar KK.

Aust Dent J 1989 34: 421-6

PURPOSE/QUESTION:

This purpose of this study was undertaken to probe the efficacy of tricalcium phosphate ceramic (TCP) as an immediate root implant in the maintenance of alveolar bone.

SOURCE OF FUNDING:

Not mentioned

TYPE OF STUDY/DESIGN:

Pilot Study with Follow-up

SUMMARY FROM AUTHORS' MANUSCRIPT

Subjects(Patients):

As a pilot study, three patients were selected from those attending the Department of Oral Diagnosis and Radiology, College of Dental Surgery, Manipal, for whom canine / premolar extractions and later prosthetic rehabilitation was advised.

Exposure:

The main exposure was patients who had canine / premolar extractions.

Main Outcome Measure:

Main outcome measures included the control and implant areas were evaluated at the 1st, 12th, 20th and 78th week on the basis of radiographic and clinical measurements.

Main Results:

The authors' results shown that the height of the alveolar bone radiographically and the control region showed a mean decrease of 2.4mm and 2.8mm when compared with the implant regions at the 20th and 78th post-implantation weeks.

The alveolar bone maintenance in the control region showed a mean decrease of 1.20mm and 1.64mm in width compared with the implant region at the 20th and 78th post-implantation week.

Alveolar bone resorbs at a faster rate at control compared with implant sites.

Conclusions:

The authors' conclusions were as follows:

(1) The TCP implant in the extraction sockets helped in the maintenance of the height and width of alveolar bone.

- (2) No immunological reactions or toxic effects occurred.
- (3) The ceramic material possessed no problems during preparation, storage or implantation and can be recommended for short clinical procedures.
- (4) The TCP implantation did not require specialized skill or sophisticated instrumentation.
- (5) The results of the authors' study justified the need for a long-term evaluation of TCP in a larger group of patients covering larger implantation sites.

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Tricalcium phosphate ceramic as immediate root implants for the maintenance of alveolar bone in partially edentulous mandibular jaws. A clinical study

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K. K. Srinivasan Nambiar, MSc§

Key words: Alveolar bone, implants, resorption, tricalcium phosphate ceramic.

Abstract

This study was undertaken to probe the efficacy of tricalcium phosphate ceramic (TCP) as an immediate root implant in the maintenance of alveolar bone. Three patients had five TCP root implants placed in fresh extraction sockets with soft tissue closure. The control and implant areas were evaluated at the 20th and 78th week on the basis of radiographic and clinical measurements. Tricalcium phosphate ceramic root implants in extraction sockets produced a significant increase in height and width of alveolar bone compared with control sites. It is believed that this method is a more effective and efficient procedure to preserve alveolar bone for the retention of dentures than other methods.

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Introduction

Dental surgeons for the past one hundred years have been striving hard to develop various techniques and materials to preserve the existing tissues of the stomatognathic system. Once the teeth are lost the alveolar bone begins to resorb. Where the loss of teeth is inevitable, prosthodontists have tried to preserve the alveolar ridge. This has been a stimulus for the development of 'Preventive Prosthodontics' which has gained momentum over the last three decades. The present study attempts to evaluate the efficacy of tricalcium phosphate ceramic (TCP) as an immediate root implant; by the processes of bioresorbability or biodegradation, new bone formation may result and probably form a firm and stable foundation for the future denture base able to withstand occlusal forces.

Review of literature

Many materials and methods have been tried for the preservation of alveolar bone. Helsham in 1960,¹ after a clinical survey, was the first to note the preservation of alveolar bone in patients with roots of teeth retained in the jaws as a result of incomplete extraction.

Lord and Teel,² Loisella and associates,³ Brewer and Fenton,⁴ Crum and Rooney,⁵ Guyer,⁶ and others⁷⁻¹¹ reported on favourable results obtained by constructing complete dentures over retained teeth and/or roots, prepared or otherwise.

All the above studies and observations showed that root retention¹² preserves the alveolar bone and this in turn offers a better contour and stability to the prosthesis, preventing a decrease in the vertical facial height. However, long-term studies have shown that these experimental teeth when exposed to the oral environment experienced the classical signs of periodontitis and eventual loss due to the failure of the oral mucosa to maintain the primary closure. Other problems were caused by prosthetic forces or delayed resorption of alveolar bone. Additionally, the cost of the materials, the skilled personnel required for the sophisticated endodontic and surgical procedures, repeated visits by the patients and, finally, the time factor led to the search for newer materials and procedures.

Lam and Poon in 1969¹³ used cold-curing methyl methacrylate resin and Lam in 1972¹⁴ used biologic and non-biologic implants for the prevention of alveolar bone resorption.

Among non-biologic materials, metals and ceramics are widely used for alveolar ridge augmentation. Smith,¹⁵ in 1963, was the first to use ceramics as a bone substitute. Bhaskar et al.,^{16,17} Hammer et al.,¹⁸ Ellegard,¹⁹ and Dennisseh and De Groot²⁰ found excellent tissue compatibility in several types of biodegradable and non-degradable ceramic materials which have shown promise as a substitute for bone.

In 1970, De Castro et al.,²¹ following tooth extraction in rats, filled the alveolar sockets with TCP. Their 'synthetic bone' caused some histologically detectable inflammation and resorption of cortical bone. But in later years, in contrast to these findings, various investigators^{16-18 22-26} have reported that the implanted biodegradable ceramic was well tolerated.

The following features have been reported in these studies:

1. Tricalcium phosphate ceramic was well accepted by tissues.
2. No inflammatory reaction was noted.
3. Bone was deposited directly against the ceramic.
4. Marrow re-establishment occurred around and within the TCP pellet.
5. The final stage of degradation was of a fine granular form which appeared to combine with the proteinaceous fluid present.
6. Degradation was approximately 95 per cent complete within 48 days.²⁷

The work described by Howden²⁷ proved that TCP ceramic was biocompatible with bone,

compatible with the immunological system, eventually was totally replaced by bone and was capable of promoting bone formation.²⁸ Bhaskar et al.¹⁷ stressed that biodegradable ceramic stimulated bone formation and disappeared from the implantation site, but it did not have the initial strength of a metal or non-degradable ceramic implant; however, when completely replaced by bone it might prove superior to the latter two.

Another potentially valuable and unique feature of TCP ceramic implant was its apparent ability to become directly bonded to bone.²⁹ A chemical bond was found to exist between the calcified tissue and the ceramic.

The factors which govern the rate of healing, bone bonding and the efficacy of calcium phosphate implants are similar to those which govern the 'take' of a bone graft. Many investigators noted that initial stabilization and tight fixation of the implant to the adjacent bone were prerequisites for effective healing.^{30,31} (In the present study the atabilization of the implant is achieved by the well-confined walls of the root socket.)

Many reporters have presented their data on the efficacy of TCP ceramic as an implant material in other fields.^{22,24,25,32,33} (Osseoplast R. Personal communication, 1982.) Based on the substantial amount of information that has been gained with TCP ceramic implants, the suitability of TCP ceramics as an immediate root implant for the maintenance of alveolar bone is unquestionable. It also appears that calcium phosphate is probably the most compatible synthetic hard tissue implant material known.³⁴ By virtue of possessing both the ability to become chemically bonded to bone,²⁹ and therefore an integral part of the living tissue,¹⁷ and a chemical composition devoid of toxicity, the TCP ceramic in this study is expected to function as a hard and stable support foundation for dentures.

Materials and methods

As a pilot study, three patients were selected from those attending the Department of Oral Diagnosis and Radiology, College of Dental Surgery, Manipal, for whom canine/premolar extractions and later prosthetic rehabilitation was advised. Dense TCP ceramic was implanted in a total of five extraction sockets of the lower jaw and their 'mirror image' on the contralateral side served as controls.

In accordance with established medical procedure, each patient was fully informed about the relevant details regarding the study.

The following criteria were taken into account for the selection of cases:

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Table 1. Mean difference in height and width of alveolar bone between the implant and control region

	At the time of extraction or immediately after extraction	At 20th week	At 78th week
Long cone paralleling technique measured in height in mm (LCP)	0.2 mm	2.4 mm	2.8 mm
Diagnostic casts measured in width in mm	0.94 mm	1.20 mm	1.64 mm

1. The future of bilateral 'mirror image' extraction cases involving canines/premolars on the lower jaw.
2. Freedom from disease status.
3. The absence of any long-term medication.
4. Normal haemogram and blood sugar levels.

Those patients who fulfilled the above criteria underwent oral prophylaxis and oral hygiene instruction, and diagnostic casts with special trays and border moulding were taken of the extraction sites. The control and implant sites were randomly selected from either side of the lower jaw.

Radiographs were taken with a right-angle paralleling technique incorporating a Fixott-Everett grid³⁵ with a beam aligning device (xCP)³⁶ that was adjusted by employing bite blocks.

TCP ceramic in dense polycrystalline form was prepared as described by Jarcho et al.³⁰

The implant material was made into 50 mg packets and sterilized in a hot air oven at 160 °C for 60 minutes. It was mixed with normal saline to form a paste at the time of implantation.

Procedure

Patients were placed under penicillin cover at least 12 hours before implantation and the procedure was performed under local anaesthesia. A standard full-thickness, mucoperiosteal flap was raised, and on completion of the extractions, the surgical sites were repeatedly irrigated with sterile normal saline and TCP ceramic mixed in normal saline was condensed after encouraging enough bleeding into the socket by a curettage so that it would permit the ingress of multipotential cells from the marrow space.³⁷ The implant was packed so as to just fill the socket as over-filling would interfere with the closure. The flaps were then repositioned and sutured. Post-operative instructions were given.

Methods of evaluation

Pre-implantation

Diagnostic casts were obtained with special trays and measurements of the buccolingual width of the alveolar bone at the implantation and control sites were recorded with the help of vernier calipers and tabulated.

Immediately after implantation

Radiographs using a right-angled paralleling technique incorporating the Fixott-Everett grid^{13, 30} (where the adjacent natural tooth root apex served as a fixed reference point) were taken immediately after the extractions both at the implant and control sites so that the exact height of the remaining bone could be assessed.

Evaluation data at the 20th and 78th post-implantation weeks were obtained as above and tabulated for comparison.

Observations and results

The observations and results were based on three patients included in this study and provided ten sockets in all. Tricalcium phosphate ceramic was implanted in five sockets and five served as controls. Patients were recalled at the end of the 1st, 12th, 20th and 78th weeks for assessment and evaluation. Healing was uneventful and there was no evidence of any inflammatory reaction. The non-biologic TCP used in this study was well tolerated by all patients and there was no evidence of any immunological rejection of the TCP at any of the recalls. In most of the implant sites an apparent prominence in height and width was noticed.

Osseous configuration

The height of the alveolar bone was measured radiographically and the control region showed a mean decrease of 2.4 mm and 2.8 mm when compared with the implant regions at the 20th and 78th post-implantation weeks (Table 1).

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Table 2. Maintenance of alveolar bone (%) in height at implant and control regions — long cone paralleling technique

Bone height immediately after extraction	Implant region (mm) (mean)		Bone height immediately after extraction	Control region (mm)	
	At 20th week	At 78th week		At 20th week	At 78th week
9.2	8.6	8.4	9.0	6.2	5.6
Maintenance of alveolar bone height at 20th week (%)	$\frac{9.2-8.6}{9.2} \times 100 = 6.52\%$			$\frac{9.0-6.2}{9.0} \times 100 = 31.1\%$	
Maintenance of alveolar bone height at 78th week (%)	$\frac{9.2-8.4}{9.2} \times 100 = 8.69\%$			$\frac{9.0-5.6}{9.0} \times 100 = 37.7\%$	

Table 3. Maintenance of alveolar bone (%) in width at implant and control region

Width of alveolar bone at the time of implantation	Implant region (mm) (mean)		Width of alveolar bone at the time of extraction	Control region (mm) (mean)	
	Width of alveolar bone at 20th week	78th week		20th week	78th week
10.64	8.58	8.58	9.7	7.38	6.94
Maintenance of alveolar bone width at 20th week (%)	$\frac{10.64-8.58}{10.64} \times 100 = 19.3\%$			$\frac{9.7-7.38}{9.7} \times 100 = 23.9\%$	
Maintenance of alveolar bone width at 78th week (%)	$\frac{10.64-8.58}{10.64} \times 100 = 19.3\%$			$\frac{9.7-6.94}{9.7} \times 100 = 28.4\%$	

The alveolar bone maintenance in all the cases was clinically evaluated by diagnostic casts by measuring the width at the implant and control regions with a vernier caliper. The control region showed a mean decrease of 1.20 mm and 1.64 mm in width compared with the implant region at the 20th and 78th post-implantation week (Table 1).

Although there was no conclusive evidence of bone regeneration at the implant site, Tables 2 and 3 clearly indicate that alveolar bone resorbs at a faster rate at control sites compared with implant sites. It follows that alveolar bone resorption can be minimized to a considerable extent with TCP root implants.

Discussion

This study was undertaken to probe the efficacy of TCP as an immediate root implant for the preservation of human alveolar bone. This ceramic was selected for evaluation on the basis of the interest shown in reported findings on this material used as an implant in other areas.^{22-24, 26} Tricalcium phosphate ceramic is reported to stimulate bone formation^{17, 27} and degradation of the implant with replacement by new bone has been shown histologically by Cutright et al.²³ There is, therefore, every possibility for the implant to be completely replaced

by new bone in the present study of 78 weeks duration. According to Bhaskar et al.¹⁷ the newly-replaced bone would prove superior to metal or any non-degradable ceramic implants. Moreover, TCP, when used as an immediate root implant in fresh extraction sockets, is likely to become firmly attached to the bone by the cementing medium as reported in a histological study described by Jarcho et al.³⁰ A histological study was not carried out because of the very limited number of extraction sockets and the unwillingness of the patients.

The mandibular premolar and canine regions were selected because resorption occurs mainly in the buccolingual direction³⁸ and can be easily evaluated in this region. The mandibular alveolar bone was selected because its resorption rate is reported to be about four times greater than that of the maxillary alveolar bone³⁹ and comparisons could be more readily made.

The controls were 'mirror images' largely because they were contralateral to the implant site in the same jaw, and the studies were undertaken only on single-rooted teeth.

A study conducted to evaluate the effectiveness of an implant material involves an accurate assessment of the quantitative and qualitative records of the results. Various methods are available for the

l regions —

At 78th week

5.6

$\times 100 = 31.1\%$

$\times 100 = 37.7\%$

region

78th week

6.94

$\times 100 = 23.9\%$

$\times 100 = 28.4\%$

78 weeks duration et al.¹⁷ the superior to metal implants. Moreover, root implant in became firmly bonding medium as described by Jarcho not carried out of extraction the patients.

anine regions occurs mainly in be easily evaluated alveolar bone ate is reported at of the maxilla could be more

largely because ant site in the taken only on

effectiveness accurate assess- tive records of available for the

assessment of implant studies in alveolar bones. Those commonly used are radiographs, study models, re-entry procedures, radioisotopes, microradiographs, and computer-assisted analysis, but many are beyond the scope of this study. Re-entry procedures were not attempted because of the possibility of bone resorption,⁴⁰ patient reluctance, and the lack of any resulting benefit to the patient.

Alveolar bone height at the 20th and 78th post-implantation weeks at the implant region was found to be almost its original measurement except for a negligible amount of resorption, namely, 6.52 per cent and 8.69 per cent, respectively, compared with the 31.11 per cent and 37.77 per cent resorption at the control region (Table 2). Thus it is evident that the maintenance of the alveolar bone height at the implant region was due to the scaffolding effect of the TCP. The slight decrease of the alveolar bone height at the implant region at the 20th and 78th post-implantation weeks could be attributed either to crestal remodelling or to the occlusal load of the removable partial denture aggravating the crestal remodelling process (all the patients started wearing removable partial dentures after the 12th post-implantation week). However, long follow-up studies are necessary to substantiate the above interpretations. The percentage of resorption of alveolar bone in width at the implant regions at the 20th and 78th post-implantation weeks were 19.3 per cent and 19.3 per cent compared with 23.9 per cent and 28.4 per cent at the control sites (Table 3).

As there were no reports of TCP being used as immediate root implants for alveolar bone maintenance in human beings in the literature reviewed, a comparison with the present study could not be made.

This study is significant in that it is the first such report of a well-controlled study with a definite measure of success with TCP implants in human alveolar extraction sockets. Normally, after extraction, within a period of six months to two years^{39,41} crestal remodelling occurs regardless of the graft or implant utilized.¹⁶ It is obvious that TCP was well tolerated by the tissues as there was no untoward tissue reaction and the implant remained firmly attached to the surrounding structure as evidenced by the radiographic evaluation.

Summary and conclusions

This study was undertaken to probe the efficacy of TCP as an immediate root implant in the maintenance of alveolar bone in human beings. An evaluation of the study and its results led to the following conclusions.

1. The TCP implant in extraction sockets helped in the maintenance of the height and width of alveolar bone
2. No immunological reaction or any toxic effects occurred.
3. The ceramic posed no problems during its preparation, storage or implantation and it can be recommended for short clinical procedures.
4. No specialized skill or sophisticated instrumentation is needed for TCP implantation.
5. The results of this study justify the need for a long-term evaluation of TCP in a larger group of patients covering larger implantation areas.

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APPENDIX IV

Article Analysis and Evaluation

ARTICLE TITLE AND BIBLIOGRAPHIC INFORMATION:

Intraindividual comparative animal study of alpha- and beta-tricalcium phosphate degradation in conjunction with simultaneous insertion of dental implants.

Merten HA, Wiltfang J, Grohmann U, Hoenig JF.

J Craniofac Surg 2001; 12: 59-68

PURPOSE/QUESTION:

This purpose of this study was to determine whether the new, pure phased α - and β -tricalcium phosphate (TCP) ceramics with defined physiochemical and stoichiometric characteristics show predictable degradation kinetics and whether they are biologically equivalent.

SOURCE OF FUNDING:

Not mentioned

TYPE OF STUDY/DESIGN:

Animal Study

SUMMARY FROM AUTHORS' MANUSCRIPT

Animals:

In this intraindividual comparative study of proximal tibial marrow defects in nine adult Goettinger miniature pigs (GMPs) was investigated. The average weight of 47.5 ± 8 kg were used as test animals.

Exposure:

The main exposure were as follows: The left side of the defect was filled with granular beta-tricalcium phosphate (TCP) ceramic ad modum Cerasorb, and the right side was filled with granular alpha-TCP ceramic ad modum Biobase alpha pore.

Main Outcome Measure:

Main outcome measure was to determine the reorganization and degree of bone regeneration, dynamics of ceramic degradation, and remodeling characteristics of the bone regenerate referring to osseo-integration of the dental implants were examined histomorphologically in nondecalcified specimens.

Main Results:

The authors' results demonstrated that both ceramic types were osteoconductive exclusively. Centripetally oriented angiogenic bone regeneration occurred at the margins of the circular defects. Ceramic degradation was performed hydrolytically and within cells. Furthermore, it was demonstrated that decomposition of the intratrabecularly integrated ceramic residues underlies a dynamic process of degradation. Within 86 weeks, nearly 80% to 90% of the larger alpha-TCP granules, and nearly 90% to 95% of the beta-TCP granules were degraded. The residual height of the alveolar crest in the posterior maxilla was 6.8 ± 1.6 mm on average. The implant lengths ranged from 10 to 16 mm (mean implant length 12.2 ± 1.4 mm).

Conclusions:

The interconnecting microporosity of the investigated the special β -TCP, which should be no smaller than $5\mu\text{m}$, resulted in faster degradation and micro-osseous conduction, and exhibited better tissue response toward the ceramic in comparison with α -TCP.

In contrast to bone substitutes, both α - and the special β -TCP ceramic types are resorbed and substituted by bone in a predictable time, and are suitable as bone rebuilding material.

Commentary

The authors also recommended that because of the initially pronounced accumulation of macrophages, dental implants should not be inserted simultaneously with ceramic, but after further progress of ceramic degradation (5 to 6 months after TCP implantation).

Intraindividual Comparative Animal Study of α - and β -Tricalcium Phosphate Degradation in Conjunction with Simultaneous Insertion of Dental Implants

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Jörg Wiltfang, DMD, MD, PhD
Ulrike Grohmann, MD
Johannes Franz Hoenig, MD, DMD, PhD

Goettingen, Germany

An intraindividual comparative study of proximal tibial marrow defects in nine adult Goettinger miniature pigs (GMPs) was undertaken. The left side of the defect was filled with granular β -tricalcium phosphate (TCP) ceramic ad modum Cerasorb, and the right side was filled with granular α -TCP ceramic ad modum Biobase α pore. Simultaneously, dental screw implants were inserted in each ceramic and fixed within the orthotopically replanted corticalis lids. Control defects were made in two other animals. The survival period ranged from 4 to 86 weeks (control study, 16 and 20 weeks). The reorganization and degree of bone regeneration, dynamics of ceramic degradation, and remodeling characteristics of the bone regenerate referring to osseo-integration of the dental implants were examined histomorphologically in nondecalcified specimens. The results reveal that both ceramic types were osteoconductive exclusively. Centrally oriented angiogenic bone regeneration occurred at the margins of the circular defects. Ceramic degradation was performed hydrolytically and within cells. Furthermore, it was demonstrated that decomposition of the intratrabecularly integrated ceramic residues underlies a dynamic process of degradation. Within 86 weeks, nearly 80% to 90% of the larger α -TCP granules, and nearly 90% to 95% of the β -TCP granules were degraded. At this time, especially for the α -TCP modification,

ceramic microparticles were found in the marrow, either unbound or within polynuclear macrophages. The predictable degradation of both ceramic types provides an early functional adaptation of bone regenerates and facilitates a biofunctional, anisotropic orientation of the neotrabeculae without delay. It is concluded that because of the initially pronounced accumulation of macrophages, dental implants should not be inserted simultaneously with ceramic, but after further progress of ceramic degradation (5 to 6 months after TCP implantation).

Key Words: Bone regeneration material, TCP ceramic, bone defect substitution materials, dental implants, minipig

Concerning the application of ceramic bone substitution materials, an important feature is the demand for controlled bony substitution of ceramic with the potential for biofunctionally orientated degradation of the bone-ceramic compound and consecutive topographic-anatomic and biofunctional restitutio ad integrum.¹⁻¹⁷ Resorbable ceramics of synthetic and biological origin often have unpredictable retention times in the tissue and therefore can act as functional foreign substances.¹⁸⁻²³

Of interest is whether the new, pure phased α - and β -tricalcium phosphate (TCP) ceramics with defined physicochemical and stoichiometric characteristics show predictable degradation kinetics and whether they are biologically equivalent. Furthermore, it is interesting to note how much osseo-

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integration of simultaneously inserted dental implants is influenced by ceramic degradation.

MATERIALS AND METHODS

In an intraindividual experimental animal study conducted on Goettingen miniature pigs (GMPs), we investigated the dynamic degradation of α - and β -TCP and the bone remodeling process with regard to osseointegration of dental implants.

Test Conditions

A total of nine adult GMPs with an average weight of 47.5 ± 8 kg were used as test animals. The animals were premedicated with 2 mg per kilogram Stressnil (azaperone), 10 mg per kilogram Hypnodil (metomidate), and 0.3 mg per kilogram atropine, all administered intramuscularly. Oxygen-halothane anesthesia was induced through a customized animal mask. Endotracheal intubation followed with controlled respiration and electrocardiographic control throughout the entire operation.

Surgical Technique

In a left-to-right comparison, in seven adult GMPs, after osteotomy of a cortical bone window, intraosseous defects of a critical size (3.5–4.7 mL) were created in the proximal tibial condyles. The left sides were filled with granular β -TCP ceramic (Fig 1; spherical; granule size, 1–2 mm; microporous; ad modum Cerasorb [Fig 2]), and the right sides were filled

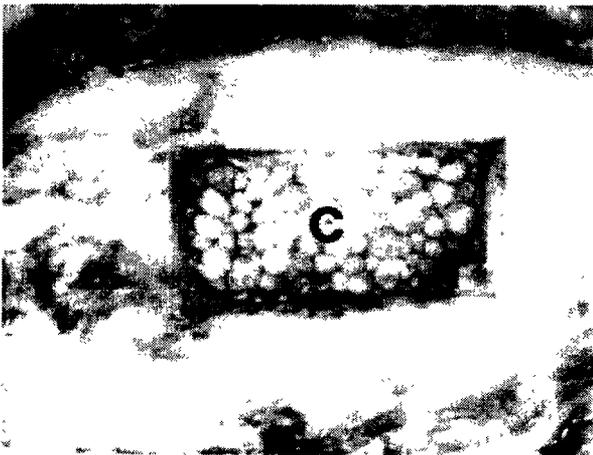


Fig 1 Intraoperative view after defect filling with β -tricalcium phosphate (TCP) granules. In contrast to polygonal α -TCP granules, the spherical β -TCP granules allow a tighter package. The capillary, microporous structure stabilizes the primary blood coagulum.



Fig 2 Electronic microscopic view of the microporous β -tricalcium phosphate (TCP) granules. Arrows mark the so-called "sinter necks" generated by sintering of TCP ceramic. P = micropore; CF = ceramic fragments.

with granular α -TCP ceramic (polygonal; granule size, 3.2–5.0 mm; micromacroporous; ad modum Bio-base α pore [Fig 3]). Control defects in another two animals remained unfilled. In the orthotopically replanted corticalis lids, fixed with miniplates, additional dental full-screw implants (ITI; 3.2 \times 12 mm) were implanted in the defects filled with the TCP ceramics.



Fig 3 Electronic microscopic view. Micromorphometric aspect of macroporous α -tricalcium phosphate (TCP) granules. In contrast to β -TCP granules, the micropore diameter of α -TCP ceramic is smaller than 5 μ m. A continuous interconnection of macropores is questionable. Arrows mark the so-called "sinter necks" generated by sintering of TCP ceramic. P = micropore; CF = ceramic fragments.

Labeling

To evaluate the dynamic process of bone regeneration, we performed polysequential labeling. The following stains were administered as subcutaneous injections paravertebrally and intravitaly in individual applications²⁴ at weekly intervals: 90 mg per kilogram Xenole orange, 20 mg per kilogram Calcein blue, 15 mg per kilogram Rolitetracycline, and 30 mg per kilogram Alizarin Complexone.

End of Trial

After weeks 4, 16, 20, 28, 46, 68, and 86 (the control animals survived 16 and 20 weeks), the GMPs were sacrificed by narcosis, and intravital microangiography with Berlin Blue and Micropaque stain was performed. The tibias were explanted en bloc, fixed immediately in 4% formalin solution, and treated according to the methods of Donath and Breuner²⁵ for uncalcified specimens.

Production of Uncalcified Specimens

The specimens were fixed in a 4% neutral formalin solution at a temperature of 4°C. Dehydration was performed in an incrementally increasing alcohol series followed by vacuum infiltration with composite methacrylate (LR-white Hard-Grade, Science Servicer, München, Germany). Staged polymerization followed in a thermal unit, starting at 30°C for 8 hours, up to 50°C for 12 hours, and at 60°C for 4 hours. The specimens were cut to a thickness of 200 µm using an Exakt sectioning system (Mesmer, Ost-Einbeck, Germany), and later were polished to a thickness of 120 to 140 µm for light optical and fluorescence optical evaluation. The tissue of the specimens was stained with Toluidine blue and Pyronine G dye.

Evaluation of nondecalcified sections thinned by grinding was performed using transmission microscopy, including double polarization and fluorescence microscopy (Zeiss microscopes, Jenar, Germany).²⁵ Contact microradiographs were acquired for selected specimens. Histomorphological evaluation occurred using a semiquantitative method to evaluate ceramic degradation profiles (semi-automatic count processing; Zeiss-Videomat 2, Jenar, Germany),^{26,27} shape and degree of bone formation, and degradation of ceramico-osseous regenerate. Furthermore, inguinal lymph nodes were examined with regard to ceramic deposition.

RESULTS

Throughout the entire course of the study, no inflammation or fractures were observed, making all animals candidates for the study and thus allowing a detailed histomorphological evaluation. All implants healed up to the preset removal date.

Concerning bone regeneration patterns, the different TCP ceramic types showed no significant differences. Only the osteoconductive characteristics of the materials could be observed. With optical fluorescence, centripetally arranged angiogenic bone neoformation was observed originating regularly from the tissue defect margins. No multilocular reossification was seen (Fig 4). Five months after implantation, both TCP modifications showed strong decomposition, with a higher degradation rate of β -TCP (approximately 70% ceramic decomposition) compared with the α -TCP (approximately 40% ceramic decomposition; Fig 5). At that time, ceramic residues were localized mainly in the newly built trabeculae. In addition, microparticles were found in the newly generated, hematopoietically active marrow and in polynuclear giant cells respectively. Macrophages contained α -TCP ceramic remnants primarily (Fig 6).

Continuous degradation of both TCP modifications occurred via hydrolytic halisteresis (physical

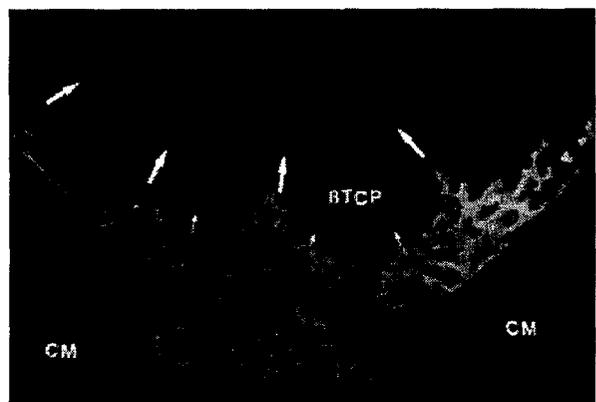


Fig 4 Fluorescent optical detection of bone neoformation generated exclusively by the cortical defect margins (CM). The ceramic granules provide an osteoconductive guide for the centripetally outgrowing bone cones (arrows; so-called "implant hopping" of bone regeneration). A multilocal formation of new bone can be excluded. (Tibial cross-section of the weakly regenerating defect center 4 weeks after defect filling with β -TCP granules, subcutaneous calcein application, 3 weeks after defect filling, nondecalcified thin section, 200 µm, undyed, magnification $\times 4$, FZ blue excitation.)

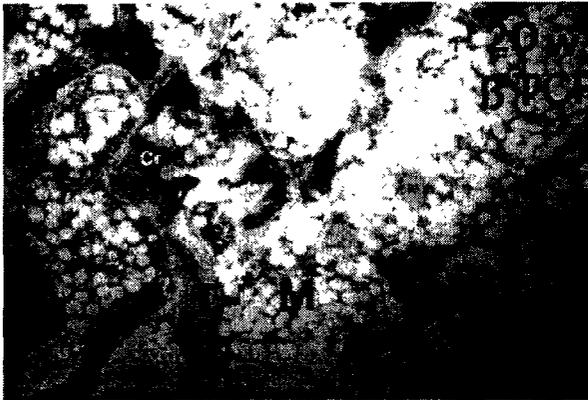


Fig 5 Microscopic view. The situation 5 months after ceramic implantation with obvious ceramolysis of β -tricalcium phosphate (TCP) ceramics. Ceramic residues (Cr) are incorporated within newly built trabeculae (T) as defined by compound osteogenesis. Within the trabeculae, a hematopoietically active marrow (M) is established. In the marrow, no free macrofragments of TCP ceramic can be seen. (Tibial cross-section of the weakly regenerating defect center after defect filling with β -TCP granules; nondecalcified thin section, 20 μ m, toluidine blue, magnification $\times 10$.)

and chemical erosion) similar to the same process that occurs at the cellular level by phagocytosis (polynuclear giant cells, macrophages, or osteoclasts). Compared with the β -TCP modification, a

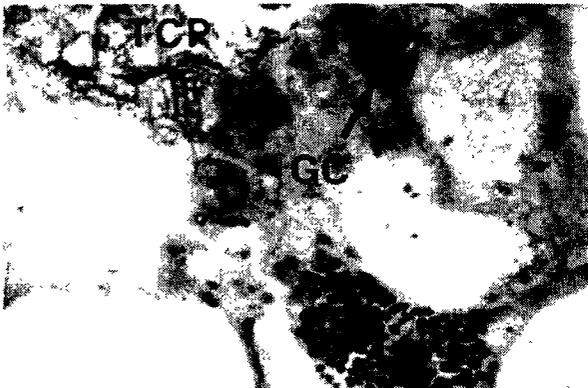


Fig 6 Microscopic view of the center of a tibial cross-section 5 months after α -tricalcium phosphate (TCP) ceramic implantation and progressive physical degradation. Ceramic residues are localized mainly in the newly built trabeculae. In addition, microparticles are found in the newly generated, hematopoietically active marrow and in polynuclear giant cells (GC) resp. macrophages, which contain mainly α -TCP ceramic remnants. (Nondecalcified thin section, 20 μ m, toluidine blue, magnification $\times 64$.)

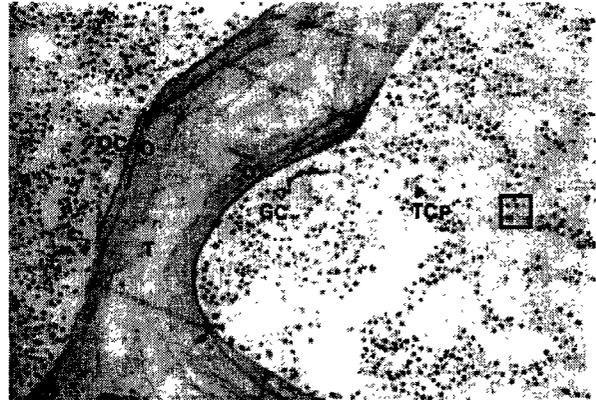


Fig 7 Local hydrolytic-cellular degradation of tricalcium phosphate (TCP) ceramic. Polynuclear giant cells (GC) phagocyte TCP microparticles removed from the trabeculae (T). Near these degradation processes, vital osteocytes (OC) and fresh osteoid bands (O) can be seen, indicating optimal reactivity. After 68 weeks, degradation products are barely detectable in the mature, lipid-rich bone marrow. (Detail of the center of a tibial cross-section 68 weeks after α -TCP implantation; nondecalcified thin section, 10 μ m, toluidine blue, magnification $\times 40$.)

more pronounced cellular accompanying reaction of the investigated α -TCP degradation was observed until the end of the trial (Figs 7 and 8).

It was obvious that trabecular ceramic integration follows the pattern of so-called *compound osteogenesis*, with the definitive degradation of TCP ceramic residues underlying the special locoregional remodeling dynamics of the trabeculae. During the

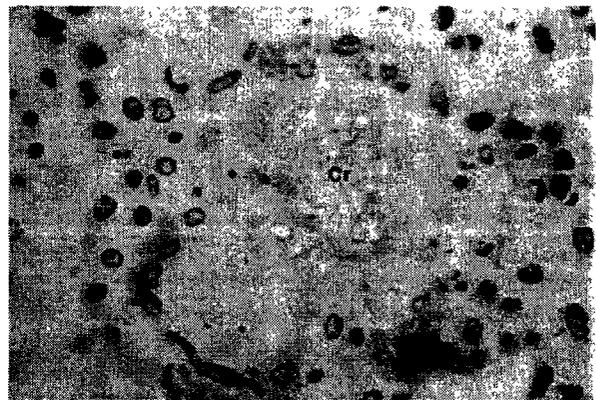


Fig 8 Magnification of a detail of the center of a tibial cross-section of the view in Figure 7 with intracellularly incorporated ceramic remnants (Cr). (Sixty-eight weeks after α -tricalcium phosphate implantation; nondecalcified thin section, 10 μ m, toluidine blue, magnification $\times 180$.)

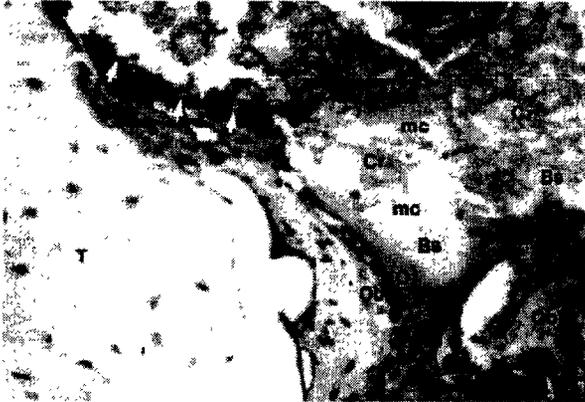


Fig 9 Microscopic view of the the center of a tibial cross-section. During the remodeling process of the newly formed trabeculae (T), the bony incorporated β -TCP ceramic remnants (Cr) were exposed successively (arrows), which means that they were demasked by the surrounding bone and followed by further cellular degradation and creeping substitution. mc = microconduction; Bs = bone substitutes; O = osteoid; Ob = osteoblasts. (Nondecalfied thin section, 10 μ m, toluidine blue, magnification $\times 63$.)

remodeling process, the incorporated bony ceramic remnants were exposed successively, which means that they were demasked by the surrounding bone and followed by further degradation (Fig 9).

Histomorphological analysis revealed that the degradation of both TCP modifications is nearly complete after 86 weeks (Table 1). At that time, ap-

proximately 80% to 90% of the larger size α -TCP granules, and nearly 90% to 95% of the β -TCP granules were degraded and substituted with bone. The remaining ceramic residues were detected within the fine-structured trabeculae. The physiological anisotropy of newly built trabeculae is nearly undisturbed by the functional ceramic adaptation (see Fig 7). In this long-term animal study, the integrated TCP modifications did not lead to any biofunctional foreign body reactions.

Furthermore, it was obvious that both TCP ceramics allowed a topographic-anatomic restitutio ad integrum after a predictable resorption time, and determined bony substitution biofunctionally (Fig 10).

In contrast to α -TCP, β -TCP did not exhibit any foreign body reaction or biofunctional disturbance even if small amounts of β -TCP residues were incorporated intraosseously (Fig 11). If the α -TCP ceramic was implanted, so-called *microcracks* were obvious in the regenerated trabeculae, with an accumulation of giant cells close to the cracks even after 86 weeks, when more than 95% of the material was degraded (Fig 12). When α -TCP was used, these intra- and transtrabecular microcracks were seen in the peri-implant region (Fig 13). The cracks were limited to the outline of the ceramic remnants. Histological examination revealed that they are not artifacts resulting from production of the specimens.

In contrast to α -TCP, the faster degraded β -TCP does not present a microcrack configuration in the peri-implant trabecular framework (Figs 14 and 15).

Table 1. Resorption Profile of α -TCP and β -TCP

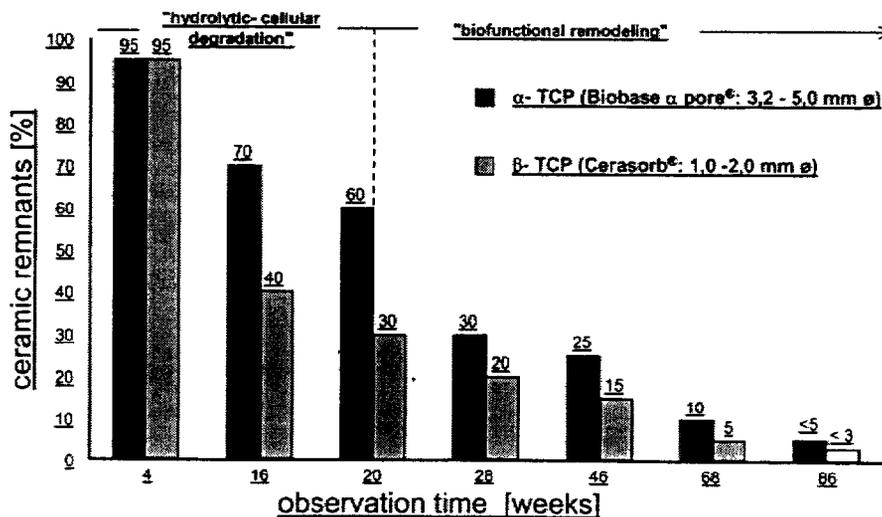




Fig 10 Nearly complete restitutio ad integrum of a tibial defect formerly filled with β -tricalcium phosphate (TCP) ceramic with generation of a physiological trabecular framework. (Tibial cross-section of the defect center 86 weeks after β -TCP implantation; formalin-fixed section, 300 μ m, microradiography $\times 1.3$.)

The predictable degradation of the TCP modifications provides an early functional adaptation of bone regenerate and facilitates a biofunctional, anisotropic orientation of the neotrabeculae without delay, as seen with polarization microscopy (see Figs 13 and 15).

During the hydrolytic-cellular degradation phase, which is characterized by progressive ceramic resorption (see Table 1), a complete osseointegration

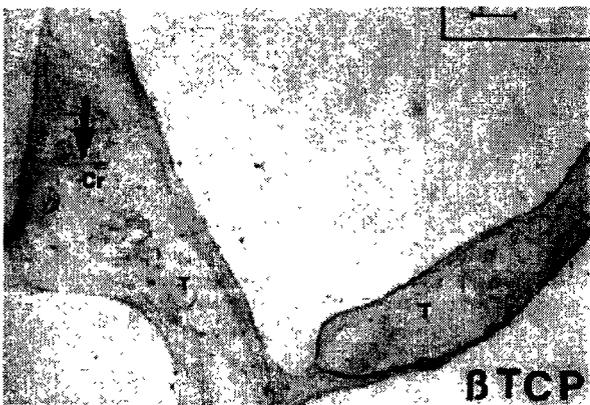


Fig 11 Microscopic view of the tibial defect formerly filled with β -tricalcium phosphate (TCP) ceramic. After 86 weeks only sporadic ceramic remnants (Cr; arrow) are obvious in the vital, newly formed, regularly structured trabecular framework (T). (Tibial defect filled with β -TCP; nondecalcified cut section, 25 μ m, toluidine blue, bar = 40 μ m.)



Fig 12 Microscopic view of the trabecular framework (T) of the tibia formerly filled with α -tricalcium phosphate (TCP) ceramic. Note the intratrabecular microcracks through the ceramic remnants (Cr) and the accumulation of the giant cells (GC) close to the cracks. Possibly the microcracks are induced by the microdebris of the α -TCP ceramic itself. (Tibial defect filled with α -TCP ceramic; nondecalcified cut section, 25 μ m, toluidine blue, bar = 60 μ m.)

of the simultaneously inserted dental implants was not seen until the end of week 20. At the peri-implant interface, trabeculae with direct contact with the dental implant surface or soft-tissue sheaths of implant surfaces could be detected. Histologically, at these

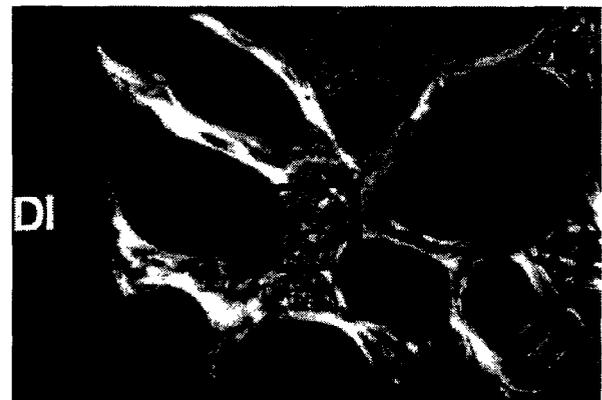


Fig 13 Polarized optical view of an osseo-integrated dental implant (DI) with anisotropic orientation of the remodeled, new trabecular framework. After 86 weeks of implantation, some remnants of intratrabecular α -tricalcium phosphate (TCP) are still obvious. Note the intratrabecular cracks (frame). They were found only in areas in which α -TCP remnants were observed. (Tibial cross-section; double polarization, undyed, 50 μ m, nondecalcified, magnification $\times 10$.)



Fig 14 Microscopic view of an osseointegrated simultaneously with β -TCP ceramic implantation inserted dental implant (DI) in the tibia. With regard to the biofunctional remodeling process, 68 weeks after implantation nearly 95% of the ceramic (arrow) is osseosubstituted. No microcracks or disturbance of the biofunctional system could be detected in the peri-implant region. (Nondecalfied thin section, 25 μ m, toluidine blue, magnification $\times 25$.)

interfaces, cellular ceramic degradation reactions were observed within the newly grown trabeculae in direct contact with the implants.

Twenty weeks after insertion of the dental implant, an osseointegration process started during the biofunctional period (Fig 16). In some rare cases, connective tissue linings were seen at some interfaces with the dental implant even 86 weeks after insertion of the implant (Fig 17).

Two animals (4 and 16 weeks of survival) with tibial defects that were filled with α -TCP ceramic ipsilaterally showed sporadic, refractile microparticles within the inguinal lymph nodes.

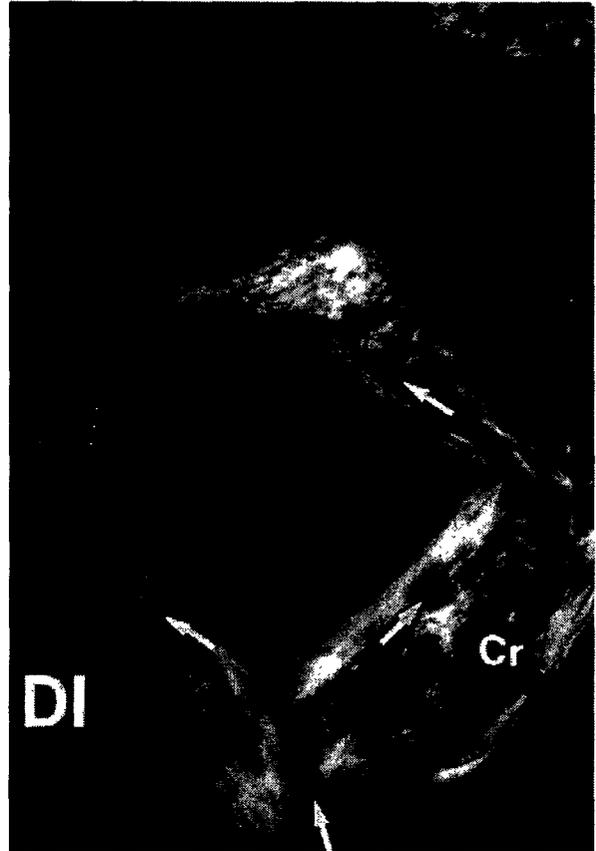


Fig 15 Functional adaptation of the dental implant (DI) with minimal ceramic residue 68 weeks after implantation. β -Tricalcium phosphate residue (Cr) can be detected only in the outline within the anisotropically structured neotrabeculae. This anisotropy results from the structure of oriented collagen fibers (white arrows) and deposited mineral crystals. (Detail of a reossified defect center; nondecalfied thin section, 50 μ m, undyed, double polarization, magnification $\times 25$.)

DISCUSSION

Tricalcium phosphate ceramics have been used as bone substitution materials for a long time.^{8,19,28-31} Because the former types of TCP ceramics were often contaminated with so-called *foreign phases*, as a result of their heterogeneous compounds, different degradation times for the α - and β -TCP modifications were reported.^{18,13,22,23} Reticulo-endothelial system (RES) charges that have been detected³² are likely to be caused by lymphogenous transport of ceramic foreign phases. An optimized biological reactivity is to be expected with the introduction of homogeneous

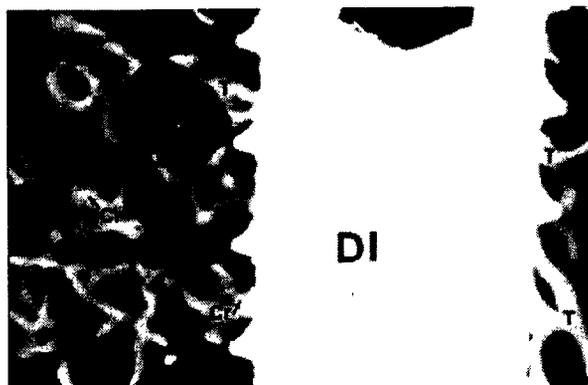


Fig 16 Microradiography of an osseo-integrated dental screw implant (DI) with a rough surface. Note the physiological orientation of the rebuilt trabecular frameworks (T), which are in multiple direct contact with the dental implant surface. Eighty-six weeks after implantation, the remodeling process is nearly complete but there are still some β -tricalcium phosphate ceramic residues (Cr) in the trabeculae (T). (Nondecalfied thin section, 300 μ m, toluidine blue, magnification $\times 6.3$.)

phase α - and β -TCP ceramic types with defined composition.^{13,33-36}

In the current study, for the first time, two of these new homogeneous phase α - (Biobase α pore)

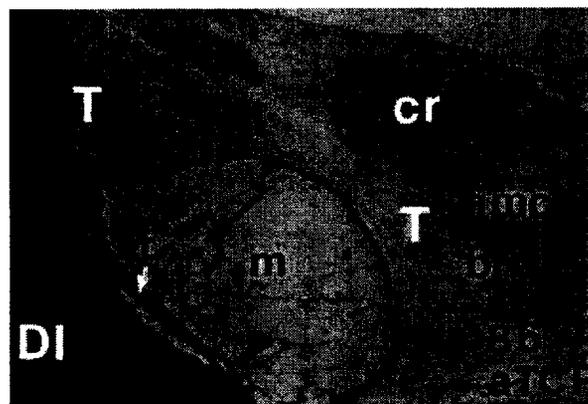


Fig 17 Microscopic view of an osseo-integrated dental implant. Simultaneously, with α -tricalcium phosphate (TCP) ceramic was the dental implant inserted in the tibia 86 weeks after implantation. It is obvious that some ceramic remnants (Cr) are still intratrabecular, and that the trabeculae (T) are in direct contact with the dental implant surface (DI). Connective tissue (t) is rarely seen at the dental interface m = bone marrow; b = functional bio-oriented new trabeculae. Note the intratrabecular microcracks (imc) that cross only the α -TCP ceramic remnants. (Nondecalfied thin section, 25 μ m, toluidine blue, magnification $\times 25$.)

and β - (Cerasorb) TCP ceramics were compared intraindividually.

Both TCP ceramic types exhibited different degradation kinetics with initially accelerated ceramolysis of the smaller size β -TCP granules. After 5 months, approximately 70% of β -TCP ceramic and nearly 40% of α -TCP ceramic were resorbed by a combined hydrolytic-cellular degradation mechanism. After 86 weeks, only minimal residues of both ceramic types could be detected histologically in the newly built trabeculae. Possibly, the smaller size β -TCP granules underwent accelerated ceramolysis. Because the spherical β -TCP granules have a higher package density and a higher microporosity, better solubility of the β -modification can be estimated.³⁷ The initially accelerated ceramolysis, however, did not impede reconstructive osteogenesis.

In general, reconstructive osteogenesis follows the pattern of primary angiogenic ossification, with centripetally oriented bone regeneration originating only from the defect margins. The ceramic granules serve as angio-osteoconductive guides for inter- and intragranular outgrowing bone regenerates.^{6,12} A multilocular reossification, as suggested by Jacobs and coworkers,³⁰ can be excluded by fluorescence microscopy. After 16 weeks, the control defects showed scarce trabecular structures with incomplete reossification whereas in the defects filled with TCP ceramic, after 6 to 8 weeks bony reorganization could be detected fluorometrically. The smaller size β -TCP granules initially generated fine-structured neotrabeculae. Because this physiologically intended, anisotropic trabecular architecture allowed early biofunctional adaptation of β -TCP granules, the more polygonal structured neotrabeculae within α -TCP-filled defects underlie an increased remodeling, leading to an increased resorption kinetic during additional healing (see Table 1).

With both ceramic types, the locally limited hydrolytic ceramolysis is accompanied by cellular resorption. Macrophages or osteoclast phagocyte the exposed ceramic microparticles without any migration tendency to the RES.^{13,18,20,21,38} Instead of two animals in the α -TCP group showing refractile microparticles within efferent lymph vessels, a permanent RES load with TCP ceramic particles seems to be less probable. Further investigation is needed to decide whether these residues consist of TCP or α -TCP-derived hydroxy apatite (HA) remnants.³⁹ Especially during the progressive degradation phase, free ceramic degradation particles could be found in the marrow. This may influence negatively the osseo-integration of dental implants inserted simultaneously within the ceramic. Furthermore, phagocytic cell accumulations

accompanying ceramic degradation can disturb the osseointegration of dental implants. Therefore, dental implants should be inserted after ceramic degradation and extensive bony substitution have progressed (usually after 5 to 6 months).

Because the definitive degradation of intratrabecularly incorporated ceramic residues is only determined by the remodeling dynamics of the trabeculae, complete ceramic degradation depends on individual factors, and therefore is limited in its predictability.

CONCLUSION

For the first time, intra- and transtrabecular microcracks could be detected, but only in α -TCP, which can lead to instability of the newly regenerated trabecular bone and loss of dental implants inserted simultaneously within the ceramic.

The interconnecting microporosity of the investigated the special β -TCP, which should be no smaller than 5 μm , resulted in faster degradation and micro-osseous conduction, and exhibited better tissue response toward the ceramic in comparison with α -TCP.

In contrast to bone substitutes, both α - and the special β -TCP ceramic types are resorbed and substituted by bone in a predictable time, and are suitable as bone rebuilding material.

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Article Analysis and Evaluation

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The endoscopically controlled osteotome sinus floor elevation: a preliminary prospective study.
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Int J Oral Maxillofac Implants 2002; 17:557-66

PURPOSE/QUESTION:

This purpose of this study was to quantify the gain in height of implant sites by endoscopically controlled osteotome sinus floor elevations (ECOSFE) with simultaneous implant placement.

SOURCE OF FUNDING:

Not mentioned

TYPE OF STUDY/DESIGN:

Prospective Cohort Study

SUMMARY FROM AUTHORS' MANUSCRIPT

Subjects(Patients):

In this study from October 1999 to December 2000, 92 sinus floor elevations were carried out with different techniques at the Department of Oral and Maxillofacial Surgery of the University of Erlangen-Nuremberg, Germany.

Fourteen patients (7 women, 7 men; mean age 51.4 ± 16.2 years, range 22 to 74 years). Out of the 92 sinus floor elevations, 18 were carried out endoscopically controlled with an osteotome technique. As augmentation material, beta-tricalcium phosphate (beta-TCP) or autogenous bone was used; 22 implants were placed.

Exposure:

The main exposure was for the sinus augmentations, 0.5 cm^3 of particulated autogenous bone from the retromolar region (7 sinus) or 0.5 cm^3 of β -tricalcium phosphate (β -TCP) granules (11 sinus) were applied.

Main Outcome Measure:

Main outcome measure was the residual height of the alveolar crest in the posterior maxilla was measured.

Main Results:

The authors' results demonstrated that the residual height of the alveolar crest in the posterior maxilla was 6.8 ± 1.6 mm on average. The implant lengths ranged from 10 to 16 mm (mean implant length 12.2 ± 1.4 mm).

There were significantly larger than the residual height of the alveolar crests ($P < .0005$). Elevation of the sinus floor with an osteotome had to be supported by conventional sinus floor elevation instruments after a mean elevation of 3.0 ± 0.8 mm to prevent perforation of the sinus membrane.

However, 1 perforation occurred, which was repaired with a periosteal patch. At stage 2 surgery, 2 implants were removed because of mobility.

Conclusions:

With the ECOSFE, perforations of the sinus membrane can be visualized; however, they cannot be avoided. Although this technique is less invasive than the lateral window technique, it cannot be recommended as a standard procedure in the posterior maxilla because of the large amount of additional equipment needed and the technically demanding procedure.

The use of the ECOSFE should be confined to scientific trials.

Commentary

Endoscopic control revealed one case in which beta-TCP could be found within the sinus; another case showed areas of polypoid mucosa on the sinus floor.

The Endoscopically Controlled Osteotome Sinus Floor Elevation: A Preliminary Prospective Study

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Friedrich W. Neukam, MD, DDS, PhD³/Jörg Wiltfang, MD, DDS, PhD²

Purpose: It was the aim of the present prospective study to quantify the gain in height of implant sites by endoscopically controlled osteotome sinus floor elevations (ECOSFE) with simultaneous implant placement and to report the number of sinus membrane perforations. **Materials and Methods:** From October 1999 to December 2000, of 92 sinus floor elevations, 18 were carried out endoscopically controlled with an osteotome technique. As augmentation material, β -tricalcium phosphate (β -TCP) or autogenous bone was used; 22 implants were placed. **Results:** The residual height of the alveolar crest in the posterior maxilla was 6.8 ± 1.6 mm on average. The implant lengths ranged from 10 to 16 mm (mean implant length 12.2 ± 1.4 mm). They were significantly larger than the residual height of the alveolar crests ($P < .0005$). Elevation of the sinus floor with an osteotome had to be supported by conventional sinus floor elevation instruments after a mean elevation of 3.0 ± 0.8 mm to prevent perforation of the sinus membrane. However, 1 perforation occurred, which was repaired with a periosteal patch. At stage 2 surgery, 2 implants were removed because of mobility. Endoscopic control revealed one case in which β -TCP could be found within the sinus; another case showed areas of polypoid mucosa on the sinus floor. **Discussion:** With the ECOSFE, perforations of the sinus membrane can be visualized; however, they cannot be avoided. Although this technique is less invasive than the lateral window technique, it cannot be recommended as a standard procedure in the posterior maxilla because of the large amount of additional equipment needed and the technically demanding procedure. **Conclusion:** The use of the ECOSFE should be confined to scientific trials. (INT J ORAL MAXILLOFAC IMPLANTS 2002;17:557-566)

Key words: dental implantation, endoscope, maxillary sinus, membrane perforation, posterior maxilla, sinus floor elevation

The edentulous posterior maxilla generally provides a limited amount of bone volume because of atrophy of the ridge and pneumatization of the maxillary sinus.¹ The residual bone is often Type IV in quality.²⁻⁴ The excessive loss of implants in this region has been described.³ Surgical techniques are of particular importance to increase the success rates of dental implants in the posterior maxilla.⁵ The

osteotome technique has been reported to improve the survival rate of implants in the residual bone of the posterior maxilla.⁶ The osteotome sinus floor elevation can be carried out with an implant survival rate higher than 95%.⁷ However, when osteotome sinus floor elevation is applied without sinusoscopic control, a direct inspection of the sinus membrane is not possible,⁸ and during preparation of the implant site a perforation may not be recognized.

Antroscopy of the maxillary sinus is a well-established diagnostic tool. It can be performed in outpatients under local anesthesia with a minimum of discomfort.⁹ The use of sinuscopy in the perioperative care of patients who have undergone sinus floor elevations is a standard technique.¹⁰⁻¹² The intraoperative use of this technique has also been described.¹³⁻¹⁵ When an internal sinus floor elevation is combined with endoscopic control for the augmentation procedure, reduced invasivity and patient morbidity has

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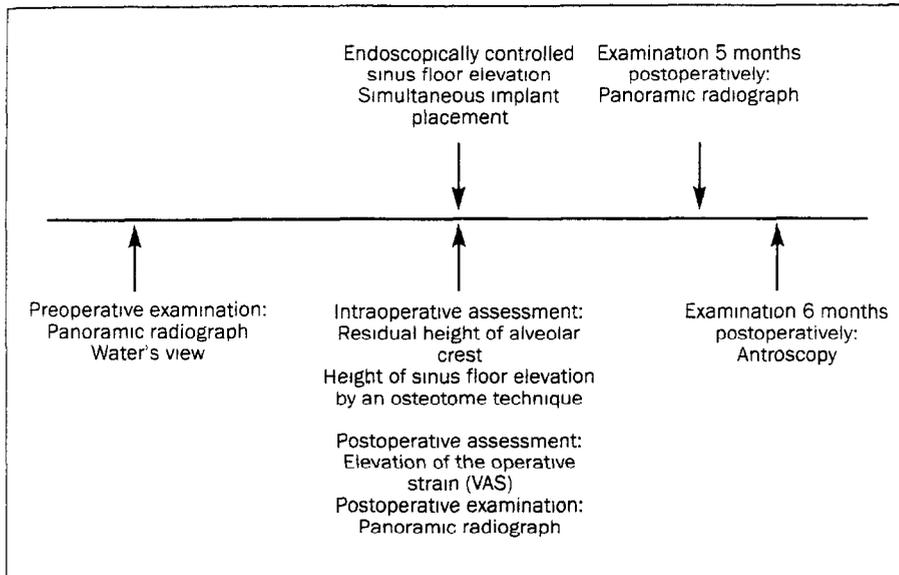


Fig 1 Prospective design of the study.

been claimed.¹⁴ Although the benefit of the osteotome technique for the internal sinus floor elevation has been described previously, there is only one report available on an endoscopically controlled procedure.¹³ However, this study did not have a prospective design.

The aim of the present prospective study was to quantify the gain in height of implant sites by endoscopically controlled osteotome sinus floor elevations (ECOSFE) and simultaneous implant placement, and to report the number of sinus membrane perforations. Moreover, control antroscopy of the maxillary sinus was carried out 6 months after implant placement to document the condition of the sinuses at the time of stage 2 surgery.

PATIENTS AND METHODS

From October 1999 to December 2000, 92 sinus floor elevations were carried out with different techniques at the Department of Oral and Maxillofacial Surgery of the University of Erlangen-Nuremberg, Germany. Fourteen patients (7 women, 7 men; mean age 51.4 ± 16.2 years, range 22 to 74 years, 2 edentulous, 12 partially edentulous patients, 18 sinuses) gave their informed consent to implant placement with the ECOSFE and an antroscopy during stage 2 surgery 6 months postoperatively. A prospective design was chosen for the study (Fig 1). Panoramic radiographs and Water's views were assessed preoperatively. Patients were excluded if they showed pathologic findings or had a history of maxillary sinus diseases or operations. A total of 22 dental implants were placed (5 Ankylos,

Degussa Dental, Hanau, Germany; 5 Brånemark Mk II, Nobel Biocare, Göteborg, Sweden; 4 Frialit-2, Friadent, Mannheim, Germany; 8 ITI, Straumann, Waldenburg, Switzerland) (Table 1).

The surgical procedure was performed using a standardized technique. Treatment of the posterior maxilla was carried out under local anesthesia with 2 mL Ultracain D-S (Hoechst Marion Roussel Deutschland, Frankfurt, Germany). No premedication or sedation was used. The maxillary sinus was punctured without flap retraction in the middle of the canine fossa with a trocar of 5 mm in diameter. Sinusscopes with view angles of 70, 90, and 120 degrees were used under video monitoring (Karl Storz, Tuttlingen, Germany). The continuous sinuscopy during the whole operation required an additional surgeon. Prior to sinus floor elevation, the sinus was examined and the natural ostium was inspected. An irrigation test with saline solution was performed to confirm communication with the nasal cavity. Inflammatory and allergic alterations of the sinus mucosa were documented. If no pathologic findings were encountered, the sinus floor elevation was carried out.

After a crestal incision, a mucoperiosteal flap was raised. To secure proper alignment of the implants, surgical templates were used. A 2-mm-deep primary pilot drilling was followed by preparation of the implant site with osteotomes of increasing diameter. The tips of the osteotomes were concave (Frialit-2 BoneCondenser, Friadent). The osteotomes D1, D2, and D3.8 were used when implants of 3.75, 3.8, or 4.1 mm in diameter were placed. For an implant diameter of 4.5 mm, the D4.5 osteotome was applied additionally. Each osteotome remained in

Table 1 Patient Data

Patient no./initials	Sex	Age (y)	Type of implant(s)	Implant location	Implant diameter (mm)	Implant length (mm)
1/B A	M	74	Brånemark Mk II	Right second premolar	4	12
				Right first molar	4	12
2/B Z	M	54	ITI	Right second premolar	4.1	12
				Left second premolar	4.1	12
3/B J	M	67	Ankylos	Right second premolar	4.5	12
				Left second premolar	4.5	12
4/FW	M	58	Ankylos	Right second premolar	4.5	12
				Left second premolar	4.5	12
				Left first molar	4.5	10
5/H E	F	41	Frialit-2	Right first premolar	3.8	13
6/K A.	F	63	Frialit-2	Left second premolar	4.5	13
7/K.M	F	44	Brånemark Mk II	Right second premolar	4	10
				Left second premolar	5	12
8/O G	M	26	ITI	Right second premolar	4.1	16
9/PG	M	58	Frialit-2	Right first molar	4.5	13
10/R.A	F	67	ITI	Left first molar	4.8	10
11/S R	F	43	Brånemark Mk II	Right first molar	4	10
12/S G	F	66	ITI	Left second premolar	4.1	14
				Left first molar	4.1	14
13/S S	M	37	ITI	Left second premolar	4.1	12
				Left first molar	4.1	12
14/T S	F	22	Frialit-2	Left first premolar	4.5	13

M = male, F = female

Mean implant diameter 4.3 ± 0.3 mm, mean implant length 12.2 ± 1.4 mm

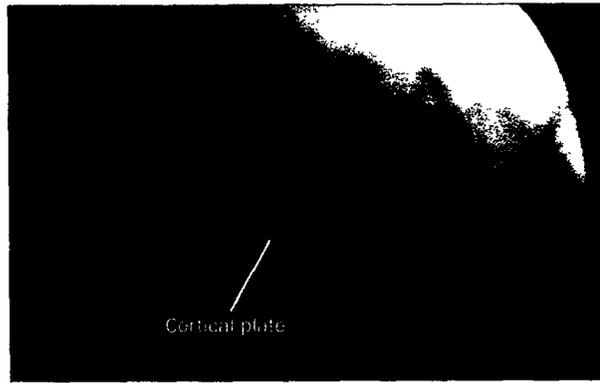
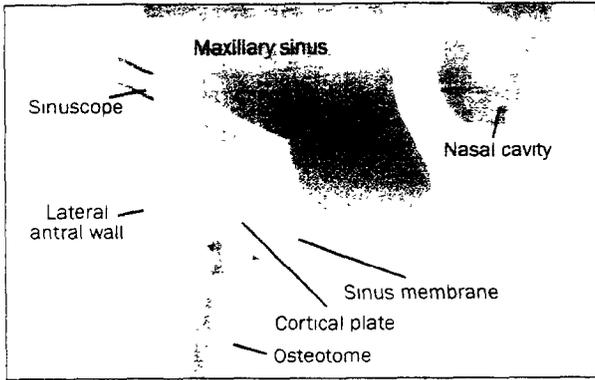
the implant site for 1 minute before the next diameter was used.

The initial osteotome was gently cut to depth with hand pressure or light malleting, without elevation of the sinus floor. Subsequently, with larger-diameter osteotomes, only a lateral compression of the spongy bone was carried out. When the final osteotome with the widest concave tip was used, the sinus floor elevation was performed under endoscopic control. The cortical plate was punched out of the sinus floor with the adherent membrane, and a tent-like formation was created (Figs 2a and 2b). The height of the residual alveolar bone was measured with a depth gauge as the distance from the sinus floor (endoscopic control) to the crest of the alveolar ridge. The cortical plate was lifted with the osteotome until no further concomitant spontaneous dissection of the sinus membrane from the sinus floor occurred in the periphery of the elevated region and visible tension of the sinus membrane revealed the risk of rupture. At this point, the height of the elevation was measured again with the depth gauge. Subsequently, the endoscopic view was used to control the dissection of the mucosa from the sinus floor, which was performed with a blunt eleva-

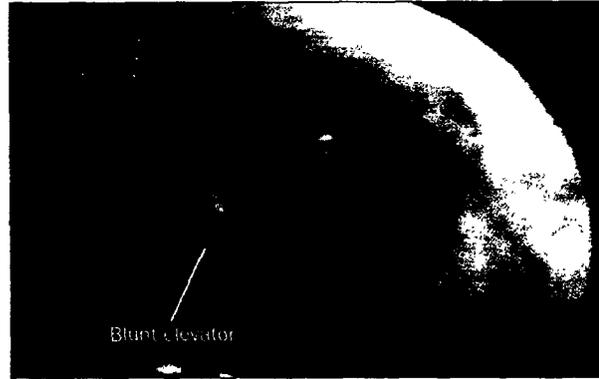
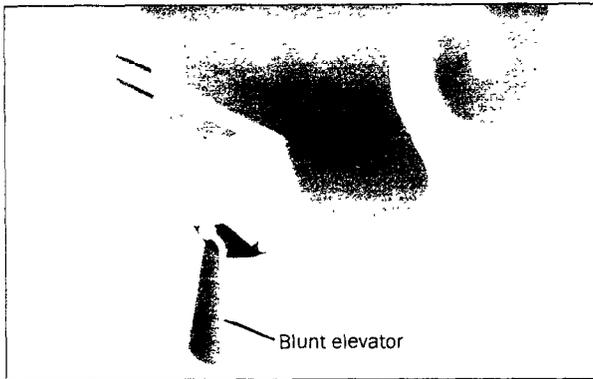
tor (Figs 3a and 3b). The extent of the dissection was limited by the geometry of the elevator and the diameter of the implant cavity. At the end of the procedure, all implant sites were tested for perforations of the sinus membrane by the Valsalva maneuver.

For the sinus augmentations, 0.5 cm^3 of particulated autogenous bone from the retromolar region (7 sinuses) or 0.5 cm^3 of β -tricalcium phosphate (β -TCP) granules (Cerasorb, Curasan Pharma, Kleinostheim, Germany; 11 sinuses) were applied. The largest osteotome was reinserted to position the grafting material in the newly formed space between the sinus membrane and the sinus floor (Figs 4a and 4b). Subsequently, the implant was placed. The mucoperiosteal flap was repositioned and sutured (Ethilon 4/0, Ethicon, Norderstedt, Germany). The operation time was measured from the mucoperiosteal incision until the final suture. A panoramic radiograph was assessed postoperatively.

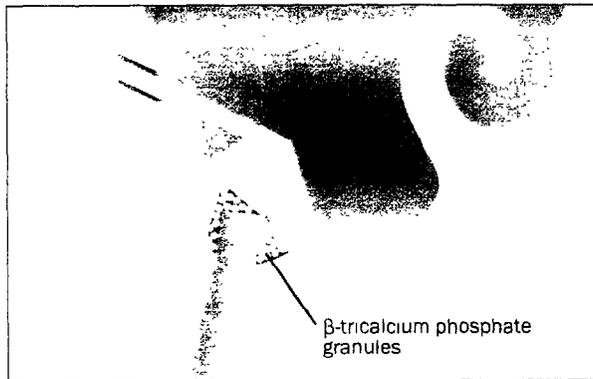
Perioperatively, an antibiotic was administered 6 hours before and 6 hours after surgery. The postoperative treatment comprised 400 mg ibuprofen (Tabalon, Hoechst Marion Roussel Deutschland) and the intranasal application of xylometazoline (Ortiven 0.1%, Novartis Consumer Health, Munich,



Figs 2a and 2b A cortical plate is punched out of the sinus floor and elevated with the adherent sinus membrane by an osteotome (*left*, schematic drawing; *right*, sinusoscopic view).



Figs 3a and 3b Dissection of the sinus membrane from the sinus floor with a blunt elevator (*left*, schematic drawing; *right*, sinusoscopic view).



Figs 4a and 4b Reinsertion of the osteotome with grafting material (*left*, schematic drawing; *right*, sinusoscopic view).



Fig 5 Endoscopic examination 6 months postoperatively. The sinus membrane shows no signs of inflammation or perforation.



Fig 6a Preoperative clinical situation—missing maxillary right first premolar.



Fig 6b Preoperative panoramic radiograph.



Fig 6c Direct postoperative panoramic radiograph.

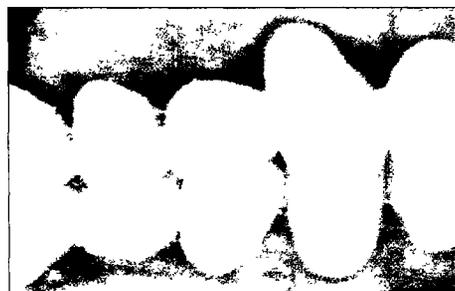


Fig 6d Prosthetic restoration 6 months after surgery



Fig 6e Panoramic radiograph 6 months after surgery

Germany) for 3 days. The sutures were removed at the seventh postoperative day.

Five months after surgery, panoramic radiographs were obtained and assessed. At the time of stage 2 surgery 6 months postoperatively, sinuscopy was again carried out through the canine fossa. The natural ostium was inspected. Inflammatory alterations of the sinus mucosa were documented (Fig 5). The implants were uncovered and the abutment connection was performed with a torque of 20 Ncm. Implants that showed mobility were removed.

After 7 postoperative days, prosthodontic treatment was initiated (Figs 6a to 6e).

Statistics

Mean values are given with standard deviations. The Wilcoxon test was used for comparisons of paired samples when normality of the variables could not be assumed because of small case numbers; *P* values equal to or smaller than .05 were considered significant. All calculations were done using SPSS for Windows (SPSS, Chicago, IL).

Table 2 Intraoperative and Follow-up Data

Patient no.	Region of placed implant	Vertical dimension of bone (mm)	Implant length (mm)	Elevation (mm)	Visible perforation	Valsalva maneuver	Augmentation material	Duration of surgery (min)	Pathologic findings		
									6 mo postop	Loss of implants	
1	15	8	12	2	Yes	Negative	β-TCP	115*	Yes*	At stage	
	16	8	12	3	No	Negative	β-TCP		Yes*	2 surgery	
2	15	7	12	3	No	Negative	A	72	No	No	
	25	8	12	2	No	Negative	A		80	No	No
3	15	9	12	3	No	Negative	β-TCP	89	No	No	
	25	8	12	3	No	Negative	β-TCP		64	No	No
4	15	5	12	5	No	Negative	A	82	No	No	
	25	7	12	4	No	Negative	β-TCP		95*	No	No
	26	6	10	3	No	Negative	β-TCP			No	No
5	14	7	13	4	No	Negative	A	47	No	No	
6	25	6	13	2	No	Negative	β-TCP	76	No	No	
7	15	9	10	3	No	Negative	β-TCP	65	No	No	
	25	7	12	3	No	Negative	β-TCP		60	No	No
8	15	9	16	3	No	Negative	A	39	No	No	
9	16	4	13	3	No	Negative	β-TCP	35	No	No	
10	26	8	10	2	No	Negative	A	69	Yes†	No	
11	16	6	10	2	No	Negative	β-TCP	58	No	No	
	25	5	14	4	No	Negative	β-TCP		56*	No	No
12	26	4	14	3	No	Negative	β-TCP	62*		No	No
	25	5	12	4	No	Negative	A		41	No	No
13	26	5	12	2	No	Negative	A	66.9 ± 20.7		No	No
	24	8	13	3	No	Negative	β-TCP		No	No	
Means		6.8 ± 1.6*	12.2 ± 1.4†	3.0 ± 0.8							

*Migration of grafting material

†Polypoid mucosa

‡P < .0005

Elevation = Height of elevation of the cortical plate by an osteotome until the concomitant dissection of the sinus membrane in the periphery stops, β-TCP = β-tricalcium phosphate, A = autograft

Region 14 = right first premolar, 15 = right second premolar, 16 = right first molar, 24 = left first premolar, 25 = left second premolar, 26 = left first molar

RESULTS

The residual height of the alveolar crest ranged from 4 to 9 mm (mean value 6.8 ± 1.6 mm). The increase in the height of the implant sites by an osteotome technique alone, up to the point where the concomitant spontaneous dissection of the sinus membrane in the periphery of the elevated region stopped and the tension of the sinus membrane revealed the risk of rupture, was 3.0 ± 0.8 mm (range 2 to 5 mm). After further sinus lifting by blunt elevators, implants 10 to 16 mm in length could be placed (mean length 12.2 ± 1.4 mm). They were significantly larger than the height of the residual alveolar crest at the implant sites (6.8 ± 1.6 mm; P < .0005). The chosen amount of 0.5 cm³ of grafting material was found sufficient in all cases. The ECOSFE operations lasted an average of 66.9 ± 20.7 minutes from the first incision until the final suture (range 35 to 115 minutes) (Table 2).

A perforation of the sinus membrane occurred in 1 patient (#1) after a 2-mm elevation of the cortical plate with an osteotome (Table 2). However, the Valsalva maneuver was negative. Further sinus floor elevation was carried out with the blunt elevator. A periosteal patch harvested from the cranial aspect of the mucoperiosteal flap and applied through the implant cavity was used to cover the perforation. Subsequently, augmentation of the sinus floor was carried out with an alloplastic material (β-TCP) and the implant was placed. In another patient (#10; Table 2), bleeding within the sinus occurred and did not stop after copious saline irrigation. Therefore, the endoscopically controlled procedure was aborted and the sinus floor elevation was carried out by the lateral window technique below the puncture for the sinuscopy. The Valsalva maneuver did not reveal a perforation of the sinus membrane (Table 2). Two implants were placed successfully.

Table 3 Review of the Current Literature

Authors	Patients	Osteotome technique	Endoscopic control	Perforations	Endoscopic follow-up	Prospective design
Baumann and Ewers 1999 ¹³	10	Yes	Yes	1	No	No
Deckwer and Engelke 1998 ⁴⁵	8	No	Yes	2	Yes	No
Deporter et al 2000 ¹⁹	16	Yes	No	?	No	Yes
Engelke and Deckwer 1997 ¹⁴	8	No	Yes	0	No	No
Horowitz 1997 ⁶	18	Yes	No	?	No	No
Ioannidou and Dean 2000 ²⁰	1	Yes	No	No	No	No
Rosen et al 1999 ⁷	101	Yes	No	?	No	No
Wiltfang et al 2000 ¹⁵	18	No	Yes	0	Yes	Yes
Yildirim et al 1998 ²²	15	Yes	No	?	No	No
Zitzmann and Schärer 1998 ³³	20	Yes	No	?	No	No

? = Not specified

The postoperative healing period proceeded uneventfully in all cases. Acute sinusitis was not observed. A follow-up radiologic examination after 5 months (panoramic radiograph) revealed no pathologic findings. After 6 postoperative months, stage 2 surgery was performed. The healing abutments were mounted with a torque of 20 Ncm. Twenty implants showed no mobility. Two implants were removed because of mobility (patient #1; Table 2). The Valsalva maneuver did not reveal perforation of the sinus membrane. However, a soft tissue closure was carried out to reduce the risk of an oroantral fistula.

The sinusoscopic control revealed 16 sinuses without pathologic findings. Saline irrigation confirmed the communication between the maxillary sinus and nasal cavity in all cases. Perforation of the implants through the sinus membrane was not visible in these patients. Migration of the augmentation material within the sinus was found in 1 patient (#1; Table 2), in whom perforation of the sinus membrane occurred during the elevation procedure; this was covered by a periosteal patch. The sinus membrane showed no pathologic findings and the perforation was no longer visible. Copious saline irrigation of the sinus and aspiration of the β -TCP were performed.

In another patient, polypoid mucosal areas were visible on the sinus floor (patient #11; Table 2). Displaced augmentation material could not be found. The patient did not suffer from clinical signs of chronic sinusitis. Therefore, no further treatment was carried out.

DISCUSSION

The osteotome technique has been well established for implant placement in the posterior maxilla.¹⁶ Experimental animal trials have shown an improved bone-to-implant contact percentage compared to conventional implant placement in the early phase of the healing period.¹⁷ Whereas survival rates of 65% have been found for preparation of the implant site in the posterior maxilla with drills, results with the osteotome technique are much more favorable,³ ranging from 85.7% to 96%.^{6,7,18} Therefore, use of the osteotome technique seems to be a safe procedure in the posterior maxilla. The technique for the internal sinus floor elevation with and without bone grafts has been described previously (Table 3).^{6-8,13,18-22} Only one report could be found in the literature that refers to an osteotome sinus floor elevation technique with endoscopic control.¹³ However, it did not provide prospective data. Therefore, the present prospective study has been carried out to assess information on: (1) the limits in gain of the height of the sinus floor elevation by an endoscopically controlled osteotome technique, (2) the number of sinus membrane perforations, (3) the postoperative condition of the sinuses, and (4) the operation time.

Sinus floor elevation procedures are routinely performed, although the function of the maxillary sinus is not totally understood. Some of its functions might be adding resonance to the voice, some degree of olfactory function, warming and humidifying inspired air, and a reduction of the weight of the

skull.^{23,24} Therefore, it seems to be reasonable to confine the augmentation volume of the maxillary sinus to a minimum. With the lateral window technique, an average augmentation volume of $3.50 \pm 1.33 \text{ cm}^3$ has been considered necessary to place an implant of 13 mm in length when the residual bone height is 5 mm.²⁵ However, when the osteotome sinus floor elevation is performed, a minimum augmentation volume of only 0.5 cm^3 is required because of the local aspect of the augmentation. Therefore, with this technique, extensive changes in antral morphology and function have not been anticipated.

Another decisive factor that encourages the use of a minimally invasive sinus floor elevation technique is the desire for undisturbed vascularization of the grafting material placed in the sinus floor during the healing period. Vascularization is provided by an endosseous and an extraosseous anastomosis between the posterior superior alveolar artery and the infraorbital artery and branches of these vessels in the sinus membrane. With the osteotome sinus floor elevation, mucoperiosteal flap retraction can be reduced to a minimum, and only a puncture of the sinus through the bony wall of the canine fossa must be carried out.^{26,27} The risk of damaging the periosteum and the blood supply in the lateral antral wall is decreased. However, the present study shows that massive bleeding because of vessel vulnerability cannot be excluded (patient #10; Table 2).

Residual bone height less than 4 mm is associated with reduced primary implant stability.²⁸⁻³¹ A finite element analysis has shown that reduced augmentation volume, as should be expected with the osteotome sinus floor elevation, leads to further decrease of implant stability.³² Therefore, it is not surprising that during the follow-up in the present study, 2 implants were lost in sites with a reduced residual alveolar crest of 4 mm, of which 1 site showed an additional perforation of the sinus membrane with migration of the grafted material (patient #1; Table 2). In cases of severely resorbed maxillae, the minimally invasive sinus floor elevation seems not to be the method of choice; a 2-stage procedure with the conventional lateral window technique would be preferred.³³ However, many implant sites in the posterior maxillae show only mild degrees of bony resorption, allowing sufficient primary stability but not an implant length of 13 mm as recommended by Kent and Block³⁴; for example, in the present study where the average residual bone height was $6.8 \pm 1.6 \text{ mm}$. Such implant sites are suitable for the osteotome sinus floor elevation. A mean height in the elevation of $3.0 \pm 0.8 \text{ mm}$ could be attained by an endoscopically controlled osteotome technique alone until no further concomitant spontaneous dis-

section of the sinus membrane in the periphery of the elevated area occurred.

Finally, implants could be placed with a mean length of over 12 mm (Table 1). However, in some patients, the risk of rupture of the sinus membrane was encountered after an elevation of 2 mm because the spontaneous dissection stopped (patients #2, #6, #10, and #11; Table 2). When there is no visualization, further dissection with a blunt elevator is difficult without harming the integrity of the sinus membrane. Although it has been said that implants perforating the sinus membrane and penetrating the sinus will have no reduced survival rate, displacement of alloplastic material through the sinus membrane can lead to transient or chronic sinusitis in 10% to 20% of sinus elevation cases, prompting the need for further treatment.³⁵⁻³⁹ Dislocated bone chips may also initiate local inflammation and subsequent severe resorption of the bone graft.⁴⁰ Spread of the grafting material can be prevented by using block grafts.^{41,42} Unfortunately, in these cases, a larger lateral window has to be created, which may harm the blood supply in this region. With the lateral window technique, rates of membrane perforation during bone grafting of the maxillary sinus of 35% have been reported.⁴²⁻⁴⁴ When using the ECOSFE, perforations of the sinus membrane cannot be excluded. They have been encountered by previous investigators and in the present study.^{13,45}

In attempting the osteotome sinus floor elevation, the pressure at the tip of the osteotomes can increase the risk of perforation of the sinus membrane.⁸ It has been proposed to take advantage of hydraulic forces created during the osteotome sinus floor elevation to avoid rupture of the sinus membrane.^{7,18} With this technique, the osteotomes do not enter the sinus. After the graft is placed into the osteotomy, it exerts pressure on the sinus membrane by reinsertion of the osteotome so as to elevate the sinus floor. However, this procedure is based only on a hypothesis that has never been proved either in experimental or in clinical studies because of the lack of an appropriate method for visualization. Intraoperative endoscopic examination will help determine whether this hypothesis is acceptable or not. In the present study, this technique was not adopted because autogenous bone from the mandible was used that had been particulated in a bone mill. With these potentially sharp-edged bone chips, perforation of the sinus membrane seemed likely to occur if the particulated material had been used to elevate the sinus membrane.

When the internal sinus floor elevation is carried out without visualization, there is little opportunity to detect perforations. In these cases, elevation

should be confined to an average height of 3 mm.^{8,33} Before insertion of the augmentation material, the Valsalva maneuver is one of the few possibilities for recognition of perforations. However, in the present study the perforation that was visible by endoscopy was related to a negative Valsalva maneuver, which shows the limited effectiveness of this test.

It has been claimed that special training is necessary before the time-consuming endoscopically controlled procedure is used.⁴⁵ The additional endoscopic equipment, the need for a second surgeon, and the technically challenging, time-consuming procedure all seem to limit the use of this technique to scientific trials. It is not surprising that previous investigators have only treated small numbers of patients.^{13-15,45} To date, the shortcomings of the ECOSFE procedure seem to outweigh the advantage of the minimally invasive aspect.

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Article Analysis and Evaluation

ARTICLE TITLE AND BIBLIOGRAPHIC INFORMATION:

Lateral ridge augmentation and implant placement: an experimental study evaluating implant osseointegration in different augmentation materials in the canine mandible.

von Arx T, Cochran DL, Hermann JS, Schenk RK, Higginbottom FL, Buser D.

Int J Oral Maxillofac Implants 2001;16: 343-54

PURPOSE/QUESTION:

This purpose of this study was to investigate the osseointegration of dental implants with a titanium plasma-sprayed surface (TPS) in regenerated and native bone in an experimental dog study.

SOURCE OF FUNDING:

ITI Foundation, Waldenburg, Switzerland

Foundation for Dental Research and Education (FDR), Waldenburg, Switzerland

Dr. H.C. Robert Mathys Foundation, Bettlach, Switzerland

TYPE OF STUDY/DESIGN:

Animal Research Study

SUMMARY

Animals:

In this study, 19 implants were placed in lab-bred American foxhounds were investigated.

Exposure:

The main exposure was lateral ridge augmentation with the following four groups:

- (1) autogenous corticocancellous block grafts,
- (2) autogenous corticocancellous block grafts and e-PTFE membrane,
- (3) tricalcium phosphate particles and e-PTFE membrane, or
- (4) canine-derived demineralized freeze-dried bone allograft particles and e-PTFE membrane without use of soft tissue flaps during the implant placement.

Main Outcome Measure:

Main outcome measure was the evaluation of histologic and histometric analysis of the specimens. Histometric quantification was carried out under a light microscope utilizing a high-resolution videocamera coupled to a computer monitor.

Main Results:

The authors' results demonstrated that all implants had high percentages (59% to 75%) of bone-to-implant contact, with no significant differences across the various treatment groups.

Conclusions:

The authors' findings concluded that the different grafting techniques did not significantly influence the location of first bone-to-implant contact and the horizontal bone width at the most coronal bone level.

Lateral Ridge Augmentation and Implant Placement: An Experimental Study Evaluating Implant Osseointegration in Different Augmentation Materials in the Canine Mandible

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The present study investigated the osseointegration of dental implants with a titanium plasma-sprayed surface (TPS) in regenerated and native bone in an experimental dog study. Initially, lateral bone defects were created in the alveolar ridge on both sides of the mandible. Two months later, lateral ridge augmentation was performed with (1) autogenous corticocancellous block grafts, (2) autogenous corticocancellous block grafts and e-PTFE membrane, (3) tricalcium phosphate particles and e-PTFE membrane, or (4) canine-derived demineralized freeze-dried bone allograft particles and e-PTFE membrane. After 4 months, membranes were removed, and non-submerged titanium implants were placed in regenerated bone (test implants) and in native bone (control implants). Two months later, the animals were sacrificed and non-decalcified orofacial sections were evaluated histometrically. All implants demonstrated high percentages (59% to 75%) of bone-to-implant contact, with no significant differences across the various treatment groups. The different grafting techniques did not significantly influence the location of first bone-to-implant contact and the horizontal bone width at the most coronal bone level. (INT J ORAL MAXILLOFAC IMPLANTS 2001;16:343-354)

Key words: autogenous bone, barrier membrane, demineralized freeze-dried bone allograft, histometry, osseointegration, ridge augmentation, titanium implant, tricalcium phosphate

Tooth restoration using implant-supported prostheses for functional and esthetic rehabilitation has become an established and widely used

treatment modality in dentistry. One of the most critical factors in treatment planning is bone volume at the future implant site. The quantity and quality of the bone supply not only influence implant osseointegration, but also affect the shape and contour of the overlying soft tissue and, hence, the esthetic outcome. In addition, prosthetic parameters such as restoration/implant axis and restoration/implant ratio are affected by the quantity and quality of bone at the implant site.

Following the evolution of root-form dental implants, a multitude of surgical techniques have evolved to enhance alveolar bone volume for implant placement. Among these techniques, guided bone regeneration (GBR) has become not only the most extensively studied technique but probably the most popular bone reconstructive procedure in implant dentistry. One major point of differentiation of GBR procedures is the scheduling of bone regeneration in relation to implant placement. In the staged approach, bony site development is performed usually 6 months prior to implant placement, whereas in the simultaneous approach, the bone regeneration

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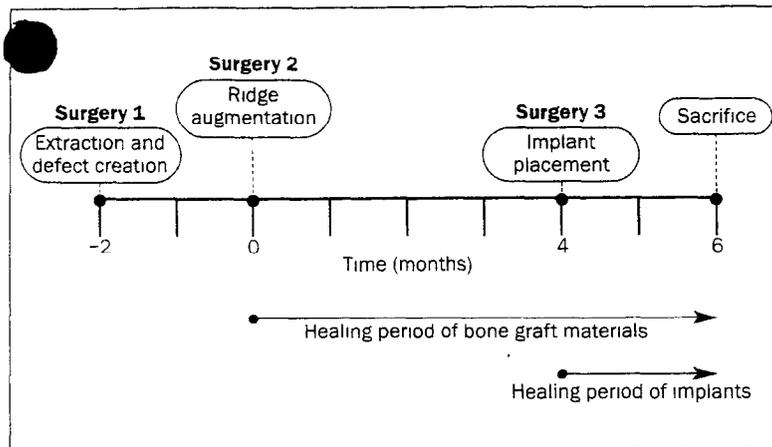


Fig 1. Time schedule of the present study.

procedure is carried out in conjunction with implant placement. Selection criteria for the appropriate surgical approach include anatomic aspects, such as the size and morphology of the bone defect. Additional and essential issues include primary implant stability and correct implant position and orientation in relation to the prosthetic restoration.¹⁻³ With respect to the staged approach, a number of clinical studies have demonstrated that implants placed subsequently into regenerated alveolar bone have excellent long-term results and maintain their peri-implant tissue status.⁴⁻⁷

These clinical results were confirmed in an experimental canine study by Buser and colleagues.⁸ In 5 dogs, acute through-and-through ridge defects were created in the mandible and immediately covered with expanded polytetrafluoroethylene (e-PTFE) membranes. No bone grafts or substitutes were applied. Following a healing period of 6 months, non-submerged implants were placed. After 3 months of implant healing, some of the implants were restored with fixed prostheses and loaded for 6 months. At the completion of the study, all implants, irrespective of loading status, demonstrated osseointegration with direct bone-to-implant contact. Peri-implant bone parameters did not differ between loaded and unloaded implants. The authors concluded that bone regenerated in membrane-protected defects responded to implant placement in the same way as non-regenerated native bone.

Other factors important in GBR are the achievement of primary soft tissue healing and the type of graft material to be used as a membrane-supporting device to avoid membrane collapse during healing.⁹ Although autogenous bone is unequivocally accepted as the gold standard for bone grafting, other filling materials have been successfully used for bone

regeneration. The main reasons to avoid the utilization of autografts are as follows: (1) the additional harvesting procedure with possible donor site morbidity, (2) a sometimes limited amount of available bone graft from intraoral sites, and (3) the higher cost and often more complex surgery for extraoral graft donor sites.

Bone regeneration with different grafting materials protected by an e-PTFE membrane was recently analyzed in an experimental study in 12 miniature pigs.¹⁰ The filler materials compared to autogenous bone included a collagen sponge, demineralized freeze-dried bone allograft (DFDBA) (from the tibia of a miniature pig), tricalcium phosphate (TCP) granules, and coral-derived hydroxyapatite granules. Autogenous bone showed the best results in the initial phase of healing (4 weeks), whereas TCP demonstrated 70% new bone formation at the completion of the study (24 weeks), compared to 54% in autografted sites.

Taking into account the findings of the above-mentioned studies,^{8,10} the authors designed the present experimental study to evaluate osseointegration of dental implants placed in bone regenerated with different grafting materials. Implants placed in augmented areas (test implants) were compared to implants placed in non-regenerated, native alveolar bone (control implants).

MATERIALS AND METHODS

Study Design and Time Schedule

Osseointegration of implants placed in regenerated bone in previously created localized bone defects was evaluated in an experimental study employing 3 dogs. Initially, all premolars and the first molar were surgically removed in the mandible (Fig 1), and 2 lat-

Table 1 Randomization of Grafting Techniques by 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 #2235	DFDBA + membrane	Autograft + membrane	TCP + membrane	Autograft alone
Dog #2240	Autograft alone	TCP + membrane	Autograft + membrane	DFDBA + membrane
Dog #2363	DFDBA + membrane	Autograft + membrane	TCP + membrane	Autograft alone

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

eral bone defects were created per side (see below). Two months later, lateral ridge augmentation was performed utilizing 4 different grafting treatments. Four months after augmentation surgery, dental implants were placed into regenerated bone (test implants) and into native bone (control implants). All animals were sacrificed 6 months after ridge augmentation, ie, 2 months after implant placement.

Parallel to this study, another 3 animals underwent the same surgeries except for implant placement. That part of the study evaluated reconstruction of the alveolar ridge using the same grafting techniques. Results have been published in a separate article.¹¹

Animals

Lab-bred American foxhounds were used in this study. At the beginning of the study, 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 the University of Texas Health Science Center at San Antonio (UTHSCSA), and the protocol was approved by the Institutional Animal Care and Use Committee.

Surgery

Pre- and postoperative medication and preparatory surgical steps were identical to those reported elsewhere.¹¹ Therefore, only a brief summary is given. All surgical procedures were performed under general anesthesia employing endotracheal intubation. In addition, local anesthesia was administered by infiltration at the respective buccal and lingual aspects of the mandibular ridge. Antibiotics were given postoperatively (benzathine penicillin, procaine penicillin G, and gentamicin).

During the first surgery, all mandibular premolars and first molars, as well as the second and third maxillary premolars, were removed. Immediately afterward, 2 lateral bone defects (14×10×8 mm) were created on each side of the mandible. Two months later, the lateral bone defects were augmented in 4 different ways,¹¹ with random assignment of each grafting condition (Table 1).

- Site 1: Corticocancellous block graft and bone particles (autograft) without membrane protection
- Site 2: Corticocancellous block graft and bone particles (autograft) with e-PTFE membrane
- Site 3: Tricalcium phosphate granules (TCP) with e-PTFE membrane
- Site 4: Canine DFDBA with e-PTFE membrane

The corticocancellous block grafts were harvested from the site of the previously extracted first molar. The autografts 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 grafts. In each dog, 1 autografted site was subsequently covered with an e-PTFE membrane (GTAM, W.L. Gore, Flagstaff, AZ). The membrane was stabilized with 2 Memfix fixation screws at its buccal base. The third defect was grafted with DFDBA particles processed from canine tibiae (Osteotech, Shrewsbury, NJ). The graft particles measured 250 to 500 µm. The remaining defect was augmented with TCP granules, 0.7 to 1.4 mm (Ceros TCP, Robert Mathys AG, Bettlach, Switzerland), for ridge reconstruction. To prevent membrane collapse, a supporting Memfix screw was inserted into the lingual cortex in the middle of the defects were treated with DFDBA and TCP. Periosteal releasing incisions allowed for tension-free wound closure, which was accomplished with horizontal mattress and interrupted sutures. Sutures were removed 2 weeks postoperatively.

Four months after ridge augmentation, the dogs were scheduled for implant placement. A midcrestal incision with vertical release incisions was made to reflect full mucoperiosteal flaps. The e-PTFE membranes and all fixation and supporting screws were removed. Commercially available implants were placed in augmented sites when bone density and volume were adequate. A single implant was placed in the anterior augmentation site, whereas 1 or 2 implants were placed in the posterior augmentation site. Control implants were placed into native bone either between the 2 augmentation

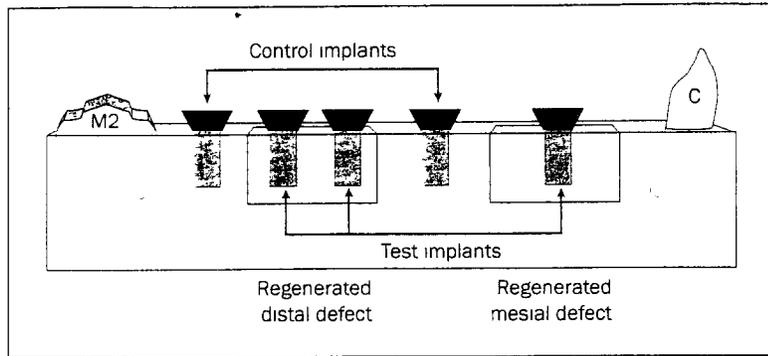


Fig 2 Schematic illustration of right mandible, showing implant placement into regenerated bone (test implants) and into native bone (control implants) C = canine; M2 = second molar.

Table 2 No. of Implants Placed per Treatment Group

Treatment	Specimens	No. of implants
Autograft alone	Test	2
Autograft + membrane	Test	5
TCP + membrane	Test	3
DFDBA + membrane	Test	3
Native bone	Control	6
Total		19

sites and/or distal to the posterior augmentation site (Fig 2). Two different types of ITI titanium plasma-sprayed dental implants (ITI Dental Implant System, Institut Straumann, Waldenburg, Switzerland) were used: 6-mm hollow-screw implants (HS-6) and 8-mm solid-screw implants (S-8), both with an outer diameter of 4.1 mm. Implants placed at anterior augmentation sites were always HS-6 implants, whereas all other sites received S-8 implants. Implant beds were prepared according to the standard ITI surgical protocol. The implants were placed in a non-submerged technique, with flaps reapproximated around the implants using multiple interrupted sutures. A total of 19 implants were placed (13 test and 6 control) (Table 2).

Oral hygiene procedures, including implant cleansing, were carried out 2 times a week using 0.2% chlorhexidine gel (Plak-Out Gel, Hawe Neos Dental, Biaggio, Switzerland). A soft diet was maintained throughout the study.

Sacrifice

All animals were sacrificed 2 months after implant placement, ie, 6 months after ridge augmentation. Euthanasia was performed with an overdose of pentobarbital sodium 0.2 mL intravenously (65 mg/kg, Euthanasia-5, Henry Schein, Port Washington,

NY). Subsequently, the mandibles were block-resected using an oscillating autopsy saw, and the recovered segments were immersed in a solution of 4% formaldehyde combined with 1% calcium chloride prior to histologic preparation.

Histologic and Histometric Analysis

The specimens were prepared for histology as described by Schenk and coworkers.¹² Briefly summarized, non-decalcified specimens were embedded in methyl methacrylate resin and stained with toluidine blue and basic fuchsin. Consecutive orofacial step sections with a thickness of approximately 80 μ m, spaced at intervals of about 1 mm, were obtained for histologic and histometric analysis. For each implant site, all sections showing the implant body were evaluated. Histometric quantification was carried out under a light microscope utilizing a high-resolution videocamera coupled to a computer monitor. A morphometry software package (Image Pro Plus, Media Cybernetics, Silver Spring, MD) with image-capturing capabilities was employed to measure the following parameters (Fig 3).

- fBIC = first bone-to-implant contact (mm) measured from the implant shoulder (at $\times 12.5$ magnification)
- HBW = horizontal bone width (mm) at level of first bone-to-implant contact (at $\times 12.5$ magnification)
- BIC = percentage of bone-to-implant contact from first bone-to-implant contact down to where the implant begins to curve at the apical end (at $\times 31.25$ magnification)

All parameters were measured on the buccal and lingual aspects of the implants. Osseointegration was defined according to Brånemark and associates¹³ as direct bone-to-implant contact without intervening soft tissues.

Statistical Analysis

The statistical analysis involved comparisons across treatment groups as well as buccal versus lingual. Histometric data were obtained for at least 3 sections taken from each implant site. The data were averaged so that each measure had a single value per implant to be used for statistical analysis. For the comparisons across treatment groups, analysis of variance was performed for each histometric parameter at the buccal and the lingual, as well as the difference between the buccal and lingual measures. When the resulting F tests were statistically significant ($P < .05$), Bonferroni-adjusted unpaired Student t tests (with $P < .05$ considered significant) were performed to identify individual treatment group differences. For each treatment group, the corresponding buccal and lingual histologic measures were compared by paired Student t tests (with $P < .05$ considered significant). Since the small sample sizes had the potential of producing Type II errors, marginally significant results ($P < .10$) involving mean differences greater than 1 mm were also reported.

RESULTS

Clinical Findings

Following ridge augmentation, 2 membrane-covered sites in the same animal showed extended membrane exposures (dog #2240, right posterior site with TCP + membrane and left posterior site with DFDBA + membrane). Three weeks after surgery 2, these exposed membranes were surgically removed. Subsequent wound healing was uneventful. The overall membrane exposure rate was 22% (2 of 9 membrane sites). In surgery 3, implants could be placed at both sites with previous membrane exposure. The number of test implants placed per grafting condition in surgery 3 varied. For instance, no implants could be placed in 2 sites because of severe resorption or loss of the bone grafting material (1 "autograft alone" site and 1 "DFDBA + membrane" site). In contrast, 2 implants instead of a single implant could be placed in 3 sites with exceptionally good bone regeneration (2 "autograft + membrane" sites and 1 "DFDBA + membrane" site). This led to diverging numbers of implants evaluated per grafting group. No implants were lost, and all implants were clinically stable at the completion of the experiment.

Histologic Observations

Experimental Implants in "Autograft Alone" Sites. Only 2 implants had been placed in autografted sites without membrane application. In 1 site, the

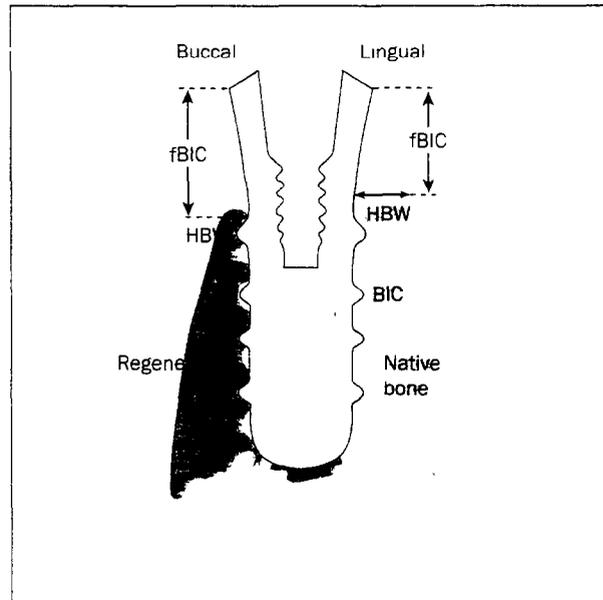


Fig 3 Schematic illustration of histometric analysis with measurements of first bone-to-implant contact (fBIC), horizontal bone width (HBW), and percentage of bone-to-implant contact (BIC) on buccal and lingual aspects.

buccal wall was critically thin but reached the level of the former alveolar crest (Fig 4a). The other site showed an inadequate crestal contour but good reconstruction of the buccal wall (Fig 4b). The grafted bone exhibited good remodeling. However, the periosteal surface showed ongoing osteoclastic resorption (Fig 4c).

Experimental Implants in "Autograft with Membrane" Sites. Five implants had been placed into sites regenerated with membrane-protected autografts. All of these sites showed a well-preserved crestal contour with adequate ridge width. All sites demonstrated good buccal bone dimensions, generally reaching the coronal TPS level of the placed implant. The outer surface of the transplanted corticocancellous block grafts usually demonstrated little surface resorption, thus re-establishing the original dimension of the buccal cortex (Figs 5a and 5b). Similarly, the cortical bulk of the block graft had undergone little remodeling, and only a limited number of new Haversian systems were present (Fig 5c). New bone formation was more extensive in the cancellous portion of the graft facing the buccal implant surface and around the block graft where the cancellous chips had been placed.

Experimental Implants in "TCP with Membrane" Sites. Three implants had been placed into regenerated sites using TCP particles with membrane coverage. Two specimens with buccal inclination of the

Figs 4a to 4c Defects treated with corticocancellous block grafts without membrane placement. Undecalcified ground sections surface-stained with toluidine blue and basic fuchsin. The buccal wall of the specimens is always oriented to the right.

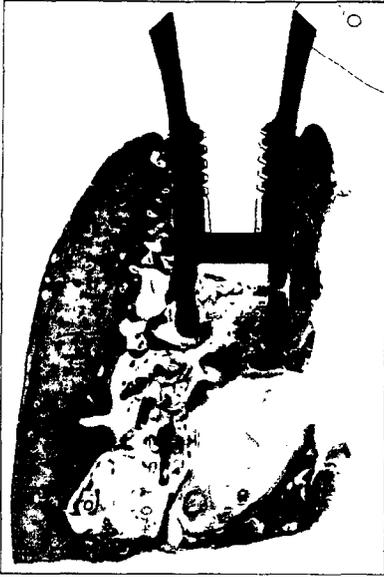


Fig 4a Implant placed just coronal to the mental foramen. The unprotected block graft underwent extensive resorption, but the bone-to-implant contact remained intact (magnification $\times 2$).



Fig 4b This specimen shows good reconstruction of the former alveolar width. Most of the corticocancellous graft is preserved, except for the buccocrestal aspect, which underwent active resorption (magnification $\times 2$).



Fig 4c Coronal portion of the autogenous block graft. The implant surface is almost completely covered with newly formed bone, except for a small area with primary contact at the lower thread. The cortical graft underwent quite intense remodeling, with most remodeling units being in the formative stage. Osteoclastic resorption dominates along the full extent of the surface exposed to the periosteum (magnification $\times 10$).

Figs 5a to 5c Defects treated with corticocancellous block grafts and e-PTFE membrane placement. Undecalcified ground sections surface-stained with toluidine blue and basic fuchsin. The buccal wall of the specimens is always oriented to the right.

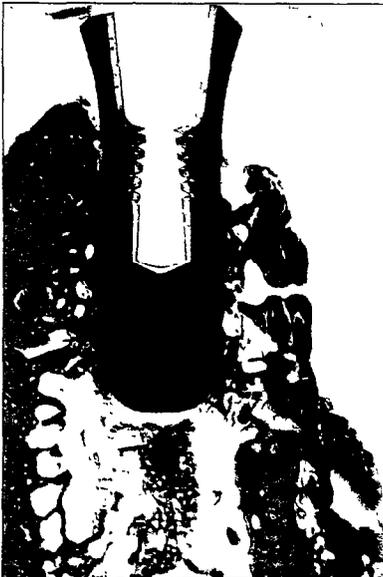


Fig 5a Worst case of the membrane-protected autograft due to the small size of the block graft. Extensive bone-to-implant contact can be seen on both implant aspects (magnification $\times 10$).



Fig 5b Best case of a membrane-protected corticocancellous autograft, demonstrating full osseointegration of the implant (magnification $\times 2$).



Fig 5c Bony ongrowth has led to extensive contact of this corticocancellous block graft with the implant surface. Most of the grafted compact bone is avascular and devitalized, and remodeling has just started. The smooth periosteal surface indicates that membrane protection has prevented osteoclastic resorption (magnification $\times 10$).

Figs 6a to 6c Defects treated with TCP particles with e-PTFE membrane placement. Undecalcified ground sections surface-stained with toluidine blue and basic fuchsin. The buccal wall of the specimens is always oriented to the right.



Fig 6a The marked asymmetry between the buccal and lingual bone plates is a result mainly of the angulation of the implant. The 2 coronal threads on the buccal aspect are covered by soft tissue (magnification $\times 2$).



Fig 6b The fully regenerated buccal bone plate is as wide as the lingual cortex but slightly reduced in height. Full bone-to-implant contact has been achieved (magnification $\times 2$).



Fig 6c Grafting with TCP particles and membrane protection has reconstructed a rather solid buccal bone plate. Extensive bone-to-implant contact is seen. Remnants of TCP particles are in close proximity to the implant surface and embedded in newly formed bone. Remodeling and substitution have started. Membrane protection has promoted new bone formation and has prevented osteoclastic resorption along the periosteal surface (magnification $\times 10$).

implant axis showed less than adequate bone regeneration buccally, resulting in a critically thin buccal bone plate at the crestal level (Fig 6a). This finding was associated with reduced bone height on the buccal aspect of the implant. One site demonstrated good reconstruction of the buccal bone wall (Fig 6b). Most of the previously grafted TCP particles had been incorporated into bone that had been regenerated since augmentation in the periods before and after implant placement (Fig 6c). Substitution of the graft material was not yet complete.

Experimental Implants in "DFDBA with Membrane" Sites. Three implants had been placed into regenerated bone following osteopromotion by canine DFDBA with membrane coverage. Two sites demonstrated a very thin bony layer on the buccal implant surface (Fig 7a). However, this bone almost always reached the coronal TPS level of the implant. One site showed excellent bone regeneration, with good buccal bone width (Fig 7b). The DFDBA particles were incorporated into newly formed woven and lamellar bone (Fig 7c). However, the density of regenerated bone was low.

Control Implants in "Native Bone" Sites. Six implants had been placed into non-regenerated bone. The buccal bone height almost always reached the coronal TPS level and demonstrated adequate width

unless the implant was angulated to the buccal aspect (Fig 8a). Since the cortical bone wall had not been removed at the control sites, normally dense, compact bone was found at both the buccal and lingual implant aspects (Fig 8b). This bone showed characteristic remodeling, with newly formed osteons in the area adjacent to the implant surface (Fig 8c).

Histometric Results

The mean data per treatment group of the 3 histometrically evaluated parameters are listed in Table 3. A summary of the statistical data is given in Table 4.

Analysis of fBIC. Treatment means calculated for first bone-to-implant contact (fBIC) ranged from 3.80 to 4.70 mm (controls, 3.87 mm) for buccal aspects and from 2.67 to 3.98 mm (controls, 3.2 mm) for lingual aspects. The most coronal levels of bone were found in "DFDBA + membrane" sites. A significantly greater lingual fBIC ($P < .05$) was calculated for "autograft alone" sites compared to "DFDBA + membrane," "autograft + membrane," and control sites, but no significant difference was observed at "TCP + membrane" sites. The lingual fBIC of "TCP + membrane" was also significantly greater than that of "DFDBA + membrane" sites ($P < .05$). No statistically significant differences were found between buccal and lingual fBICs within any of the treatment

Figs 7a to 7c Defects treated with DFDBA particles and e-PTFE membrane placement. Undecalcified ground sections surface-stained with toluidine blue and basic fuchsin. The buccal wall of the specimens is always oriented to the right.



Fig 7a The buccal wall is thin but reaches the smooth/rough implant border. Extensive bone-to-implant contact is present (magnification $\times 2$).



Fig 7b The buccal wall is remarkably wide. It consists mostly of cancellous bone, confined by a thin cortical layer formed underneath the membrane (magnification $\times 2$).



Fig 7c This case of augmentation with DFDBA particles and membrane protection provided a result comparable to the TCP graft. A somewhat higher magnification ($\times 16$) was chosen for easier identification of remnants of DFDBA particles (arrow) that, after incorporation in new bone, underwent recalcification.

Figs 8a to 8c Undecalcified ground sections from non-augmented control sites surface-stained with toluidine blue and basic fuchsin. The buccal wall of the specimens is always oriented to the right.



Fig 8a This control specimen illustrates the asymmetry between the lingual and buccal walls resulting from the buccally angulated implant position. Structure and bone remodeling as well as bone-to-implant contact are identical on both sides of the implant (magnification $\times 2$).



Fig 8b This control implant is in an axial position and supported by almost symmetric lingual and buccal walls, both consisting of compact bone with comparable remodeling activity (magnification $\times 2$).

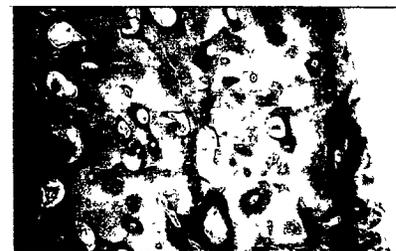


Fig 8c This part of the buccal wall underwent intense remodeling, a result of the interruption of the blood supply during implantation. Extensive secondary bone-to-implant contact ensures osseointegration. The periosteal surface has not been subjected to osteoclastic resorption (magnification $\times 12.5$).

Table 3 Data of Test and Control Sites (Mean \pm SD)

Parameter	Autograft alone	Autograft + membrane	TCP + membrane	DFDBA + membrane	Control sites
fBIC buccal (mm)	4.62 \pm 0.67	3.92 \pm 0.84	4.70 \pm 1.41	3.80 \pm 0.49	3.87 \pm 0.86
fBIC lingual (mm)	3.98 \pm 0.15	3.13 \pm 0.13	3.46 \pm 0.57	2.67 \pm 0.37	3.20 \pm 0.15
HBW buccal (mm)	0.85 \pm 0.53	1.22 \pm 0.64	1.04 \pm 0.44	0.32 \pm 0.20	1.09 \pm 0.76
HBW lingual (mm)	3.08 \pm 1.09	2.63 \pm 0.76	2.41 \pm 0.84	2.26 \pm 0.31	2.10 \pm 0.79
BIC buccal (%)	58.8 \pm 19.6	74.1 \pm 6.6	75.0 \pm 2.5	74.2 \pm 11.6	73.7 \pm 7.5
BIC lingual (%)	65.2 \pm 17.0	76.3 \pm 5.5	66.8 \pm 8.6	69.1 \pm 19.6	76.4 \pm 9.9

fBIC = first bone-to-implant contact measured from implant shoulder, which is placed 2.8 mm coronal to the alveolar crest, HBW = horizontal bone width at fBIC, BIC = bone-to-implant contact along implant surface from fBIC to bottom of implant

Table 4 Summary of Statistically Significant Differences for Evaluated Parameters

Parameter	Buccal means compared among groups	Lingual means compared among groups	Buccal compared to lingual means within groups	Difference of buccal and lingual means among groups
fBIC, by grafting technique	$F = 0.72, P > .58$ No significant differences	Autograft alone > DFDBA/membrane, autograft/membrane, control ($P < .05$) TCP/membrane > DFDBA/membrane ($P < .05$) $F = 7.04, P < .01$	Buccal > lingual for autograft/membrane (marginal, $P = .08$)	$F = 0.38, P > .81$ No significant differences
HBW, by grafting technique	$F = 1.13, P > .38$ No significant differences	$F = 0.75, P > .57$ No significant differences	Lingual > buccal for autograft/membrane and for DFDBA/membrane ($P < .025$)	$F = 0.57, P > .68$ No significant differences
BIC, by grafting technique	$F = 1.33, P > .30$ No significant differences	$F = 0.78, P > .55$ No significant differences	No significant differences ($P > .17$)	$F = 1.38, P > .28$ No significant differences

conditions, but buccal was marginally ($P = .08$) greater than lingual for "autograft + membrane" sites.

Analysis of HBW. Treatment means calculated for the horizontal bone width (HBW) measured at the level of the first bone-to-implant contact ranged from 0.32 to 1.22 mm (controls, 1.09 mm) on buccal aspects and from 2.26 to 3.08 mm (controls, 2.1 mm) on lingual aspects. Buccally, "autograft + membrane" sites had the highest mean HBW, whereas lingually, "autograft alone" sites showed the greatest mean HBW. Generally, the mean buccal HBWs were 2 to 7 times smaller than their lingual counterparts when the lingual dimension exceeded 2 mm. However, a significantly smaller buccal HBW ($P < .025$) compared to the lingual HBW was seen for only "autograft + membrane" and for "DFDBA membrane" sites. Comparisons across the different grafting conditions and control sites revealed no statistically significant differences for mean buccal or lingual HBW measurements.

Analysis of BIC. Treatment means calculated for BIC ranged from 58.8% to 75.0% (controls, 73.7%) on the buccal implant surface and from 65.2% to 76.3% (controls, 76.4%) on the lingual implant surface. Sites treated with TCP and DFDBA had more BIC on the buccal compared to the lingual implant surface, whereas autografted sites (with or without a membrane) and control sites had higher BIC on the lingual surface. A comparison of buccal versus lingual BICs revealed no significant differences across and within the different treatment conditions.

DISCUSSION

The first experimental study evaluating an osteopromotive technique (subsequently termed *guided bone regeneration*, or *GBR*) in conjunction with root-form dental implants was published by Dahlin and coworkers.¹⁴ Thirty submerged titanium implants

with a machined surface were placed in the tibiae of 15 rabbits in such a way that 3 to 4 of the coronal threads were left exposed on one side of each implant. Subsequently, test implants received an e-PTFE membrane for defect coverage, whereas control implants were not covered. Animals were sacrificed after 6, 9, and 15 weeks, respectively. A significantly better ($P < .0001$) bone gain of 99.5% was found for test implants, compared to 66.4% for control implants irrespective of the time of sacrifice. However, no data were reported on direct bone-to-implant contact within the regenerated area.

Since that pioneer study, a multitude of animal studies have evaluated different histometric and histomorphometric parameters of peri-implant bone regeneration. Most of these studies have examined the effect of a non-resorbable, bioinert e-PTFE membrane on bone regeneration around partially exposed implant surfaces with simultaneous implant placement. Though it was demonstrated in several experimental studies that the bone-promoting effect of this technique and indication was reproducible, complications such as membrane exposure or membrane collapse were also often reported.¹⁵⁻¹⁸ Recently, experimental studies evaluating bone-promotion techniques with simultaneous implant placement have focused on bioabsorbable membranes,¹⁹⁻²² on new bone grafting materials,²³⁻²⁵ or even on the use of biologic mediators.²⁶

The present study investigated the osseointegration of non-submerged dental implants placed into previously augmented sites. Four grafting techniques employing 3 different bone grafting materials were tested in the canine mandible and compared to native bone. Irrespective of the type of grafting technique, all implants achieved osseointegration during a healing period of 2 months. All implants demonstrated intimate contact of the rough and microporous TPS surface with bone, which in turn showed remodeling and osteons adjacent to the implant surface. Within a specific site, BIC on the buccal aspect (ie, the implant surface contacting regenerated bone) was statistically similar to the BIC on the lingual aspect (ie, the implant surface in contact with the non-regenerated lingual bone) among the 4 tested grafting conditions. Also, no difference was found in comparison to control implants placed in native bone.

In another canine study, Berglundh and Lindhe²⁷ reported lower BIC for implants placed in a staged approach compared to the present study. After extractions in that study, defects in test sites were filled with a demineralized deproteinized bovine bone material; however, no membrane was applied. Control sites were not filled and were left to spon-

aneous healing with a blood clot. Three months later, nonsubmerged implants with a TPS surface were placed (8×3.3 -mm ITI dental implants). Following a healing period of 4 months, bone-to-implant contact measured along the entire TPS surface was 44.1% for test implants and 45.8% for control implants. The smaller BIC percentage in that study compared to this study may have resulted from the possibility that the smaller-diameter implants may not have engaged the buccal and lingual cortices and may have contacted only cancellous bone within the previous alveoli.

Bone-to-implant contact may differ when implants are placed in a staged approach compared to a simultaneous approach. The reasons for this are not known but may be related to the number of times the bone is stimulated.²⁸ For instance, implant placement in a staged approach following an osteo-promotion procedure stimulates bone formation at 2 separate timepoints. In contrast, a single activation of bone formation occurs when an implant is placed concomitantly with the osteopromotion procedure. The present study had a triple activation of bone formation, since tooth removal, ridge augmentation, and implant placement were all performed at separate timepoints. In addition, the implants immediately had intimate contact with both previously regenerated and native bone.

Few experimental studies have examined the behavior of regenerated bone around implants prior to loading. Rasmussen and associates²⁹ investigated changes in augmented bone after membrane removal around unloaded dental implants placed in the tibial metaphysis of rabbits. Membranes were removed after 8 weeks of healing, and the implants were followed for 16 more weeks. They reported substantial morphologic changes in membrane-protected newly formed bone. However, fewer dimensional changes were observed for the bone formed adjacent to the implant body compared to bone regenerated at distant areas, indicating that a solid surface may have a stabilizing effect on newly formed bone. Because that study was performed in long bones, it was not known whether a similar finding would occur in jawbone. The present study, however, has demonstrated such a phenomenon. Regenerated bone in direct contact with the buccal implant surface was consistently located more coronally than regenerated bone away from the implant surface. This was observed particularly in "DFDBA + membrane" sites, which had the most coronal fBIC (mean = 3.80 mm). In these sites, the thinnest buccal bone width was found (mean HBW = 0.32 mm). Bone resorption is thought to occur if a critical thickness of bone is not maintained. In the present

study, only "autograft + membrane," "TCP + membrane," and control sites demonstrated a mean buccal HBW greater than 1 mm, whereas lingual mean HBWs for all sites were greater than 2.1 mm irrespective of treatment.

Implant position and angulation in the bone may also affect the level of the fBIC, as well as the buccal and lingual width of the crestal bone around implants. However, to the authors' knowledge, no study has ever investigated such a possible correlation. It must be emphasized that no attempt was made to standardize the angulation and position of implants upon placement in the present study. It was rather a post-experimental observation that the long axis of the placed implants seldom matched the long axis of the alveolar ridge. The inadvertent buccal inclination of many of the evaluated implants may be explained by 2 reasons: (1) placement of implants in intubated dogs lying on their side makes tilting of drills toward the surgeon more likely, and (2) augmentation sites, particularly those with a granular bone grafting material, may demonstrate low resistance on the buccal aspect, facilitating swerving of drills.

Maintenance of a reconstructed alveolar crest is important for the final outcome of any osteopromotion technique. A bone grafting material or a mechanical support are measures attempting to prevent membrane collapse into the defect.³⁰ In the present study, the membranes covering the sites grafted with TCP- and DFDBA-particles had been supported by a tent pole-like screw anchored in the middle of the defect into the lingual cortex. Nevertheless, partial membrane collapse was observed at surgery 2 around the supporting screw, compromising the amount of the localized ridge augmentation. Possible explanations for this finding might be pressure of the soft tissue onto the membrane during the initial healing period and displacement of loose grafting particles prior to their osseous integration. In contrast to particulate grafting materials, cortico-cancellous block grafts are rigid and provide better biomechanical stability. However, without a barrier membrane or titanium mesh, block grafts may also undergo considerable resorption.³¹⁻³³ The beneficial effect of placing a membrane in conjunction with block autografts was also demonstrated in the present study. Sites treated with membrane-protected autografts showed better mean buccal fBIC and HBW measurements than sites treated with autografts alone. Also, the original contour was more ideally preserved in membrane-protected autografts. The same findings were shown in a pilot study evaluating different bone fillers with or without membrane application for lateral ridge augmentation.¹¹

CONCLUSIONS

The findings in the present study support the following conclusions:

1. Non-submerged implants with a rough titanium surface (TPS) placed into regenerated bone obtained a high percentage of bone-to-implant contact, irrespective of which of 4 different tested grafting techniques was used.
2. No statistically significant differences were calculated for any of the 3 histometrically evaluated parameters (fBIC, HBW, and BIC) on the buccal implant aspect facing regenerated bone among the 4 different grafting conditions and compared to native bone.
3. Based on the BIC results, regeneration of bone using the presented techniques of lateral ridge augmentation resulted in a similar proportion of direct connection between the implant surface and the bone.

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Article Analysis and Evaluation

ARTICLE TITLE AND BIBLIOGRAPHIC INFORMATION:

Autogenous bone versus beta-tricalcium phosphate graft alone for bilateral sinus elevations (2- and 3-dimensional computed tomographic, histologic, and histomorphometric evaluations): preliminary results.

Szabo G, Suba Z, Hrabak K, Barabas J, Nemeth Z.
Int J Oral Maxillofac Implants 2001; 16: 681-92

PURPOSE/QUESTION:

This purpose of this study was to investigate and to compare 2 different graft materials, beta-tricalcium phosphate (Cerasorb) and autogenous bone, used in the same patient.

SOURCE OF FUNDING:

Not mentioned

TYPE OF STUDY/DESIGN:

Human Research Study, Case Series

SUMMARY

Subjects(Patients):

In this study, 4 edentulous patients scheduled for bilateral sinus floor grafting and concurrent onlay plasty.

Exposure:

The main exposure was lateral ridge augmentation with the following two treatments:

- (1) Cerasorb only was used on the experimental side, and
- (2) autogenous bone only was used on the control

Main Outcome Measure:

Main outcome measure was the evaluation of the histologic and histomorphometric results. Histologic sections were then examined under light microscopy.

Main Results:

The authors' results demonstrated that when the formation of new bone was slow, it was slow on both sides; when it was fast, then it was fast on both sides.

Conclusions:

The authors' findings concluded that individual patient factors strongly influenced the fates of the various graft materials in the organism. The comparisons of the present results with the findings of other authors demonstrated that beta-tricalcium phosphate is a good graft material, even without autogenous bone. With the application of platelet-rich plasma, the rate of bone formation may be accelerated still further.

Autogenous Bone Versus β -Tricalcium Phosphate Graft Alone for Bilateral Sinus Elevations (2- and 3-Dimensional Computed Tomographic, Histologic, and Histomorphometric Evaluations): Preliminary Results

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The aim of this research was to compare 2 different graft materials, β -tricalcium phosphate (Cerasorb) and autogenous bone, used in the same patient. Bilateral sinus grafting was performed on 4 selected patients; Cerasorb only was used on the experimental side, and autogenous bone only was used on the control side. In all 4 patients, the maxilla was atrophied to such an extent that the reconstruction included not only sinus grafting but also onlay plasty. The procedure was followed by implant placement 6 months later. In addition to routine panoramic radiographs, 2- and 3-dimensional computed tomographic (CT) examinations were performed pre- and postoperatively and after implantation. Information from CTs is necessary when alveolar bone atrophy is extensive, complications appear probable, and in difficult cases, when exact documentation is important. A total of 16 bone biopsies were taken at the time of implant placement. The histologic and histomorphometric results indicated that when the formation of new bone was slow, it was slow on both sides; when it was fast, then it was fast on both sides. Individual patient factors strongly influenced the fates of the various graft materials in the organism. Comparisons of the present results with the findings of other investigators demonstrated that β -tricalcium phosphate is a satisfactory graft material, even without autogenous bone. (INT J ORAL MAXILLOFAC IMPLANTS 2001;16:681-692)

Key words: autogenous bone, bone grafting, calcium phosphates, computed tomography, histology, histomorphometry, maxillary sinus

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Autogenous graft or allogeneic graft? For many years, the reconstruction of bone defects has been achieved using a variety of bone substitute materials. The question of the "best" graft material has been addressed intensively by researchers, and as a result, a large number of experimental and clinical publications have appeared on this topic.¹⁻¹³ In 1996, a consensus conference on sinus grafting made an attempt to summarize and evaluate the research findings.¹⁴ One of the most important conclusions of the conference was that retrospective analyses did not reveal any bone substitute material that was equivalent to autogenous spongiosa. Accordingly, "... many participants believed that autografts were the most efficacious ..." and "the doubts raised revealed the need for controlled prospective multicenter clinical trials."

In essence, the question lies in how to avoid morbidity at bone graft donor sites.^{15,16} It is increasingly clear that, in addition to basic animal experiments, there is a need for clinical investigations that apply the gold standard principle to compare autogenous bone and various bone substitute materials.

An important publication in this respect is that of Groeneveld and coworkers.¹⁷ They compared 4 materials: osteogenic protein 1 (on a collagen carrier), human freeze-dried demineralized bone matrix, autogenous bone, and nongrafted alveolar crest. In a total of 12 patients (3 for each of the materials), histologic and histomorphometric methods were used to detect new bone formation during sinus floor elevation and implantation. All grafted sinuses exhibited an increased proportion of osteoid, as compared with nongrafted sinuses. It was concluded that in human sinus floor elevation, osteogenic protein has a potential bone-inductive capacity; however, the results with this material were inconsistent.

Yildirim and associates¹⁸ used a combination of Bio-Oss and venous blood as a graft material. Six months after sinus floor augmentation, they found 14.7% new bone, 29.7% Bio-Oss, and 55.6% soft tissue in the tissue samples (soft tissue = blood vessels and connective tissue composed of various proportions of fibroblasts and collagenous fibers). It is interesting to compare these results with the data reported in 1991 by Schenk,¹⁹ who found that the bone content of the human iliac crest was 20% to 25%, depending on age. Naturally, one of the problems to be considered in this regard is the extent to which Bio-Oss is resorbed.

In the literature, the resorption of bovine bone substitute materials has been the subject of controversy. Schlegel and Donath^{20,21} were able to identify the presence of Bio-Oss granules even after a resting time of up to 7 years. It was demonstrated histologically by Skoglund and colleagues²² that Bio-Oss particles could be found in the maxilla 44 months after implantation. Some publications based on animal experiments have furnished histologic evidence of the resorption of Bio-Oss.^{18,23-25}

An example of control is provided by the paper by Tadjodin and coworkers.²⁶ Bilateral sinus grafting was performed on 10 patients; a 1:1 mixture of autogenous bone particles and bioactive glass particles was used on the experimental side, and autogenous bone alone was used on the control side. At 6 months, bone tissue on the experimental side had increased to 32%, differing only slightly from the control side, which contained 38% bone by volume. At 16 months, the total bone volume on the experimental side was similar to that on the control side. After 16 months, the quality and density of bone in

the augmented sinus floor were similar, regardless of whether or not bone particles or a mixture of bone particles and bioactive glass particles had been applied.

In addition to histology and histomorphometry,²⁷⁻³² modern imaging procedures³³⁻⁴¹ are being applied more frequently for sinus graft examination. At the sinus consensus conference,¹⁴ panoramic radiographs appeared logical for the comparison of a large number of patients. Long-term results of sinus grafting may be monitored by a number of known computer tomographic methods, but these have seen limited use. Kent,³⁴ for example, examined bone levels from the new sinus floor to the alveolar crest and the apex of the implant. Alveolar bone height was considered satisfactory if the new bone exceeded the apex of the implant by at least 2 mm even after 5 to 10 years.

These data and the consensus conference¹⁴ have raised the question (among others) of how the immediate and long-term success of planned sinus grafting can be monitored, not only histologically, as with delayed implant placement, but also more accurately. When and to what extent is it worthwhile to use a state-of-the-art imaging technique? One of the aims of the present work was to clarify these questions.

The significance of pure-phase β -tricalcium phosphate as a bone substitute material has increased in recent years. It has been used in maxillofacial preprosthetic surgery, implant dentistry, traumatology, orthopedics, and hand surgery.⁴²⁻⁴⁹ The treatment modes in maxillofacial surgery have included the filling of large cysts, sinus grafting, augmentation, and the filling of periodontal lesions. It has been demonstrated that β -tricalcium phosphate is fully resorbed in 12 to 18 months and is replaced by bone that is similar both functionally and anatomically to the original bone. In view of these favorable properties, the authors sought to determine whether this bone substitute alone is an appropriate sinus graft material and whether it is suitable for the filling of large bone cysts.⁴⁹ Accordingly, prospective controlled studies were planned in selected patients.

The aim of the present work was to compare 2 different graft materials, β -tricalcium phosphate (Cerasorb, Curasan Pharma GmbH, Kleinostheim, Germany) and autogenous bone, when used in the same patient. Evaluations were performed by means of 2- and 3-dimensional (2D and 3D) computed tomography (CT) and histologic and histomorphometric examinations. The duration of the study was 6 months, which is the usual waiting period after sinus grafting. Answers to the following questions

were sought: (1) To what extent is 2D and 3D CT reconstruction suitable for assessment of the incorporation of the sinus graft, and (2) Can the above methods demonstrate any difference between Cerasorb and autogenous bone as graft materials that would circumvent the use of autogenous bone?

MATERIALS AND METHODS

Patient Selection

Four edentulous patients were scheduled for bilateral sinus floor grafting and concurrent onlay plasty. All patients had conventional denture retention problems because of severe anterior and posterior maxillary alveolar ridge atrophy. All had a residual sinus floor of less than 5 mm in height (bone loss was graded as between 3 and 4 in 1 of the 4 patients and between 5 and 6 in the other 3, according to the classification scale of Cawood and Howell⁵⁰). In all 4 patients, the maxilla was atrophied to such an extent that the sinus graft alone would not have resolved the problem; in all 4, a large part of the residual alveolar arch had thinned to a fine edge in the horizontal and sagittal directions. This situation is clearly demonstrated by the preoperative 3D CT photos (Figs 1a to 1d). The situation of the residual sinus floor is illustrated by the 2D CT photos (Figs 2a to 2d). The ages of these patients (2 men and 2 women) ranged from 42 to 62 years.

After routine oral and physical examinations, patients were selected and bone reconstruction procedures were planned. In all cases, this reconstruction included bilateral sinus floor grafting and onlay plasty in the anterior and part of the posterior maxilla, followed by implant placement 6 months later. All patients were healthy without any disease that could have influenced the treatment outcome (eg, diabetes, immunosuppressive chemotherapy, chronic sinus inflammation, rheumatoid arthritis). The patients were informed extensively about the procedures, including the surgery, the bone substitute material, the implants, and the uncertainties of using a relatively new bone-regenerative material. They were asked for their cooperation during treatment and research. All gave their written informed consent, and the research protocol was approved by the University Ethics Committee.

Methods

Radiographs and Computed Tomograms. In addition to routine panoramic radiographs, 2D and 3D CT examinations were performed pre- and postoperatively and 6 months after implant placement using a General Electric Pro-Speed Plus Instrument

(General Electric Medical Systems, Milwaukee, WI). The later exposures were taken in the same plane and direction as preoperatively. For further technical details relating to this procedure, the reader is referred to an earlier publication.³³

Surgery. In all 4 patients, surgery was carried out under general anesthesia. Before the sinus grafting or at the same time (by a second team), a 3×4 to 3×6-cm² piece of cortical bone was taken from the left iliac crest, together with 5 to 6 cm³ from the spongiosa below it. The bone wound was closed with periosteum, and the soft tissues above it were then sutured.

The bilateral sinus grafting procedure followed Tatum's classical description.⁵¹ In brief, a door was created with a round hollow bur in the lateral maxillary sinus wall. After mobilization, the door was reflected inward. The space created by this procedure was filled on one side only with 1.5 to 2 g Cerasorb (1,000 μm). This was the experimental side; the other side was the control side, which was filled with autogenous spongiosa (3 to 4 cm³). The sides for the various grafting materials were chosen at random. Care was taken to keep the inner epithelial lining intact in so as to avoid spilling the grafting material.

Onlay Plasty. To enhance successful implantation subsequently, it was necessary to widen the alveolar crest, which had become extremely thin in places. This was performed at the same time as the bilateral sinus grafting. The harvested cortical bone was attached to the lateral half of the anterior and posterior compromised maxilla with microscrews (Figs 3a and 3b). Next, the uneven bone edges were smoothed with spongiosa, the buccal and labial periosteum was extended in the customary way, and the wound was closed in a tension-free manner. The sutures were removed 7 to 10 days later. The following postoperative regimen was applied to avoid infection: Ciprofloxacin 500 mg 2 times daily (Ciprobay, Bayer, Germany); and ibuprofen 400 mg 3 times daily to reduce pain and swelling (Klinge Pharma, München, Germany). The patients were instructed to not wear any removable prosthesis for 30 days and not to blow their noses for 7 days.

After a healing time of 6 months, implants were placed. Sixteen cylindrical bone biopsies from the grafted posterior maxilla were taken (2 from the experimental and 2 from the control side) from every patient using a trephine bur (Straumann Instruments, Straumann Institut, Waldenburg, Switzerland) with an inner diameter of 2 mm and an outer diameter of 3 mm. Implants were placed in the osteotomy sites prepared at the time of biopsy sampling. (The cortical bone used for the onlay plasty was not in the sample.)

Figs 1a to 1d Preoperative 3D computerized tomograms of the 4 patients. A large part of the residual alveolar crest has thinned to a fine edge in the horizontal and sagittal directions.



Fig 1a Patient 1.



Fig 1b (Right) Patient 2.



Fig 1c Patient 3.



Fig 1d (Right) Patient 4.

Figs 2a to 2d Preoperative 2D computerized tomograms of the 4 patients. The situation at the residual sinus floors is well illustrated. The bony recesses in the sinus are clearly revealed.

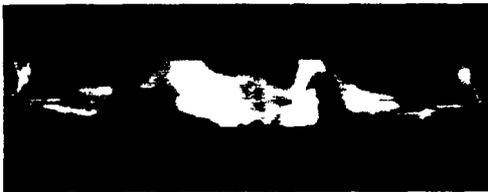


Fig 2a Patient 1.



Fig 2b Patient 2.



Fig 2c Patient 3.

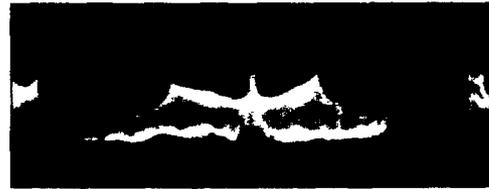
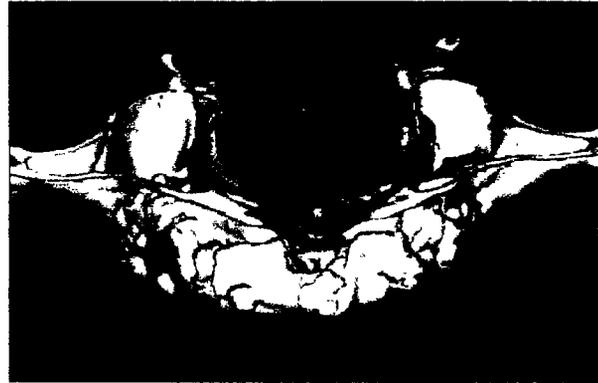
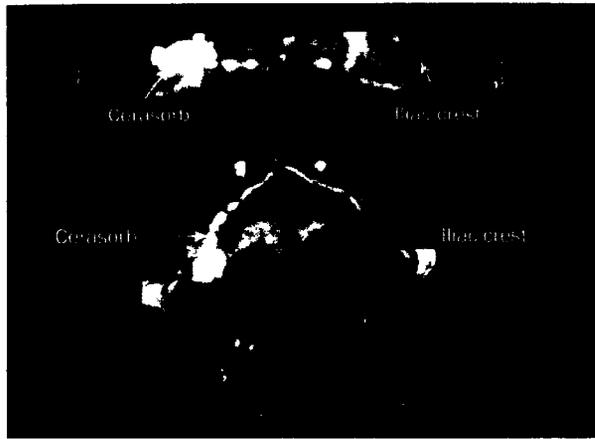


Fig 2d Patient 4.



Figs 3a and 3b Two- and 3-dimensional CT reconstructions of patient 4 after the first surgery. In Fig 3a, the bilateral sinus grafts are easily visible from horizontal and axial photographs. In the 3D rendition (Fig 3b), the onlay plasty is clearly revealed. (The 2 to 3 cm of cortical bone and the microscrews on the lateral wall of the maxilla can be seen.)

Histology and Histomorphometry. Biopsy samples were fixed in 4% formaldehyde, dehydrated in an ascending alcohol series, and embedded in methylmethacrylate resin. Histologic sections were made in the longitudinal plane with a Jung-K microtome. Sections were stained with hematoxylin and eosin, toluidine blue, and Goldner's trichrome method for light microscopy. The Cerasorb particles were achromatic. If they had broken out of the section, their places were recognizable because of their characteristic shape and size, or because of the granule remnants at the interface between the Cerasorb granules and the surrounding tissue.

Sections for histomorphometry were taken from 4 levels of each sample, with an interval of 150 μm between them. Measurements were performed semiautomatically by means of a microscope equipped with a drawing tube (Leitz, Wetzlar, Germany), cursor, and digitizing tables that was connected to a computer using Osteoplan software. The measured values were: total biopsy area (mm^2), bone area (mm^2), graft area (mm^2), and soft tissue area (mm^2).

RESULTS

Clinical Observations

No postoperative complications occurred in any of the patients. Normal wound healing was observed after both the first and the second operations. A minor nosebleed was observed in only 1 patient.

Radiology

General Observations. Routine panoramic radiographs clearly showed the positions of both types of graft material and the height of the new sinus floor. The autogenous bone was initially less visible than the Cerasorb on the radiographs. New bone formation could be clearly followed for both materials. The 2D CTs supplemented the panoramic radiographs. In the planning of surgery, the thickness and width of the alveolar bone and the process of new bone formation could be better assessed with the sagittal and axial images than with a panoramic radiograph image (Figs 3a and 3b). As for the 3D CT reconstruction, most information was provided by the anteroposterior views from among the sagittal exposures (Figs 4a to 4c), the lateral views from among the horizontal photographs, and the inferosuperior views from among the axial exposures (Figs 5a and 5b).

Detailed Observations. In treatment planning, the 2D CTs clearly revealed the bony recesses in the sinus. Simulation of the sinus grafting was more dramatic in the 2D exposures than in the 3D exposures (Figs 6a to 6c). The postoperative sinus graft height and new sinus floor were best seen in the anteroposterior views, and the ossification process was best followed here (Figs 4a to 4c).

With 3D images taken laterally, good assessments could be made of the mass of the sinus graft, the relative conditions of the new sinus floor, and the implants (Figs 6a to 6c). From photographs taken soon after the first surgery, by assessment of the density of the graft, the incorporation could be followed well in the later images (Figs 4a to 4c).

Figs 4a to 4c Consecutive 3D computerized tomograms of patient 1.

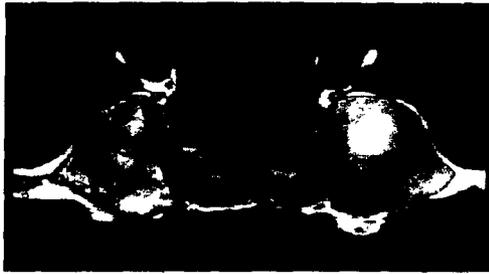


Fig 4a Preoperative image. It is clearly visible that, on the right side, continuity of the bony sinus floor is missing for 2 cm. On the left side, it is less than 3 mm.



Fig 4b Postoperative picture. The bilateral sinus grafts are clearly visible (Cerasorb in the right maxilla, and autogenous bone in the left maxilla). The symmetric onlays (cortical bone), screwed outside the maxilla, can be seen under the sinus grafts.

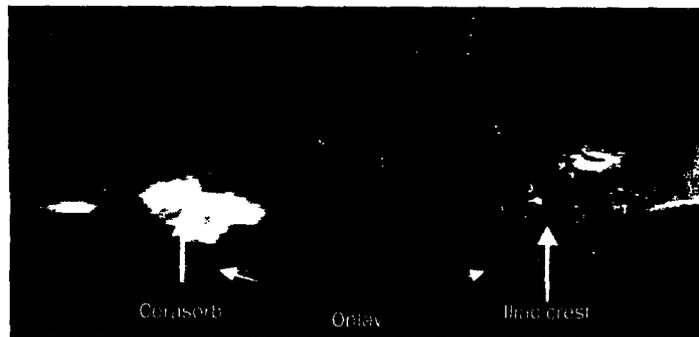
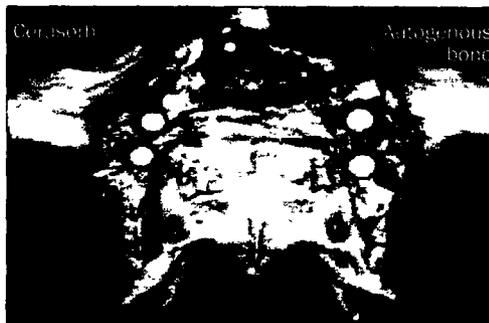


Fig 4c Six months later, just after bilateral implantations, the new sinus floors are clearly visible. On the right side, the Cerasorb graft is less radiopaque than in the postoperative view.



Figs 5a and 5b Three-dimensional CT reconstructions of patient 1 after implantation. (Left) The situation of the 4 implants in the reconstructed maxilla is visible. (Right) The volume of the incorporated sinus graft, the healed new sinus floor, and the position of the 2 implants may be established.

The 2D axial radiographs were well supplemented by the 3D radiographs. It was possible to assess the intact new sinus floor and, in the consecutive images, to follow the healing of the new sinus floor (Figs 5a and 5b). (The Cerasorb graft is less radiopaque than before, and the autogenous bone is outlined better than previously.)

The consecutive images also clearly revealed changes in the graft materials and their incorporation. Cerasorb is markedly more radiopaque than the autograft. After 6 months, the Cerasorb could be seen to have changed slightly in the CT images; the contour of the bony parts around the graft merely became more defined. Together with the absorption of Cerasorb and the simultaneous formation of new bone, the graft became similar to the bone (Figs 4a to 4c). Decreased graft height was not observed in the 3D computerized tomograms; 2D CT is more suitable for determining this.

Histology

Biopsy samples taken from the control side 6 months postoperatively showed formation of mature lamellar bone. The bone marrow was partly fibrous and partly cellular. In the bone trabeculae, osteocytes could be observed in their lacunae. Signs of remodeling were relatively rare; osteoblast activity at the osteoid surface and lacunar resorption by osteoclasts were rare findings. Autogenous bone graft remnants could be seen in the 4 patients as homogeneous, partially resorbed bone tissue without osteocytes (Fig 7a).

Biopsies from the experimental side contained remnants of Cerasorb granules. Clear identification of some Cerasorb particles in the histologic preparation remained possible after 6 months (Fig 7b). These were embedded in newly formed bone, osteoid tissue, and soft tissue in various proportions. Their form was different because of the partial resorption. The bone tissue was predominantly lamellar type. Bone deposition could be observed frequently along the surface of the remnants of partially resorbed Cerasorb granules. Intermingled with the disintegrated Cerasorb granules, connective tissue proliferation and angiogenesis were the predecessors of bone formation (Figs 8 and 9). Inflammatory reactions or foreign-body giant cell reactions did not occur in the experimental samples.

Histomorphometry

After 6 months, relatively low bone density was observed both on the experimental side and on the control side in the samples from patient 1. On the experimental side, partially resorbed Cerasorb granules were embedded in newly formed bone and soft tissue, their areas comprising 8.1% and 7.7%,

Figs 6a to 6c Consecutive 2D CTs of patient 2. Simulation of the bilateral grafting. The postoperative situation is similar to that planned.



Fig 6a Preoperative situation.

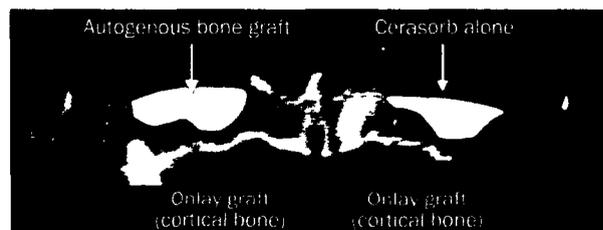


Fig 6b Treatment planning.



Fig 6c Postoperative situation

respectively, of the 2 samples. The majority of the newly formed bone tissue proved to be of mature lamellar type; it accounted for 21.2% and 29.9% of the total area of the 2 samples. On the control side in the same patient, the graft area was 8.9% and 8.45% and the bone area was 20.16% and 27.75% in the 2 samples examined.

In the second patient, a relatively high quantity of Cerasorb granule remnants could be observed on the experimental side (Fig 10a), with areas of 30.23% and 21.62% in the 2 samples. Newly formed bone comprised 13.9% and 19.35% of the total area. On the control side, some graft remnants could be observed. Newly formed bone was relatively extensive, at 42.2% and 41.2% (Fig 10b).

In the third patient, small remnants of Cerasorb granules covered 9.3% and 8.7% of the total area on the experimental side. The new bone production was relatively high, at 35.8% and 33% for the 2 parallel samples. On the control side, small remnants



Fig 7a Patient 1, control side. Lamellar bone formation and osteocytes in their lacunae can be seen (Goldner's trichrome, original magnification $\times 25$). B = bone, S = soft tissue.

Fig 7b Patient 1, experimental side. Lamellar bone formation intermingled with Cerasorb remnants can be observed (hematoxylin and eosin, original magnification $\times 25$). B = bone, C = Cerasorb; S = soft tissue.



Fig 8 Patient 2, experimental side. New bone formation can be seen along the surface of the resorbing Cerasorb granule (Goldner's trichrome; original magnification $\times 10$). B = bone; C = Cerasorb, S = soft tissue.

Fig 9 Patient 3, experimental side. Connective tissue proliferation is apparent in the center of the Cerasorb granule, along with peripheral bone apposition (hematoxylin and eosin; original magnification $\times 40$). B = bone, C = Cerasorb; S = soft tissue.

of the old bone graft could be seen. The newly formed bone area was 40.5% and 45.47%.

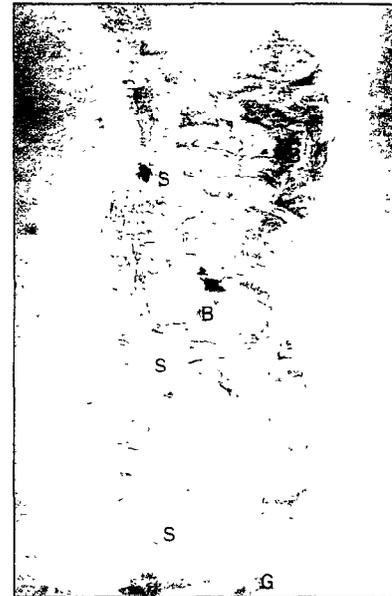
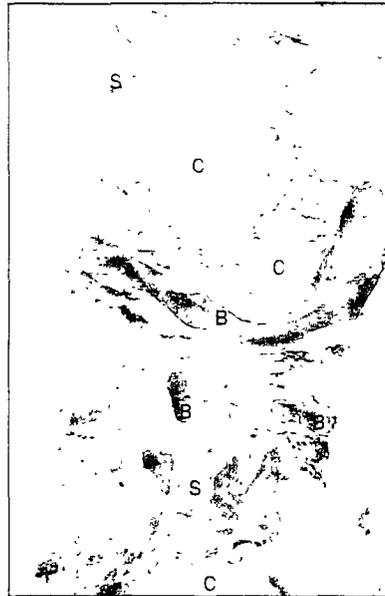
In the fourth patient, bone production was satisfactory on both sides (Figs 11a and 11b). The area of Cerasorb granule remnants on the experimental side was not very high (11.8% and 9.03%, respectively). The newly formed bone area comprised 37.7% and 44.08% of the 2 samples. On the control side, some old bone particles could be observed (7.99% and 5.52%), while the newly formed bone area made up 42.19% and 36.9% of the samples. In this case, the extent of bone formation was similar on the 2 sides (Table 1).

DISCUSSION

To what degree do 2D and 3D images aid in the planning, control, and evaluation of sinus grafting? What images are necessary, and when and in what situations? In an earlier study³³ in which prospective study methods were used to follow 12 patients with the aid of 2D and 3D CT after sinus elevation with various graft materials, 4 radiographs were obtained: preoperatively, postoperatively, before loading of the implants, and 1 year after loading. In the present study, just 3 exposures were made, since the overall duration of the investigation barely exceeded 6 months.

Fig 10a Patient 2, experimental side. Section reveals low bone density and high quantity of Cerasorb granules (Goldner's trichrome, original magnification $\times 4$). B = bone; C = Cerasorb, S = soft tissue.

Fig 10b Patient 2, control side. Satisfactory bone formation is apparent (Goldner's trichrome; original magnification $\times 4$). B = bone; S = soft tissue; G = bone graft.



Figs 11a and 11b Patient 4. A good rate of bone formation is seen on both the experimental side (*left*) and on the control side (*right*) (hematoxylin and eosin; original magnification $\times 1$). B = bone; C = Cerasorb, S = soft tissue; G = bone graft.



Table 1 Morphometric Data of Biopsy Specimens

	Experimental side (Cerasorb)				Control side (autogenous bone)			
	Total area (mm ²)	Graft area (mm ²)	Bone area (mm ²)	Soft tissue area (mm ²)	Total area (mm ²)	Graft area (mm ²)	Bone area (mm ²)	Soft tissue area (mm ²)
1 Sample I	12.63	1.03 (8.1%)	2.67 (21.2%)	8.93 (70.7%)	13.39	1.20 (8.9%)	2.70 (20.16%)	9.49 (70.94%)
Sample II	10.52	0.82 (7.7%)	3.15 (29.9%)	6.55 (62.4%)	10.90	0.92 (8.45%)	3.02 (27.75%)	6.96 (63.8%)
2 Sample I	4.73	1.43 (30.23%)	0.66 (13.9%)	2.64 (55.87%)	10.43	1.01 (5.7%)	4.40 (42.2%)	5.02 (52.1%)
Sample II	9.30	2.01 (21.62%)	1.80 (19.35%)	5.49 (59.03%)	9.58	0.70 (11.6%)	3.95 (41.2%)	4.93 (47.2%)
3 Sample I	11.02	1.01 (9.3%)	3.95 (35.8%)	6.06 (54.9%)	5.35	0.53 (10.0%)	2.17 (40.5%)	2.65 (49.5%)
Sample II	9.26	0.81 (8.7%)	3.06 (33.0%)	5.39 (58.3%)	8.82	0.69 (7.83%)	4.01 (45.47%)	4.12 (46.7%)
4 Sample I	11.15	1.32 (11.8%)	4.21 (37.70%)	5.62 (50.50%)	8.49	0.70 (7.99%)	3.56 (42.19%)	4.23 (49.82%)
Sample II	10.32	0.96 (9.03%)	4.52 (44.08%)	4.84 (46.89%)	11.08	0.61 (5.52%)	4.09 (36.9%)	6.38 (57.58%)

The preoperative radiographs are indispensable for orientation and planning. The 2D and 3D radiographs can be utilized for classification of the edentulous jaw, and hence for establishment of the parameters that could suggest one form of treatment rather than another (Figs 1 and 2). The 3D CTs permitted a decision in the present patients in favor of bilateral sinus floor elevation and simultaneous onlay plasty. Similarly to the Sim/Plant method (Columbia Scientific, Columbia, MD), planning is simpler from 2D CTs; the simulation was also performed in this way. (Figs 5a and 5b). The simulation is more important for educating patients than in preparing the objective surgical plans.

From a comparison of the postoperative CT and the CT of the planned graft, it is possible to establish the height of the graft and to learn whether the graft uniformly fills the planned volume (this refers mainly to the palatal area). After implants are placed, the distance between the apices of the implants and the new sinus floor may be measured. Conclusions may be drawn as to the incorporation of the graft from the changes in density. The 2D CT images employed in the planning are well known on the basis of the Sim/Plant software. The postoperative examination, however, is not as well known. In fact, in the literature dealing with sinus grafts, radiographs similar to the present study have not been seen.

It should be stressed that CT does not replace panoramic radiographs; no matter how useful the information gained from the various CT images, panoramic radiographs will remain the routine method in the future. Indeed, panoramic radiographs are indispensable for an appropriate evaluation of the CT images. The CT information provided is necessary when:

- Alveolar bone atrophy is so extensive that only a delayed approach is possible;
- Complication appears probable;
- Healing is slower than expected;
- In more difficult situations, exact documentation is necessary for the surgeon and for the patient.

Results of the CT examinations relating to the use of autogenous bone versus Cerasorb permit conclusions concerning the healing and incorporation of the graft. It is not only a question of the opposite changes in density (the density of Cerasorb decreases, while that of the autogenous bone increases as a function of time); the process of normal healing can be well followed. Graft integration can be seen and followed better for Cerasorb than

for autogenous bone. Because of the high density of the material, immediate observation can determine whether the granules do not reach the planned site.³³ This is scarcely possible with autogenous bone. Histologic and histomorphometric methodology can be used to demonstrate any apparent differences between autogenous bone and bone substitutes as graft materials.

Comparison of the present results with those of human studies by other authors reveals the following similarities and differences. The data of Tadjoedin and associates²⁶ and Yildirim and coworkers¹⁸ indicated a similar rate of new bone formation. Tadjoedin and associates²⁶ applied virtually the same method on the control side, but on the experimental side they mixed autogenous bone with bioactive glass in a ratio of 1:1. In their evaluation, they noted that "... bioactive glass particles in the size range 300 to 355 μm clearly show a bone augmenting capacity, and the cotransplantation of autogenous bone may not be necessary for sinus floor augmentation. However, further studies to reduce the graft amount are necessary." The present work may be considered one such study, since the β -tricalcium phosphate too was totally resorbed. Calcium and phosphorus are needed for bone-building, whereas the role of the silicate in bioactive glass is questionable.

Yildirim and coworkers¹⁸ applied Bio-Oss as a graft material in combination with venous blood. After 6 months, they observed close to 15% new bone formation, while 29% of the Bio-Oss remained. However, there was no direct or indirect control. Moy and colleagues²⁹ performed 8 sinus augmentations on 5 patients (3 bilateral and 2 unilateral). They employed the same material on both sides (4 different graft materials). Accordingly, a comparison of the use of different materials in the same patient was not possible, and only individual cases were evaluated.

Both the published data and the present findings^{42,43,47,49} indicate that pure-phase β -tricalcium phosphate resorbs completely. Furthermore, the current investigation lends support to the view that its use eliminates the necessity for the cotransplantation of autogenous bone. The present study involved only 4 patients; strong patient selection was necessary mainly for ethical reasons. The onlay plasty required autogenous bone, and a control was therefore given. It was considered important that a control be present in the same individual.

Comparison of the bone-production capacity of 2 different graft materials (Cerasorb and autogenous bone) revealed that new bone formation in the surgical area can be influenced by several factors. In

patient 1, the relatively low rate of new bone formation was similar on both sides. This supports the idea that slow bone formation is a result not only of local circumstances, but rather of general factors.

In patient 2, the bone-forming capacity was excellent on the control side. On the experimental side, remnants of Cerasorb granules reduced the quantity of bone tissue, but clinically the implants exhibited good primary stabilization. This demonstrated that not only is Cerasorb an adequate, osteoconductive bone-replacing material, but its remnants apparently harden the new bone and promote primary stabilization of implants. Later, as resorption of the Cerasorb occurs, the newly formed bone will ensure stabilization.

Patients 3 and 4 provided good examples of successful bilateral bone grafting. The bone density was quite similar on the 2 sides, and the clinical results were quite satisfactory. In these patients, quantitative measurements confirmed the positive effect of Cerasorb on new bone formation.

CONCLUSIONS

In 3 of the 4 patients, new bone formation was similar on the 2 sides. Where the Cerasorb was less well resorbed, the new tissue formed proved to be good supportive tissue. Accordingly, when comparing the present results with the findings of other authors, β -tricalcium phosphate may be considered a good graft material even without autogenous bone. Through the application of platelet-rich plasma, a relatively simple procedure, the rate of bone formation may be accelerated still further.

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APPENDIX V

CURRICULUM VITAE

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1997-98 Chief Resident in Oral and Maxillofacial Surgery, The Mount Sinai Hospital and Mount Sinai School of Medicine, New York, New York
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LICENSURE:

1991- Massachusetts State Dental License Registration Number 18019 (Expires 03/31/2004)
1992- New York State Dental License Registration Number 044230 (Expires 09/30/2005)
1992-98 Illinois State Dental License Registration Number 023077 (Expired 09/30/1998) (Inactive)
1996-98 New York State Medical License Registration Number 205171 (Expired 11/30/1998) (Inactive)
1998- DEA Federal Registration Number BC 6134162 (Expires 08/31/2004)
1998- DEA Massachusetts State Registration Number MC 0354198C (Issued 11/24/1998, Re-Issued 04/19/2002)
1999- Massachusetts State General Anesthesia Permit License Number 1801920 (Expires 03/31/2004)

CERTIFICATION:

1991 Diplomate, National Board of Dental Examiners
1991 Harvard School of Dental Medicine, Interim Diploma
1991 North East Regional Board of Dental Examiners
1992 Passed 4 examinations (#100, #110, #135, #140) for Associateship (ASA) of the Society of Actuaries
1993- American Heart Association, Basic Cardiac Life Support (BCLS) Certification
1995 Luxar Corporation; Certified Use of Carbon Dioxide Laser in Oral and Maxillofacial Surgery

- 1995 New York State Mandatory Infection Control Training at The Mount Sinai Hospital, New York, New York (Expires 03/16/1999)
- 1996 Diplomate, United States Medical Licensing Examination (USMLE) / National Board of Medical Examiners (NBME) / The Federation of State Medical Boards of the U.S. (FSMB)
- 1997 Luxar Corporation for completing a clinical training course on the CO2 Surgical Laser Techniques and application held at Mount Sinai School of Medicine, New York, New York
- 1997 Luxar / ESC Medical Systems in completion of a clinical training course in CO2 Laser Applications in General Dentistry at : The Americus Continuing Education Center, New York, New York on November 22, 1997
- 1998- American Heart Association, Advanced Cardiac Life Support (ACLS) Certification

ACADEMIC APPOINTMENTS:

- 1994-98 Clinical Fellow in the Division of Oral and Maxillofacial Surgery, The Mount Sinai Hospital and Mount Sinai School of Medicine, New York, New York 10029
- 1998-02 Research Fellow in the Department of Oral Health Policy and Epidemiology, Harvard School of Dental Medicine, Boston, Massachusetts 02115
- 2002- Instructor, Department of Oral and Maxillofacial Surgery, Harvard School of Dental Medicine, Boston, Massachusetts 02115

HOSPITAL APPOINTMENTS:

- 1998- Attending, Oral and Maxillofacial Surgery Service, Carney Hospital, 2110 Dorchester Avenue, Dorchester, Massachusetts 02124; Medical Staff Provider Number 2101
- 2002- Clinical Staff, Assistant in Oral and Maxillofacial Surgery Service, Massachusetts General Hospital, Boston, Massachusetts 02114

HONORS AND AWARDS:

- 1983-86 New York University Undergraduate Dean's List, all semesters
- 1986 Caducean Society, National Pre-Medical Honor Society, New York University
- 1986 155th Anniversary Founders Day Award, University Honors Scholar, New York University
- 1986 Mathematics Achievement Award, New York University
- 1986 Phi Beta Kappa, National Honor Society in the Humanities, New York University
- 1986 Pi Mu Epsilon, National Honor Mathematics Society, New York University
- 1986 Bachelor of Arts (BA) with magna cum laude, New York University, College of Arts and Science
- 1986-87 New York University, Stern School of Business, Graduate Division, Dean's List, all semesters
- 1987 Teaching Assistantship/Fellowship, New York University, Stern School of Business, Graduate Division
- 1987 Master of Science (MS) with distinction (Honors), New York University, Stern School of Business, Graduate Division
- 1987-92 Harvard School of Dental Medicine Course Honors: Oral Biology, Occlusion, Removable Partial Prosthodontics, Treatment Planning, Third Year Massachusetts General Hospital Oral and Maxillofacial Surgery Case Presentation, Oral Comprehensive Examinations I and III, Biostatistics, Research Methodology, Pediatric Dentistry, Oral and Maxillofacial Surgery Clinical Elective
- 1992 52nd Annual Soma Weiss Student Research Assembly, Harvard Medical School
- 1992-95 Mount Sinai School of Medicine Clinical Course Honors: Community Medicine, Otolaryngology, Psychiatry, Research in Health Policy and Management Elective, Independent Clinical Research in Biomathematics Elective, Maxillofacial Surgery Elective
- 1992-98 The first resident to begin the integrated six-year combined MD degree, General Surgery and Oral and Maxillofacial Surgery Residency Training Program at The Mount Sinai Hospital and Mount Sinai School of Medicine
- 1993 National Institutes of Health Summer Research Fellowship (No. T35 DK07420-11) at The Mount Sinai Hospital and Mount Sinai School of Medicine
- 1995-98 Physician's Recognition Award (PRA), American Medical Association
- 1996 Designated as Chief Resident in Oral and Maxillofacial Surgery to attend Chief Residents Retreat of The Mount Sinai Hospital and Mount Sinai School of Medicine
- 1997 Designated as Chief Resident in Oral and Maxillofacial Surgery to attend Chief Residents Retreat of The Mount Sinai Hospital and Mount Sinai School of Medicine

- 1998 The best chief resident in oral and maxillofacial surgery that rotates through Jamaica Hospital Medical Center in Jamaica, New York City during the academic year 1997-1998
- 1998-01 Physician's Recognition Award (PRA), American Medical Association
- 1998-01 James M. Dunning Teaching and Research Fund, Harvard School of Dental Medicine
- 1998-02 National Institutes of Health / National Institute of Dental Research Career Development Award (K16 DE00275) Institutional Dentist Scientist Award (DSA) at the Harvard University School of Dental Medicine
- 2002 AADR Hatton Competition Finalist – Senior Category, March 5, 2002, San Diego, California
- 2002-04 American Association of Oral and Maxillofacial Surgeons (AAOMS) Clinical Investigation Fellow at Massachusetts General Hospital

MEMBERSHIPS IN PROFESSIONAL SOCIETIES:

- 1989-90 Harvard School of Dental Medicine, Student Council for Class of 1992
- 1987-92 American Student Dental Association
- 1992- Academy of General Dentistry
- 1992- American Dental Association
- 1992-98 American Association of Oral and Maxillofacial Surgeons, Resident Member
- 1992- Chinese American Medical Society
- 1992- Medical Society of the State of New York
- 1992- American Medical Association
- 1992- American Statistical Association
- 1995- American College of Oral and Maxillofacial Surgeons, Resident Member
- 1998- American Association of Oral and Maxillofacial Surgeons, Member
- 1999- Massachusetts Society of Oral and Maxillofacial Surgeons, Member
- 2002- International Association for Dental Research / American Division (P331685)

SERVICE TO PROFESSIONAL ORGANIZATIONS:

- 2001- Epidemiology / Statistical Editor – Journal of Evidenced-Based Dental Practice

TEACHING AND WORK EXPERIENCE:

- 1985-86 Mathematics Grader at the New York University, Courant Institute of Mathematical Sciences; Grader in undergraduate Pre-Calculus, Calculus I, II, III, and Linear Algebra
- 1986-87 Teaching Assistant and Fellow at the New York University, Leonard N. Stern School of Business, Graduate Division; Taught and tutored undergraduate and Master of Business Administration (MBA) students in Business Calculus, Statistics, Operations Research and Operations Management

- 1992 Teaching Assistant at the Harvard University, School of Dental Medicine; Assisted Pre-doctoral dental students in Biostatistics
- 1996-97 Teaching Resident at The Mount Sinai Hospital and Mount Sinai School of Medicine, Department of Dentistry; Hospital Dentistry Lecture Series 1996-97 for General Practice Residency residents
- 1997-98 Teaching Resident at Jamaica Hospital Medical Center, The Mount Sinai Hospital and Mount Sinai School of Medicine, Department of Dentistry, Hospital Lecture Series 1997-98 for General Practice Residency residents
- 2001 Tutor at the Harvard University, School of Dental Medicine; Assisted third year pre-doctoral dental students in epidemiology and biostatistics
- 2002 Tutor for the course "Advanced Surgical Treatment" at the Harvard University, School of Dental Medicine; Assisted third year pre-doctoral dental students in oral and maxillofacial surgery

COMPUTER SKILLS AND STATISTICAL SOFTWARE:

DOS, SAS, Stata, S-plus, Windows 2000, Unix/Sun

RESAERCH AND CREATIVE ACTIVITY:

Extramural

- 1993 (Past)
NIH / NIDDK grant number T35 DK07420
National Institutes of Health Summer Research Fellowship for Medical Students at The Mount Sinai Hospital and Mount Sinai School of Medicine, New York, New York; T35 DK07420-11 (07/01/1993-08/31/1993: \$1,667)
- 1998-02 (Past)
NIH / NIDCR grant number K16 DE000275
Institutional Dentist Scientist Award (DSA); National Institutes of Health / National Institute of Dental Research Career Development Award and Institutional Dentist Scientist Award (DSA) at the Harvard School of Dental Medicine and Harvard School of Public Health, Boston, Massachusetts; K16 DE00275-08 (07/01/1998-06/30/1999: \$49,871), K16 DE00275-09 (07/01/1999-06/30/2000: \$61,228), K16 DE00275-10 (07/01/2000-06/30/2001: \$63,078); K16 DE00275-11 (07/01/2001-06/30/2002: \$65,000); Harvard University Institutional Dentist Scientist Award
- 2002-04 (Current)
American Association of Oral and Maxillofacial Surgeons (AAOMS) Clinical Research Fellowship at the Massachusetts General Hospital and Harvard School of Dental Medicine, Boston, Massachusetts; (07/01/2002-06/30/2003: \$ 100,000); (07/01/2003-06/30/2004: \$ 100,000)

2003-07 (Pending)
NIH / NIDCR grant number K22 DE 0014776
National Institutes of Health / National Institute of Dental and Craniofacial
Research Career Development Award
NIDCR Scholar Development and Faculty Transition Award (K22)
K22 DE014776-01A1 (07/01/2003-06/30/2004: \$125,000); K22 DE014776-
02 (07/01/2004-06/30/2005: \$125,000); K22 DE014776-03 (07/01/2005-
06/30/2006: \$125,000); K22 DE014776-04 (07/01/2006-06/30/2007:
\$125,000)

BIBLIOGRAPHY:

Original Reports Published in Peer-Reviewed Journals:

1. Berkey CS, Chuang SK, Douglass CW, Garcia RI. Longitudinal statistical models for or loss of sound surfaces. Community Dentistry and Oral Epidemiology 1993 Apr; 21(2): 62-6.
2. Chuang SK, Berkey CS, Douglass CW, Antczak-Bouckoms AA, Garcia RI. Epidemiologic study of sound surface trends in a 10-year longitudinal study. Community Dentistry and Oral Epidemiology 1994 Feb; 22(1): 13-20.
3. Shaari CM, Wu BL, Biller HF, Chuang SK, Sanders I. Botulinum toxin decreases salivation from canine submandibular glands. Otolaryngology - Head and Neck Surgery 1998 Apr; 118(4): 452-7.
4. Cohen S, Anastassov GE, Chuang SK. Posttraumatic pseudoaneurysm of the sphenopalatine artery presenting as persistent epistaxis: diagnosis and management. Journal of Trauma 1999 Aug; 47(2): 396-9.
5. Merchant A, Husain SS, Hosain M, Fikree FF, Pitiphat W, Siddiqui AR, Hayder SJ, Haider SM, Ikram M, Chuang SK, Saeed SA. Paan without tobacco: an independent risk factor for oral cancer. International Journal of Cancer 2000 Apr 1; 86(1): 128-31.
6. August M, Dodson TB, Nastri A, Chuang SK. Nasopharyngeal carcinoma: Clinical assessment and review of 176 cases. Oral Surgery Oral Medicine Oral Pathology Oral Radiology Endodontics 2001 Feb; 91(2): 205-214.
7. Chuang SK, Tian L, Wei LJ, Dodson TB. Kaplan-Meier Analysis of Dental Implant Survival: A Strategy for Estimating Survival with Clustered Observations. Journal of Dental Research 2001 Nov;80(11): 2016-20.

8. Vehemente VA, Chuang SK, Daher S, Muftu A, Dodson TB. Risk factors Affecting Dental Implant Survival. *Journal of Oral Implantology* 2002; 28: 74-81.
9. Chuang SK, Wei LJ, Douglass CW, Dodson TB. Risk Factors for Dental Implant Failure: A Strategy for the Analysis of Clustered Failure Time Observations. *Journal of Dental Research* 2002 Aug;81(8): 572-577.
10. Chuang SK, Tian L, Wei LJ, Dodson TB. Predicting Dental Implant Survival Using Marginal Approach of the Semi-Parametric Survival Methods for Clustered Observations. *Journal of Dental Research* (To appear, December 2002)
11. Halpern LR, Carter JB, Chuang SK, Dodson TB. A comparison of two consultation and treatment strategies for the management of impacted third molars. *Journal of Oral and Maxillofacial Surgery* (Accepted, Mid-July 2002)
12. Janket SJ, Baird AE, Chuang SK, Jones JA. Meta-Analysis of Periodontal Disease and Risk of Coronary Heart Disease and Ischemic Stroke. *Oral Surgery Oral Medicine Oral Pathology Oral Radiology Endodontics*. (Accepted on Mid-October 2002)

Manuscripts Submitted or Planned to be Submitted to Peer-Reviewed Journals:

1. McDermott NE, Chuang SK, Vehemente VA, Dodson TB. Complications of Dental Implants: Identification, Frequency and Associated Risk Factors. *International Journal of Oral and Maxillofacial Implants* (Submitted, May 22, 2002)
2. Vehemente VA, Chuang SK, Muftu A, Daher S, Dodson TB. Dentoalveolar Reconstructive Procedures as a Risk Factor for Implant Failure. *Journal of Oral and Maxillofacial Surgery*. (To be submitted)
3. Chuang SK, Douglass CW, Wei LJ, Dodson TB. Semi-Parametric Multivariate Marginal Cox Regression Models of Dental Implant Survival: A Strategy for Evaluating Covariate Effects with Clustered Observations. *Journal of Dental Research* (To be submitted)
4. Chuang SK, Hatch JP, Rugh J, Dodson TB. Multi-Center Randomized Clinical Trials in Oral and Maxillofacial Surgery: Modeling of Fixed and Random Effects. *International Journal of Oral and Maxillofacial Surgery* (To be submitted)

Chapters in Books:

1. Chuang SK, Dodson TB. Evaluation and management of pediatric midface injuries. In: *Oral and Maxillofacial Surgery Knowledge Update*, American Association of Oral and Maxillofacial Surgeons, Volume III, 2002.

Thesis:

1. Chuang SK. Epidemiologic study of sound surface trends in a ten year longitudinal study. Doctor of Dental Medicine thesis. Harvard University, School of Dental Medicine, Boston, Massachusetts. Original copy located at the Countway Library of Medicine, Harvard Medical School, Boston, Massachusetts. 1992.
2. Chuang SK. Semi-Parametric Survival Methods in Dental Research for Clustered Observations. Doctor of Medical Sciences thesis. Harvard University, Faculty of Medicine, Harvard Medical School and Harvard School of Dental Medicine, Boston, Massachusetts. Original copy located at the Countway Library of Medicine, Harvard Medical School, Boston, Massachusetts. 2002.

Co-Thesis Advisors:

Dr. Thomas B. Dodson, D.M.D., M.P.H.. Associate Professor of Oral and Maxillofacial Surgery, Massachusetts General Hospital and Harvard School of Dental Medicine

Dr. Lee-Jen Wei, Ph.D.. Professor of Biostatistics, Harvard School of Public Health

Abstracts and Other Reports:

1. Chuang SK. Analysis of repeated binary longitudinal data using markov chain models. Project summary report for NIH summer fellowship at The Mount Sinai Hospital and Mount Sinai School of Medicine, New York, New York. 1993.
2. Chuang SK. Meta-analysis and the outcomes of therapy for temporomandibular joint disorders (TMD). Community Medicine Clerkship for the degree of Doctor of Medicine, Mount Sinai School of Medicine, New York, New York. 1994.
3. Aziz SR, Chuang SK, Schneider RE, Kaban LB, Buchbinder D. The Association of Alcohol With the Etiology and Healing of Mandibular Fractures. *Journal of Oral and Maxillofacial Surgery, Educational Summaries and Outlines*, Volume 54, Number 8, Supplement 3, Page 50, August 1996.

4. Merchant A, Pitiphat W, Chuang SK. Risk factors for oral cancer in Pakistan, a matched case control study. Annual Poster Day held at Harvard School of Public Health, Boston, Massachusetts on March 4, 1999 (Accepted for Poster Presentation)
5. Chuang SK, Testa MA, Dodson TB. Meta-Analysis and Random-Effects Models of Multi-Center Clinical Trials in Craniofacial and Maxillofacial Surgery. Oral Epidemiology and Biostatistics Forum. International Association of Dental Research held at Vancouver, Canada, March 9 – March 12, 1999 (Accepted for Oral Presentation)
6. Chuang SK, Testa MA, Dodson TB. Random-Effects Models of Multi-Center Clinical Trials in Craniofacial and Maxillofacial Surgery. International Society of Craniofacial Surgery 8th International Congress held at Chang Gung Memorial Hospital in Taipei, Taiwan, October 31-November 1, 1999 (Accepted for Oral Presentation)
7. Chuang SK, Mucci LA, Dodson TB, Hayes C. The Cross-Over Design in Oral and Maxillofacial Surgery. Oral Epidemiology and Biostatistics Forum. International Association of Dental Research held at Washington, D.C., April 4 – April 8, 2000 (Oral Presentation on April 4, 2000)
8. August M, Dodson T, Nastri A, Chuang S. Nasopharyngeal Carcinoma: Clinical Assessment and Review of 166 Cases. Journal of Oral and Maxillofacial Surgery, Educational Summaries and Outlines, Volume 58, Number 8, Supplement 1, Page 66, August 2000. American Association of Oral and Maxillofacial Surgeons (AAOMS) 82nd Annual Meeting and Scientific Sessions held at San Francisco, California, September 20 – September 23, 2000.
9. Vehemente V, Chuang SK, Daher S, Muftu A, Dodson TB. Survival Analysis of Bicon Dental Implants. 7th Annual Northeast PostDoctoral Symposium in Implant Dentistry held at The Inn at Children's Conference Center, Best Western Boston Conference on October 5-6, 2000.
10. Chuang SK, Tian L, Wei LJ, DodsonTB. Correlated Kaplan-Meier Estimates for Clustered Dental Implant Observations. Special NIDCR Session. New Dental Scientists – Future Leaders of Research and Education. American Association of Dental Research held at Hyatt Regency, Regency Ballroom B, Chicago, Illinois on March 6, 2001 (Poster Presentation on March 6, 2001)
11. Chuang SK, Dodson TB, Wei LJ. Correlated Survival Analysis for Clinical Trials in Dental Research Using Frailty Models. Oral Epidemiology and

Biostatistics Forum. American Association of Dental Research to be held at Chicago, Illinois on March 6, 2001 (Oral Presentation on March 6, 2001)

12. Vehemente V, Chuang SK, Wei LJ, Muftu A, Daher S, Dodson TB. Overall Survival and Risk Factors Affecting the Long-Term Clinical Success of Dental Implants. Harvard School of Dental Medicine - Forsyth 5th Annual Research Symposium Day (Development and Neoplasia) and Poster Competition in Honor of Dr. Gerald Shklar, Charles A. Brackett Professor of Oral Pathology, Emeritus on February 2, 2001. Awarded First Prize for the Poster Competition.
13. Chuang SK, Tian L, Wei LJ, Muftu A, Daher S, Dodson TB. Correlated Kaplan-Meier Estimates for the Survival of Dental Implants. Journal of Dental Research, Volume 80, Special Issue for Abstracts, Page 235, Abstract Number 1597, January 2001. American Association of Dental Research to be held at Chicago, Illinois March 7 – March 10, 2001 (Oral Presentation on March 10, 2001, Abstract Number 1597)
14. Janket SJ, Baird A, Chuang SK, Jones JA. Meta-Analysis of Periodontal Disease and Risk of Cardiovascular Disease. International Association of Dental Research to be held at Chiba, Japan June 27 – June 30, 2001 (Accepted for Poster Presentation, Abstract Number 1558). Awarded Second Prize for the Morita Junior Investigator Award in Geriatric Research.
15. Vehemente V, Chuang SK, Wei LJ, Muftu A, Daher S, Dodson TB. Overall Survival and Risk Factors Affecting the Long-Term Clinical Success of Dental Implants. American Association of Implant Dentistry meeting. (November 2001)
16. Chuang SK, Wei LJ, Dodson TB. Risk Factors for Dental Implant Failure: A Strategy for the Analysis of Clustered Failure Time Observations. International Association of Dental Research to be held at San Diego, California March 6 – March 9, 2002 (AADR Hatton Award Finalist – Senior Category on March 5, 2001, Abstract Number 4121)
17. McDermott N, Chuang SK, Vehemente V, Daher S, Muftu A, Dodson TB. Dental Implant Complications: Types, Frequency, and Associated Risk Factors. International Association of Dental Research held at San Diego, California March 6 – March 9, 2002
18. McDermott N, Chuang SK, Dodson TB et al. Dental Implant Complications: Types, frequency and associated risk factors. Pan-Boston Oral Science Research Symposium. Held at The Forsyth Institute "Beyond the Genome - Biology of Host Tissues and Pathogens in Oral Infectious Disease" February 8, 2002.

19. Vehemente VA, Chuang SK, Dodson TB et al. Dentoalveolar reconstructive procedures as a risk factor for implant failure. Pan-Boston Oral Science Research Symposium. Held at The Forsyth Institute "Beyond the Genome - Biology of Host Tissues and Pathogens in Oral Infectious Disease" February 8, 2002.
20. Samouhi P, Valauri D, Montazem A, Chuang SK. Laboratory Testing of Various Miniplate Fixation Configurations of Simple Mandibular Angle Fractures. Journal of Oral and Maxillofacial Surgery, Educational Summaries and Outlines, Volume 60, Number 8, Supplement 1, Page 77. August 2002. American Association of Oral and Maxillofacial Surgeons (AAOMS) 84th Annual Meeting and Scientific Sessions held at Chicago, Illinois, October 2 –October 5, 2002.
21. Vehemente VA, Chuang SK, Muftu A, Daher S, Dodson TB. Dentoalveolar Procedures as a Risk Factor for Implant Failure. Journal of Oral and Maxillofacial Surgery, Educational Summaries and Outlines, Volume 60, Number 8, Supplement 1, Page 94, August 2002. American Association of Oral and Maxillofacial Surgeons (AAOMS) 84th Annual Meeting and Scientific Sessions held at Chicago, Illinois, October 2 –October 5, 2002.
22. Chuang SK, Wei LJ, Douglass CW, DodsonTB. Semi-Parametric Mixed-Effects Frailty Failure Time Models in Dental Research: Survival Analysis with Clinical Applications for Clustered Observations in Dental Implants. American Association of Dental Research to be held at San Antonio, Texas, March – March 2003
23. Gentile MA, Chuang SK, Dodson TB. 6 by 6 implants. American Association of Dental Research to be held at San Antonio, Texas, March – March 2003
24. Chuang SK, Dodson TB. Risk Factors for Failure of Dental Implants Using Frailty Failure Time Survival Methods. American Association of Dental Research to be held at San Antonio, Texas, March – March 2003
25. Chuang SK, Dodson TB. Risk Factors for Early Failure of Dental Implants Using Accelerated Failure Time Survival Methods. Academy of Osseointegration (AO) meeting held at Boston, Massachusetts February – March 2003.
26. McDermott NE, Chuang SK, Dodson TB. Sinus grafting as a risk factor for implant failure. Academy of Osseointegration (AO) meeting held at Boston, Massachusetts February – March 2003.

Letter to Editor-in-Chief:

1. Chuang SK, Dodson TB. Letter to Editor regarding the paper “Impact of Implant Interdependency When Evaluating Success Rates: A Statistical Analysis of MultiCenter Results” by Herrmann, Lekholm, Holm, Karlsson (International Journal of Prosthodontics 1999; Mar-Apr; 12 (2): 160-166). Letter to Editor appeared in International Journal of Prosthodontics 2000; Sep-Oct; 13 (5): 432-432.
2. Janket SJ, Baird A, Chuang SK, Jones JA. Heart of the matter. Letter to Editor regarding the paper “Examining the link between coronary heart disease and the elimination of chronic dental infections” by Hujuel PP, Drangsholt M, Spiekerman C, Derouen TA. (Journal of American Dental Association 2001; Jul; 132(7): 883-9). Letter to Editor to appear in Journal of American Dental Association 2001; Dec; 132 (12): 1648, 1650, 1652.

Special Mention in Paper for Contribution and Participation:

1. Ramer M, Montazem A, Lane SL, Lumerman H. Glandular odontogenic cyst. Report of a case and review of the literature. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics 1997; 84: 54-57.