

## **Injectable Bone Applied for Ridge Augmentation and Dental Implant Placement: Human Progress Study**

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n the field of implant surgery, bone availability is the key to successful placement of endosseous implants in the posterior maxilla and mandible. When the thickness of the bone between the sinus and alveolar crest is less than 5 mm, increasing the thickness of the alveolar sinus floor through grafting is necessary to support the required length of implants. On the other hand, the distance from the mandibular canal is a critical condition to avoid serious nerve injury during implant installation. In a case with insufficient alveolar bone, vertical ridge augmentation through onlay grafting is needed to increase the alveolar bone height.

Dahlin *et al*<sup>1</sup> reported an experimental study on rabbits involving the formation of new bone around titanium implants using the membrane technique. In addition, various bone grafting materials have been used for augmentation including autogenous grafts, freezedried bone allograft, hydroxyapatite, and xenografts.<sup>2,3</sup> Although the results of these investigations indicate that augmentation is clinically successful for various graft materials, it is questionable whether these materials, except for autogenous bone, have osteogenic potential and biomechanical properties.<sup>4,5</sup> On the other hand, autogenous bone, which

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Purpose: The aim of this study was to clinically evaluate the success of implants placed in conjunction with a new material, tissue-engineered bone, and the stability of the regenerated bone after functional loading on a long-term basis.

Methods: The tissue-engineered bone was applied to 14 cases, in which 6 patients were with partially or totally edentulous arches scheduled for sinus floor grafting and 8 patients underwent concurrent onlay plasty.

**Results:** This study showed that the injectable bone formation induced

currently remains the material of choice, is available for bone reconstructive procedures.<sup>6</sup> However, its use is limited due to donor site morbidity and limited amounts of graft material available for harvesting. Recently, zygoma implant has been used for the treatment of severely resorbed maxilla. If zygoma implant is used, onlay bone grafting or sinus grafting may not be necessary, because the zygoma implant can be placed from the alveolar crest and pass through the sinus cavity close to the crest of zygomatic bone. A zygoma implant can offer the patient shorter treatment time without grafting. However, there are some problems with application of zygoma implant such as its invasiveness to the patient for installation of a long fixture.

Because of these circumstances, we attempted to regenerate bone in a significant osseous defect with minimal invasiveness and good plasticity, and to provide a clinical alternative to the previously mentioned graft materials. The new technology that we developed is

bone in this anatomical site in 100% of the patients. The results also indicate that it might be possible to achieve the osseointegration of simultaneous implant placements with the grafts.

**Conclusions:** It may be possible that injectable bone can shorten the period of implant treatment and reduce the patient's burden and expect good long-term prognosis. (Implant Dent 2008:17:82–90)

Key Words: human study, injectable tissue-engineered bone, mesenchymal stem cells, dental implant

called "injectable bone,"7,8 and involves the morphogenesis of new tissue using constructs formed from isolated cells with biocompatible scaffolds and growth factors, which had been established by means of a tissue engineering concept.9 Preliminarily, we have reported about a few clinical cases that the injectable bone induces excellent bone regeneration and promotes osseointegration between implant and regenerated bone.<sup>10</sup> However, implants placed in conjunction with a new material should be evaluated on a long-term basis with respect to the success of the implants and the stability of the regenerated bone. The aim of this study was to clinically evaluate, after functional loading, periimplant tissues of titanium fixtures that had been placed in regions augmented using the injectable bone.

#### MATERIALS AND METHODS **Cell Preparation**

One month before the operation, mesenchymal stem cells (MSCs) were

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isolated from the patient's iliac crest marrow aspirates (10 mL) according to the reported method.<sup>11</sup> Briefly, the basal medium, low-glucose Dulbeccdo's Modified Eagle's Medium, and growth supplements (50 mL of serum, 10 mL of 200 mM L-glutamine, and 0.5 mL of penicillin-streptomycin mixture containing 25 units of penicillin and 25  $\mu g$  of streptomycin) were purchased from Cambrex Inc. (Walkersville, MD). Three supplements, dexamethasone, sodium  $\beta$ -glycerophosphate, and L-ascorbic acid 2-phosphate, for inducing osteogenesis were purchased from Sigma Chemical Co. (St. Louis, MO). The cells were incubated at 37°C in a humidified atmosphere containing 95% air and 5% CO<sub>2</sub>. The MSCs were replated at densities of  $3.1 \times 10^3$  cells/cm<sup>2</sup> in 0.2 mL/cm<sup>2</sup> of control medium. The differentiated MSCs were confirmed by detecting alkaline phosphatase activity using pnitrophenylphosphatase as a substrate. In culture, MSCs were trypsinized and used for implanting. For the safety of cultured cell, the culture media were examined for contaminations of bacterium, fungus, and mycoplasma before transplantation.

#### **Platelet-Rich Plasma Preparation**

Preoperative hematological assessments included a complete blood count with platelet levels. The resulting pellet of platelets (PRP) was extracted 1 day before surgery. The PRP was isolated in a 200-mL collection bag containing the anticoagulant citrate under a sterilized condition at the blood transfusion service department of Nagoya University Hospital, Japan. Briefly, the blood was first centrifuged for 10 minutes at 350g. Subsequently, the yellow plasma containing the buffy coat, which contained the platelets and leukocytes, was removed. A second centrifugation at 3500g for 10 minutes was performed to combine the platelets into a single pellet and the plasma supernatant, which was plateletpoor plasma and contained relatively few cells, was removed. The buffy coat/ plasma fraction (PRP) was resuspended in 20 mL of residual plasma and used in the platelet gel.

#### **Injectable Bone Preparation**

The PRP was stored at 22°C in a conventional shaker until used. Hu-

Table 1. Patient Data					
	Age (y)	Sex	Location	Operation	Number of Implants
1	51	F	7667	Maxillary sinus lift	6
2	60	F	56 7	Maxillary sinus lift	3
3	44	F	76	Maxillary sinus lift	2
4	54	F	765 567	Maxillary sinus lift	6
5	50	F	654	Maxillary sinus lift	3
6	56	F	56 7	Maxillary sinus lift	3
7	52	F	76	Onlay graft	3
8	74	Μ	7654	Onlay graft	4
9	54	F	76	Onlay graft	3
10	54	Μ	32	Onlay graft	2
11	54	F	32	Onlay graft	2
12	58	F	7654	Onlay graft	4
13	52	F	5 - 2 2 - 5	Onlay graft	8
14	52	F	5 - 1 1 - 5	Onlay graft	8

man thrombin in a powder form (5000 units) was dissolved in 5 mL of 10% calcium chloride in a separate sterile cup. Next, 3.5 mL of PRP, MSCs  $(1.0 \times 10^7 \text{ cell/mL})$ , and air were aspirated into a 5-mL sterile syringe. In a second 2.5 mL syringe, 500  $\mu$ L of the thrombin/calcium chloride mixture was aspirated. The cells were resuspended directly into the PRP. The 2 syringes were connected with a T connector and the plungers of the syringes were alternatively pushed and pulled allowing the air bubble to transverse the 2 syringes. Within 5 to 30 seconds, the contents assumed a gel-like consistency as the thrombin affected the polymerization of the fibrin to produce an insoluble gel.

#### **Patient Selection**

There were 14 cases aged from 44 to 74 years (mean age 54.6 years). Six patients with partially or totally edentulous ridges were scheduled for sinus floor grafting and 8 patients underwent concurrent onlay plasty. All patients had conventional denture retention problems because of severe anterior or posterior alveolar ridge atrophy. In cases of the maxilla, patients had a residual sinus floor of less than 5 mm in height, to such an extent that the sinus graft and implant would have resolved the problem (Table 1); in the other patients, a large part of the residual alveolar arch was atrophied in

the horizontal and sagittal directions (Table 1).

After routine oral and physical examinations, patients were selected and injectable bone grafting was planned because the patients preferred not to undergo any surgery for harvesting of the autogenous bone. In all cases, the reconstruction included sinus floor grafting and onlay plasty in the anterior or part of the posterior maxilla and mandible with simultaneous implant replacement. All patients were healthy and free from any disease that may have influenced the treatment outcome (e.g., diabetes, immunosuppressive chemotherapy, chronic sinus inflammation, rheumatoid arthritis). The patients were informed extensively about the procedures, including the surgery, graft material, implants, and uncertainties of using a new bone-regenerative method. They were asked for their cooperation during treatment, and the research protocol was approved by the university ethics committee (Fig. 1).

#### **Surgical Technique**

*Sinus augmentations.* In all 6 patients, surgery was carried out under general anesthesia. The sinus grafting procedure followed Tatum's classical description.<sup>12</sup> In brief, after the elevation of a mucoperiosteal flap, a door was created with a round hollow bur in the lateral maxillary sinus wall. After mobilization, the door was reflected

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inward. The space created by this procedure was filled with 1.5 to 5.8 g of tissue-engineered injectable bone, and simultaneous implant placement was performed. Care was taken to keep the inner epithelial lining intact to avoid spilling the grafting material. The mucoperiosteal flap was repositioned and sutured in the usual manner.

Alveolar ride augmentation. The regular titanium fixtures were placed into the atrophied maxilla or mandible at a depth of at least 5 mm, with the coronal part of the fixture exposed. The injectable bone was applied around the implant to completely cover the exposed threads. After coagulation of the tissue-engineered bone, the grafted area was covered by collagen membrane lined with titanium plate (W.L. Gore & Associates, Inc., Tokyo) to protect the flap compression. The membrane was fixed with cover screws, and/or microscrews or pin. Finally, the buccal and labial periosteum was extended in the customary manner, and the wound was closed tension-free.

The patients were instructed not to wear any removable prosthesis for 14 days in all cases and not to blow their noses for 7 days in cases of sinus graft. Second stage surgeries were performed approximately 4 to 8 months later.

#### RESULTS

#### Clinical and Radiographic Observations

The MSCs were trypsinized at day 7 and used for the implants at a concentration of  $1.0 \times 10^7$  cells/mL. The PRP mean platelet count was 972,269 (range 524,480–2,033,000). The values confirmed the platelet sequestration ability of the process, which showed that the mean concentration was 446% above the baseline platelet counts. None of the patients had postoperative problems besides normal swelling and inflammation at the sur-

gical sites. The main complications during surgery were sinus membrane perforation and wound separation. Perforation of the sinus mucosa was recorded in 4 procedures and resulted in only minor postoperative nasal bleeding without severe inflammatory sign in maxillary region during total observation period. In case of sinus floor augmentation, evaluation was done from 2 to 5 years after the first surgery. Twenty-three fixtures were installed with injectable bone. The clinical observation was carried out on the grafted area. Cumulative survival and success rates for fixtures placed in conjunction injectable bone were 100%. Postoperative radiographic findings were consistent with integration between the implant and the regenerated bone (no bone loss or peri-implant radiolucency). Pre- and postoperative radiographic evaluations showed that the increasing in mineralized tissue was 8.7 mm.

Table 1 also describes the vertical ridge augmentation procedure for each patient and the survival data for implants available at re-examination. Also the clinical conditions associated with the 34 remaining fixtures placed in conjunction with ridge augmentation using injectable bone are presented in the table.

At the second surgery, which was performed after a mean healing period of 4.8 months, the mucosal flap was elevated to observe the grafted site.

In all cases of vertical ridge argumentation, the spaces around the titanium fixtures were filled with newly formed tissue, which seemed to be calcified tissue. In 2 of 8 cases with wound separation, the bone regeneration was not enough. Average increasing of bone height was 5.0 mm. At 6 months after loading, as tested after removal of the prosthetic reconstruction, all implants maintained stability. Marginal bone resorption at 6 months after loading did not exceed 1.5 mm.

## CASE REPORTS

#### Case 1

A 44-year-old woman (patient 3 in Table 1) presented with an edentulous right maxilla. She complained of inability to wear her maxillary denture and comfortably chew hard food. Her

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**Fig. 2.** A, Preoperative macro view. B, Observation of second-stage surgery 6 months after the implant installation. The exposed thread was surrounded by newly formed bone and confirmed successful osseointegration. C, Last prothesis observation by porcelain fused to a metal crown. These did not exceed 2 mm, and a healthy and firm peri-implant mucosa had been established. D, Panoramic radiograph of patient 3 in Table 1, preoperative. E, Panoramic radiograph of patient 3 in Table 1, postoperative 2, postoperative 1 year. G, Panoramic radiograph of patient 3 in Table 1, postoperative 2 years. H, Panoramic radiograph of patient 3 in Table 1, postoperative 3 years.

physical examination revealed flabby posterior maxillary soft tissue and severe maxillary atrophy (Fig. 2, *A*). Insufficient bone was present for placement of implants in the maxilla. After the exposure of the maxilla, the door trap was designed by a round bur on the lateral wall of maxilla under water irrigation. The lateral wall of the maxilla was rotated medially with elevation of the sinus membrane. Two implants were placed into each alveolar ridge of the maxilla, however, the fixtures exposed in sinus cavity. The injectable bone (with beta-tricalcium phosphate) was applied in the maxillary sinus and around the fixtures completely to cover the exposed thread (Fig. 2, *B*). A spark-erosion prosthesis was made over the implants (Fig. 2, *C*).

The radiographs showed the parallel position of the maxilla and insufficient bone in the maxillary floor (Fig. 2, D, E). However, at 12 months progressive bone regeneration was observed (Fig. 2, F). A radiograph showed a bone filling around the previously exposed threads, reaching the tip of the implants (Fig. 2, F-H). The 3 years follow-up examination showed no signs or symptoms of implant failure (Fig. 2, H).

#### Case 2

A 52-year-old woman (patient 14 in Table 1), she had only both first molar teeth and lost other teeth with a severely atrophied mandibular alveolar crest. The patient required treatment by 8 implants and ridge augmentation with injectable bone. Occlusal view of mandible before the ridge augmentation procedure showed the narrow ridge and the concave shape of the lateral side of mandible. An incision was made over the crest with vertical release. The mandible has been absorbed vertically and need for the ridge augmentation. Eight fixtures were installed in the crestal part of mandible after flap elevation.

She had problems with her denture due to cosmetic reason and wanted it to be improved. The coronal parts of the fixtures protruded from the alveolar crest to the level of the implant neck (Fig. 3, A). The injectable bone was applied to cover the exposed part of fixture (Fig. 3, B). At the stage of second surgery, the grafted area was observed. The fixtures were covered by newly formed bone, and bone increase on the lateral side of the mandible was seen (Fig. 3, C). Final oral implant bridge was achieved (Fig. 3, D) and the patient was pleased. The 2 years follow-up examination showed no signs or symptoms of implant failure.

#### DISCUSSION

This study evaluated the performance of an injectable bone in 1-stage alveolar augmentation with simultaneous implant placement. As a general consensus, the 1-step procedure should be reserved for patients who have at least 5 mm of alveolar bone in the posterior maxilla or mandible to stabilize the implants. If there is less than 5 mm of available host bone, it is insufficient to mechanically maintain the endosteal implants, and thus the 2-step procedure combined with augmenta-

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**Fig. 3.** A, Macro view of fixtures insertion into a prepared implant site. The coronal part of fixtures was protruded from the alveolar crest to level the implant neck with next natural teeth. B, Macro view of a tissue-engineered bone application. C, Observation of second-stage surgery 4 months after the implant installation. The exposed thread was surrounded by newly formed bone and confirmed successful osseointegration. D, Final prosthesis observation.

tion procedure is recommended for these patients.<sup>13–15</sup> On the other hand, the 1-step procedure offers the advantages of less surgical treatment for the patient and coordinated consolidation of the graft around the implants during healing, thus reducing the surgical and healing times for the patient. Another advantage is that it not only eliminates the need to harvest autogenous bone via its inherent morbidity, but also decreases the surgical recovery time.<sup>16</sup> In this study, all cases of posterior maxilla had more than 5 mm in the sinus floor and in the mandible. The patients underwent the 1-step augmentation procedure with injectable bone application and simultaneous implant placement. The macro findings showed that injectable bone induced bone regeneration and that the dental implant thread was not exposed. Thus, these results indicate that ridge augmentation caused by injectable bone and that simultaneous implantation is possible.

The results of this study provide evidence of the safety and technical feasibility of injectable bone for maxillary sinus floor augmentation and vertical ridge augmentation in agreement with those from earlier animal studies that have indicated that treatment with injectable bone dose not result in toxicity, significant immunologic reactions, or other serious adverse effects.<sup>17–20</sup> Adverse experiences (*e.g.*, pain, swelling after operation) observed with injectable bone were consistent with the usual morbidity observed in the maxillary sinus floor augmentation procedure and vertical ridge augmentation.

Radiographic assessments indicated that injectable bone induced new bone growth in the maxillary sinus floor in 100% of the patients treated, and showed 8.7 mm mean increase in mineralized tissue. In the meantime, in clinical human testing, protruding into the sinus cavity stimulated reactive bone regeneration by human bone morphogenetic protein-2 that is limited to 8.51 mm in height.<sup>21</sup> This is almost the same as that regenerated by injectable bone in this study. Furthermore, in the case of vertical ridge augmentation the mean increase of mineralized tissue was 5 mm, which was affected by the stability of the grafted area. These effects might be dependent on MSCs and PRP. The MSCs in the bone marrow are induced into cells with osteogenic capacity, the MSCs are considered to be more feasible for this tissue engineering because the former proliferates faster because of a lower degree of differentiation. In addition, the PRP contains not only fibrinogen

that forms a fibrin network acting as a matrix but also cytokinetic substances such as platelet-derived growth factor, transforming growth factor beta, and fibroblast growth factor. These growth factors contribute to cellular proliferation, matrix formation, collagen synthesis, osteoid production, and other processes that accelerate tissue regeneration.

#### CONCLUSION

This study showed that injectable bone induced bone in the anatomical site in 100% of the patients. The results also indicate that it might be possible to achieve osseointegration of simultaneous implant placements with injectable bone grafts. It may be possible that the injectable bone can shorten the period of implant treatment and reduce the patient's burden physically and mentally. The potential for injectable bone in general and in particular is exciting for both patients and dental practitioners. The release for general clinical use seems to be very near, although it has not yet been approved for use by the Japanese Food and Drug Administration.

#### Disclosure

The authors claim to have no financial interest in any company or any of the products mentioned in this article.

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#### REFERENCES

1. Dahlin C, Sennerby L, Lekholm U, et al. Generation of new bone around titanium implants using a membrane technique: An experimental study in rabbits. *Int J Oral Maxillofac Implants*. 1989;4:19-25.

**86** INJECTABLE BONE APPLIED FOR RIDGE AUGMENTATION AND DENTAL IMPLANT PLACEMENT Copyright © Lippincott Williams & Wilkins. Unauthorized reproduction of this article is prohibited. 2. Hersh JM, Ericsson I. Maxillary sinus augmentation using mandibular bone grafts and simultaneous installation of implants. *Clin Oral Implants Res.* 1991;2:91-96.

3. Smiler DG, Johnson PW, Lozada JL, et al. Sinus lift grafts and endosseous implants. Treatment of the atrophic posterior maxilla. *Dent Clin North Am.* 1992;36: 151-186.

4. Wheeler SL, Holmes RE, Calhoun CJ. Six-year clinical and histologic study of sinus-lift grafts. *Int J Oral Maxillofac Implants*. 1996;11:26-34.

5. Moy PK, Lundgren S, Holmes RE. Maxillary sinus floor augmentation. *Int J Oral Maxillofac Implants*. 1993;51:857-862.

6. Wood RM, Moore DL. Grafting of the maxillary sinus with intraorally harvested autogenous bone prior to implant placement. *Int J Oral Maxillofac Implants*. 1988;3:209-214.

7. Yamada Y, Boo JS, Ozawa R, et al. Bone regeneration following injection of mesenchymal stem cells and fibrin glue with a biodegradable scaffold. *J Craniomaxillofac Surg.* 2003;31:27-33.

8. Yamada Y, Ueda M, Naiki T, et al. Autogenous injectable bone for regeneration with mesenchymal stem cells and platelet-rich plasma: Tissue-engineered bone regeneration. *Tissue Eng.* 2004;10: 955-964.

9. Langer R, Vacanti JP. Tissue engineering. *Science*. 1993;260:920-926.

10. Ueda M, Yamada Y, Ozawa R, et

al. A clinical report of injectable tissueengineered bone applied for alveolar augmentation with simultaneous implant placement. *Int J Periodontics Restorative Dent*. 2005;25:129-137.

11. Pittenger MF, Mackay AM, Beck CB, et al. Multilineage potential of adult human mesenchymal stem cells. *Science*. 1999;284:143-147.

12. Tatum H. Maxillary and sinus implant reconstructions. *Dent Clin North Am*. 1986;30:207-230.

13. Jensen J, Simonsen EK, Sindetpedersen S. Reconstruction of the severely resorbed maxilla with bone grafting and osseointegrated implants: A preliminary report. *J Oral Maxillofac Surg.* 1990; 48:27-32.

14. Marx RE. Clinical application of bone biology to mandibular and maxillary reconstruction. *Clin Plast Surg.* 1994;21: 377-392.

15. Raghoebar GM, Brouwer TJ, Reintsema H, et al. Augmentation of the maxillary sinus floor with autogenous bone for placement of endosseous implants: A preliminary report. *J Oral Maxillofac Surg*. 1993;51:1198-1203.

16. Marx RE, Morales MJ. Morbidity from bone harvested in major jaw reconstruction. *J Oral Maxillofac Surg*. 1988;48: 196-203.

17. Smith JL. Osseous regeneration in preclinical models using bioabsorbable delivery technology for recombinant human bone morphogenetic protein 2

(rhBMP-2). *J Control Release*. 1995;36: 183-195.

18. Gerhart TN, Kirker-Head CA, Kriz MJ, et al. Healing segmental femoral defects in sheep using recombinant human bone morphogenetic protein. *Clin Orthop Relat Res.* 1993;293:317-326.

19. Toriumi DM, Kotler HS, Luxenberg DP, et al. Mandibular reconstruction with a recombinant bone-inducing factor: Functional, histologic, and biomechanical evaluation. *Arch Otolarnygol Head Neck Surg.* 1991;117:1101-1112.

20. Sigurdsson TJ, Lee MB, Kubota K, et al. Periodontal repair in dogs: Recombinant human bone morphogenetic protein-2 significantly enhances periodontal regeneration. *J Periodontol.* 1995;66:131-138.

21. Boyne P, Marx RE, Nevins M, et al. A feasibility study evaluation rhBMP-2/ absorbable collagen sponge for maxillary sinus floor augmentation. *Int J Periodontics Restorative Dent*. 1997;17:11-25.

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# **ID** Abstract Translations

## **GERMAN / DEUTSCH**

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Injizierbares Knochengewebe in Anwendung beim Aufbau der Kieferleiste sowie bei der Einpflanzung von Implantaten: eine Fortschrittsstudie am Menschen

**ZUSAMMENFASSUNG:** Zielsetzung: Die vorliegende Studie zielte darauf ab, den Erfolg einer Implantierungsbehandlung zu bewerten, sofern diese in Verbindung mit einem neuen Material, einem dem natürlichen Gewebe nachempfundenen Knochen, angewendet wird. Außerdem sollte die Stabilität des regenerierten Knochengewebes nach funktionaler Belastung auf lange Sicht beurteilt werden. Methoden: Der dem natürlichen Gewebe nachempfundene Knochen fand in insgesamt 14 Fällen Anwendung. Dabei wurde bei 6 der Patienten mit teilweise oder komplett zahnlosem Bogen eine Transplantierung am Sinusboden vorgesehen und bei 8 Patienten wurde gleichzeitig eine Onlay-Plastik eingesetzt. Ergebnisse: Die Studie konnte zeigen, dass das injizierbare Knochengewebe bei 100% der Patienten zu einer Bildung von Knochengewebe an der Versuchsstelle führte. Die Ergebnisse weisen außerdem aus, dass mit diesen Transplantaten unter Umständen eine Knochengewebsintegration der gleichzeitig erfolgenden Implantierungsbehandlungen erzielt werden könnte. Schlussfolgerungen: Möglicherweise kann das injizierbare Knochengwebe die Implantierungsbehandlungszeit verkürzen und die Belastungen des Patienten verringern sowie für eine gute langfristige Prognose sorgen.

*SCHLÜSSELWÖRTER:* Studie am Menschen, injizierbares, dem natürlichen Gewebe nachempfundenes Knochengewebe, Mesenchym-Stammzellen, Zahnimplantat

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## SPANISH / ESPAÑOL

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Hueso inyectable aplicado para el aumento de la cresta y la colocación de un implante dental: Estudio sobre el progreso humano

ABSTRACTO: Propósito: El objetivo de este estudio fue evaluar clínicamente el éxito de los implantes colocados junto con un nuevo material, hueso con tejido sintético, y la estabilidad a largo plazo del hueso regenerado luego de la carga funcional. Métodos: El hueso con tejido sintético se aplicó a 14 casos, que fueron 6 pacientes con arcos parciales o totalmente edentulosos programados para un injerto del piso del seno y 8 pacientes recibieron a la vez una plastia de restauración de la cara oclusal. Resultados: Este estudio demostró que la formación de hueso inyectable indujo hueso en este lugar anatómico en un 100% de los pacientes. Los resultados también indican que podría ser posible lograr la oseointegración de la colocación simultánea de implantes con los injertos. Conclusiones: Podría ser posible que el hueso inyectable puede acortar el período de tratamiento con el implante y reducir los problemas para el paciente y esperar un buen pronóstico a largo plazo.

**PALABRAS CLAVES:** estudio humano, hueso inyectable con tejido inyectable, células madres mesenquimáticas, implantes dentales

## **PORTUGUESE / PORTUGUÊS**

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Osso Injetável Aplicado para Aumento do Rebordo e Colocação de Implante Dentário: Estudo do Progresso Humano

**RESUMO:** Objetivo: O objetivo deste estudo era avaliar clinicamente o sucesso de implantes colocados em conjunto com osso de material novo, trabalhado pelo tecido, e a estabilidade do osso regenerado após carga funcional em regime de longo prazo. *Métodos:* O osso trabalhado pelo tecido foi aplicado a 14 casos, os quais eram 6 pacientes com arcadas parcial ou totalmente desdentadas designados para fazer enxerto da superfície da cavidade e 8 pacientes que se subme-

teram a *onlay*-plastia simultânea. **Resultados:** Este estudo mostrou que a formação de osso injetável induziu osso neste local anatômico em 100% dos pacientes. Os resultados também indicam que poderia ser possível obter a osseointegração de colocações de implante simultâneo com os enxertos. **Conclusões:** Talvez seja possível que o osso injetável possa encurtar o período de tratamento do implante e reduzir o fardo do paciente e aguardar bom prognóstico de longo prazo.

*PALAVRAS-CHAVE:* estudo humano, osso trabalhado por tecido injetável, células-tronco mesenquimais, implante dentário

## RUSSIAN / РУССКИЙ

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Применение инъеџируемой кости для наращивания альвеолярного отростка челюсти и установки внутричелюстных зубных имплантатов: прогрессивное исследование человека

**РЕЗЮМЕ: цель** данного исследования – оценить в клинических условиях эффективность имплантатов, установленных совместно с костью, изготовленной ИЗ нового материала ткани \_ продукта биоинженерии, и устойчивость восстановленной кофункциональной сти после нагрузки на долговременной основе. Методы: ткань, являющаяся продуктом биоинженерии, применялась в 14 случаях, из которых 6 пациентам с частично или полностью отсутствующими рядами зубов была назначена трансплантация основания синуса, а 8 пациентов пластику перенесли совмещенную накладок. Результаты: данное исследование показало, что инъецируемое костеобразование породило кость в заданном анатомическом месте у 100 % пациентов. Кроме того, результаты указывают на возможность оссеоинтеграции одновременно установленных имтрансплантированными плантатов с тканями. Выводы: возможно, что инъецируемая кость может сократить период имплантационного лечения, облегчить бремя пациента и дать надежду на хороший долгосрочный результат.

*КЛЮЧЕВЫЕ СЛОВА:* исследование человека, инъецируемая костная ткань – продукт

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биоинженерии, мезенхимные стволовые клетки, внутричелюстной зубной имплантат.

## TURKISH / TÜRKÇE

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Kret Augmentasyonu ve Dental Ýmplant Yerleþtirilmesinde Uygulanan Enjektabl Kemik: Ýnsan Ýlerleme Çalýþmasý

**ÖZET:** Amaç: Bu çalışmanın amacı, yeni bir materyal olup, doku mühendisliğinden elde edilmiş kemik ile birlikte yerle-

ştirilen implantların başarı oranının yanı sıra fonksiyonel yükleme sonrasında rejenere olmuş kemiğin stabilitesini uzun vadede klinik olarak değerlendirmekti. **Yöntem:** Doku mühendisliği yoluyla elde edilen kemik, 14 olguda uygulandı. Bunlardan altısı kısmen veya tamamen dişsiz olan arkına sinüs zemini grefti yapılacak olan hastalardı. Sekiz hastaya da aynı zamanda onlay plasti uygulandı. **Bulgular:** Bu çalışma, enjektabl kemik formasyonunun hastaların %100'ünde bu anatomik yerde kemik gelişimine neden olduğunu göstermiştir. Bulgular ayrıca, eş zamanlı implantlar ile greftler arasında osseointegrasyonun mümkün olabileceğine işaret etmiştir. **Sonuç:** Enjektabl kemiğin, implant tedavisinin süresini kısaltması, hastaya zahmeti azaltması ve uzun vadede iyi prognoz sağlaması olası görülmektedir.

ANAHTAR KELÝMELER: insan çalışması, doku mühendisliği ile geliştirilen enjektabl kemik, mesenkimal kök hücreleri, dental implant

## JAPANESE / 日本語

注入型培養骨とデンタルインプラントを同時に応用した歯槽堤増大術:ヒトプログレス研究

共同研究者氏名: 上田 実(Minoru Ueda) DDS, PhD, 山田 陽一 (Yoichi Yamada) DDS, PhD, 各務 秀明 (Hideaki Kagami) DDS, PhD, 日比 英晴 (Hideharu Hibi) DDS, PhD

研究概要:目的:本研究は新素材培養骨を応用したインプラントとの同時埋入の結果、ならびにファンクショナル ローディング後の安定性の臨床評価を目的とした。

方法:14ケースに培養骨を応用した。そのうち6名の患者は部分欠損あるいは無歯顎状態で上顎洞底挙上術を行い、8名はオンレーグラフト治療を受けた。

結果:本研究は注入型培養骨組織が患者100%において解剖学的部位の骨形成を促進したという結果を示した。 さらにこの結果は培養骨と同時インプラント埋入におけるオッセオインテグレーション達成の可能性も示唆している。

結論:注入型培養骨はインプラント治療期間を短縮し、患者の負担を軽減するとともに長期間にわたり良好な見通 しを期待できる可能性がある。

キーワード: ヒト研究、注入型培養骨、間葉系幹細胞、デンタルインプラント

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## CHINESE / 中国語

#### 可注射骨質在牙脊增高與牙科植體植入的應用 - 人類進展研究

作者: Minoru Ueda、DDS、PhD; Yoichi Yamada、DDS、PhD; Hideaki Kagami、DDS、PhD; 以及 Hideharu Hibi、 DDS、PhD

#### 摘要:

**目的:**本研究的目的旨在從臨床上進行植體與新材質組織工程骨質同時植入、以及在長期功能性載入後重生骨質的穩定性的成功度評估。

方法:在 14 個病例使用組織工程骨質,其中包括為 6 名部分或全口缺牙齒弓患者排定竇底移植,另外 8 名進行同時 鑲嵌式整形手術。

**結果:**本研究顯示,可注射骨質形成能在100%患者的這個組織部位催生骨質。結果也顯示可能達成同時進行植體植入與移植的骨整合。

結論:可注射骨質可能縮短植體治療期間、減輕患者的負擔,而且可期望長期預後良好。

#### 關鍵字:人類研究、可注射組織工程骨質、間葉幹細胞、牙科植體

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### KOREAN / 한국어

#### 치조제 증강술 및 치과 임플란트 식립을 위해 적용된 주입형 골: 인간 경과 연구

**저자:** 우에다 미노라, 치과의사, 박사, 야마다 요이치, 치과의사, 박사, 카가미 히데아키, 치과의사, 박사, 히비 히데하루, 치과의사, 박사

초록

**목적:** 본 연구의 목적은 새로운 재료인 조직-공학적 골(tissue-engineered bone)과 함께 식립된 임플란트의 성공과 기능적 부하 후 재생된 골의 장기적 안정성을 임상적으로 평가하는 데 있었다.

방법: 조직 공학적 골을 14명의 환자들에 적용하였다. 이들 중 6명은 상악동저 이식이 예정되어 있던 부분 또는 전체 무치악 환자였으며 8명은 동시 중첩 이식을 받은 환자였다.

**결과:** 본 연구는 100%의 환자들에서 주입형 골이 이 해부학적 부위에서 골 형성을 유도하였음을 보여주었다. 결과는 또한, 이식편과 동시에 식립된 임플란트의 골융합이 성취될 가능성이 있을 수도 있음을 보여주었다.

**결론:** 주입형 골이 임플란트 치료 기간을 단축하고, 환자의 부담을 덜어주며, 우수한 장기 예후를 기대할 수 있도록 할 가능성이 있을 수도 있다.

핵심 단어: 인간 연구, 주입형 조직 공학적 골, 중간엽 줄기 세포, 치과용 임플란트

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