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Literaturübersicht

Algipore-Literaturübersicht

Knochenaufbaumaterialien müssen bestimmte chemische, strukturelle und biologische Grundvoraussetzungen für ihren Einsatz am Patienten erfüllen. Eine grundlegende Eigenschaft des Knochenaufbaumaterials ist dessen Biokompatibilität. Biokompatible Materialien und Werkstoffe zeichnen sich dadurch aus, dass sie keinerlei negativen Einfluss auf das jeweilige Lagergewebe haben und dort langzeitverträglich inkorporiert werden können. Die Qualität des Knochenaufbaus wird in erster Linie an seiner Fähigkeit zur Osteogenese sowie seiner mechanischen Eigenschaften gemessen. Gleichzeitig sollte er gut applizierbar sein und nach seiner Einbringung gut resorbiert sowie in ortsständigen Knochen umgebaut werden können.

In erster Linie dienen Knochenaufbaumaterialien zur Stabilisierung des Knochendefekts und als Matrix, die das umliegende Knochengewebe zur Knochenneubildung anregen soll. Diese als Osteokonduktivität bezeichnete Eigenschaft wird durch dessen poröse Grundstruktur, die der Struktur trabekulären Knochens ähnelt, begünstigt. Die dreidimensionalen Kanäle dienen dabei als Leitschiene für das Einsprossen von Gefäßen und für die Einwanderung von Osteozyten. Die osteokonduktive Potenz wird dabei entscheidend durch die Interkonnektivität der Poren und die Porengröße des Ersatzmaterials beeinflusst. Der ideale notwendige Mindestdurchmesser der Poren für eine Osteokonduktion wird dabei in der Literatur kontrovers diskutiert[1]. Einerseits werden Porengrößen von mehr als 300 Mikrometer empfohlen, um den Zellmigrationsprozess und die Neovaskularisierung zu ermöglichen und somit die Knochenneubildung hinreichend zu fördern. Andere Autoren gehen indes von einem Mindestporendurchmesser von 50 Mikrometern aus. Offensichtlich hat die Porengröße einen Einfluss auf die Art des Gewebes, das sich innerhalb der Porenstruktur ausbilden kann. Für die Bildung mineralisierter Knochengewebe wird von einem Mindestdurchmesser von mindestens 100 Mikrometern und für osteonähnliche Strukturen von 200 Mikrometern ausgegangen.

Ein im Jahre 1972 entwickeltes Verfahren (replamineform process) ermöglichte es, durch einen hydrothermalen Umwandlungsprozess bei Temperaturen von 300 Grad Celsius Fluorhydroxylapatit aus pflanzlichen Kalziumkarbonat-Exoskeletten herzustellen. Infolge des hydrothermalen Herstellungsprozesses wird ein Großteil des in den Kanälen enthaltenen organischen Bestandteils entfernt und gleichzeitig die einzigartige poröse Struktur der Algen erhalten[1,2]. Auf diese Weise wird die Grundlage für das heutzutage für Augmentationen im Mund-, Kiefer-, Gesichtsbereich verwendete phykogene (pflanzliche) Hydroxylapatit geschaffen, das im Falle von Algipore aus dem nachwachsenden Rohstoff der Rotalge gewonnen wird und das menschlichem Knochen strukturell sehr ähnlich ist[3].

Algipore wurde im Jahr 1985 entwickelt und kurz darauf gegen Ende der 1980er Jahre als Augmentationsmaterial im Mund-, Kiefer-, Gesichtsbereich klinisch eingesetzt[4]. Algipore kann man grundsätzlich in allen Indikationsbereichen einsetzen. Insbesondere wurde es bei der Augmentation des atrophierten Oberkiefers oder bei Sinusbodenaugmentationen[2,5-15] und Periimplantitistherapien[16-18] verwendet. Es eignet sich gleichermaßen als Knochenaufbaumaterial bei der Distraktionsosteogenese[19], der Ridge Preservation[20,21] und Parodontaltherapien[22].

Als sehr positiv werden seine biokompatiblen Eigenschaften eingeschätzt, die sich unter anderem in einer fehlenden Immunreaktion im In-vitro-Versuch zeigten.[23] Algipore ist in Partikelgrößen von 0,3 bis 2,0 mm und einem Porendurchmesser von ca. 1 bis10 Mikrometern erhältlich. Trotz seiner hohen Interkonnektivität werden die osteokonduktiven Eigenschaften von Algipore aufgrund seiner relativ kleinen Porendurchmesser in einigen Publikationen in Frage gestellt. Dies konnte in mehreren Studien eindrucksvoll widerlegt werden. So besitzen Materialien mit Mikroporen eine große Oberfläche, die eine erhöhte Knochenneubildung begünstigt und eine Anheftung, Proliferation und Differenzierung knochenbildender Zellen ermöglicht[3,24]. Es konnte klar gezeigt werden, dass auf dem Gerüst von Algipore-Partikeln die Proliferation und Ausdifferenzierung humaner Osteoblastenvorstufen[24] oder mesenchymaler Zellen[25] gefördert werden.

In klinischen Kohortenstudien[7,26] und klinisch kontrollierten Studien[9] konnte auch innerhalb der Poren der Algipore-Partikel neugebildeter Knochen beobachtet werden, was für dessen Fähigkeit einer De-novo-Knochenbildung spricht. Gegenüber Knochenaufbaumaterialien auf Kalziumkarbonat-Basis sind bei Algipore zudem sowohl eine signifikant höhere Kno-

chenneubildung, als auch eine gleichzeitig höhere Umbaurate erkennbar[9]. Durch Beigabe venösen Blutes zu Algipore kann die Vaskularisation innerhalb des Augmentats signifikant gesteigert werden[27].

Infolge seiner großen, porösen Oberfläche werden seine Resorption[7,28] und die Neovaskularisation[29] beschleunigt. In mehreren klinischen Studien konnte die gute Resorptionsfähigkeit von Algipore bereits sechs Monate nach Augmentation des Sinus maxillaris bestätigt werden[2,6,7]. Eine vollständige Resorption von Algipore und sein Umbau in natürlichen Knochen wurde in einem Zeitraum von 15 bis 18 Monaten beobachtet und ebenfalls auf die große Oberfläche des Materials zurückgeführt[4].

Gleichzeitig konnte – trotz der hohen Resorptionsfähigkeit von Algipore – eine gute Volumenstabilität des Augmentats beobachtet werden, die sechs Monate nach Augmentation mit einem Volumenverlust von nur ca. 10,83 bis 14,0 Prozent angegeben wurde[2,8]. Auch in Bezug auf den röntgenologisch nachweisbaren Erhalt krestalen Knochens, konnten bei Verwendung von Algipore gute Ergebnisse erzielt werden[8].

Infolge seiner großen Oberfläche und seiner Bindungsaffinität gegenüber Plasmaproteinen eignet sich Algipore als Träger für biologisch aktive und osteoinduktiv wirkende Substanzen, wie beispielsweise Transforming Growth Faktoren (TGF-beta 1)[30] dem rekombinanten humanen Bone Morphogenetic Protein (rh-BMP)[31] oder mesenchymaler Stammzellen[32].

In einer aktuellen Untersuchung wurden Langzeitergebnisse von Sinusbodenaugmentationen präsentiert, die mit einer besonderen Schichttechnik mittels Algipore und autologem Knochen durchgeführt wurden[5]. Nach Elevation der Schneider´schen Membran wurde auf den Kieferhöhlenboden eine Schicht autologen Knochens appliziert und anschließend eine weitere Lage des phykogenen Ersatzmaterials aufgeschichtet. Die Implantattherapie erfolgte nach Einheilung des Augmentats. Zum Zeitpunkt der Implantation bereits drei bis vier Monate nach Augmentation war ein äußerst geringer mittlerer Volumenverlust im Bereich des Augmentats von 1,8 mm zu beobachten. Zehn Jahre nach Implantatversorgung waren keine weiteren Volumenverluste eingetreten. Die Implantatüberlebensrate war mit 99,5 Prozent hoch und vergleichbar mit der von Implantaten, die in nicht augmentierten Bereichen inseriert worden waren.

In einer retrospektiven Langzeituntersuchung mit 208 Sinusbodenaugmentationen im stark atrophierten Oberkiefer von 118 Patienten und anschließender konventioneller Implantatversorgung wurde über einen Beobachtungszeitraum von 14 Jahren ebenfalls eine hohe Implantatüberlebensrate von 95,6 Prozent beobachtet[2]. 15 Monate nach Augmentation wurde in einer weiteren klinischen Untersuchung eine röntgenologisch messbare hohe Knochendichte im augmentierten Bereich ermittelt, die natürlicher humaner Spongiosa glich[33].

Im direkten klinischen und röntgenologischen Vergleich mit anderen Knochenaufbaumaterialien schneidet Algipore vergleichbar gut ab. So konnte in mehreren kontrollierten klinischen Untersuchungen kein signifikanter Unterschied klinischer oder radiologischer Parameter zwischen Algipore und anderen Knochenaufbaumaterialien wie gefriergetrocknetem allogenen Spenderknochen[10] bzw. autologem Knochen und Aufbaumaterialien auf Kalziumkarbonatbasis[34] ermittelt werden. Ein aktueller systematischer Review zu tierexperimentellen Studien, die eine Behandlung kritischer Knochendefekte mittels verschiedener Hydroxylapatitpräparate xenogener und synthetischer Herkunft zum Forschungsgegenstand hatte, ergab eine gute Wirksamkeit aller Materialen unabhängig vom jeweiligen Präparat[35].

Der Einsatz von Algipore zur periimplantären Defektauffüllung führte zu stabilen Verhältnissen unabhängig davon, ob der augmentierte Bereich mit einer resorbierbaren Membran abgedeckt wurde oder nicht[16,17,36].

In der Parodontitistherapie konnte in einer klinischen Humanstudie mit Algipore eine signifikante Reduktion der Sondierungstiefe und ein Zugewinn klinischen Attachments beobachtet werden[22].

Zusammenfassend lässt sich anhand der Erfahrungen zahlreicher Anwender und den Erkenntnissen aus der verfügbaren Literatur feststellen, dass sich Algipore in den 30 Jahren seines klinischen Einsatzes in vielen Bereichen der Zahnheilkunde bewährt hat. Für seinen klinischen Einsatz sprechen vor allen Dingen die hohe Biokompatibilität sowie ein gutes Resorptionsverhalten bei einer gleichzeitig vorhandenen sehr guten Volumenstabilität.

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Professor Doris Moser, DI Dr. Else Spassova-Tzekova

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Abstracts

Die Kategorisierung der Studien in der vorliegenden Auswahl der Zitate und dazugehöriger Abstracts entspricht in weiten Teilen der Einteilung nach den SIGN-Kriterien *(Harbour R, Miller J: A new system for grading recommendations in evidence based guidelines. BMJ (2001) 323: 334-336)*, welche die Studien nach der Studienqualität bzw. ihrer Übertragbarkeit der wissenschaftlichen Erkenntnisse auf die Allgemeinheit einteilt.

Die Bereiche **Narrative Reviews** und **Technische Berichte** gehören zur Sekundärforschung. Sie geben die Ansicht von Autoren wieder, die sie sich auf Grundlage der für sie verfügbaren Literatur und Erkenntnisse verschafft haben. Sie wurden nicht auf Grundlage einer systematischen Recherche erstellt und enthalten in den meisten Fällen keine kritische Würdigung oder Analytik der Fragestellung. Sie entsprechen einer „Expertenmeinung" und repräsentieren die unterste Evidenzstufe.

Die Bereiche **In vitro-Studien** und **Tierexperimentelle Studien** gehören zur Primär- bzw. Grundlagenforschung. Dort enthalten sind Material- und biologische Zellstudien sowie tierexperimentelle Untersuchungen, die nur bedingt auf den Menschen übertragbar sind, aber dennoch zu Erkenntnissen führen, die eventuell später in klinischen Humanstudien überprüft werden können.

Die **klinische Forschung am Menschen** wird in Fallstudien, Fallserien, Kohortenstudien, kontrollierten klinischen Studien und randomisiert kontrollierten klinischen Studien (RCT) repräsentiert.
Fallstudien, geben dabei Erkenntnisse wieder, die die Autoren an einem Patienten gemacht haben.
Die Studien mit der höchsten Evidenz sind die **randomisiert kontrollierten klinischen Studien (RCT)**. Diese haben in der Regel die geringsten Risiken für eine Verzerrung der Studienergebnisse durch systematische Fehler, da die Zuteilung der Patienten in die Therapiegruppen nach dem Zufallsprinzip erfolgt und ein sogenannter „Selektions-Bias" dadurch ausgeschlossen wird.

Die höchste Evidenz haben **systematische Übersichtsarbeiten und Metaanalysen**, die sich analytisch mit einer klinischen Fragestellung befassen und dazu eine systematische Literaturrecherche in verschiedenen Datenbanken heranziehen. Die Literatur wird dann bezüglich ihrer Qualität unter anderem nach den oben genannten Kriterien beurteilt (Studientyp und Risk of Bias) und in die Analyse einbezogen oder nicht.

1. Technischer Bericht

Spassova E, Gintenreiter S, Halwax E, Moser D, Schopper C, Ewers R.
Chemistry, ultrastructure and porosity of monophasic and biphasic bone forming materials derived from marine algae.
Materialwissenschaft und Werkstofftechnik. 2007; 38 (12): 1027-1034.

The research on bioceramics during the last decades has proved that the bioactivity of inorganic bone grafts depends fundamentally on an optimal combination of chemistry and structural porosity. This study presents a comparison of a resorbable monophasic hydroxyapatite (HA) and several newly developed resorbable biphasic hydroxyapatite – ß-tricalcium phosphate (HA/TCP) composites both derived from naturally grown red marine algae with respect to the phase composition, microstructure and porosity. The highly porous three dimensional mineral scaffold of the native alga is maintained in the final products all investigated materials and possesses a pronounced interconnecting microporous structure. There are generally high values of specific porosity calculated for all tested materials: 1.07 cm^3/g for pure phycogenic HA and between 0.65 cm^3/g and 1.04 cm^3/g for phycogenic biphasic HA/TCP composites with various HA/TCP ratios. The ultrastructure of the phycogenic HA/TCP composites changes significantly with the building and the increase of the ß-TCP phase due to the bigger polyedric ß-TCP crystals compared to the finer polycrystalline HA. Despite these structural changes the interconnected porous scaffold is kept throughout the production process. In all investigated materials the porosity is mainly based on pores with pore sizes between 1 and 10 µm in diameter, which is given by the structure of the natural alga. The specific chemistry combined with the structural porosity is decisive for the high in-vivo bioactivity of the studied materials.

2. Fallserie

Ewers R.
Maxilla sinus grafting with marine algae derived bone forming material: a clinical report of long-term results.
J Oral Maxillofac Surg. 2005 Dec; 63 (12): 1712-1723.

PURPOSE:
Autogenous bone grafting continues to be considered the gold standard for sinus grafting. For the past 15 years the author has used an alternative graft material and followed-up the input/output statistic of implants to evaluate if this material results similar to the autogenous bone graft. Histomorphometric evaluations of graft materials show how much new bone is formed and if the graft material is resorbed.

MATERIALS AND METHODS:
In our study we used a marine derived carbonated red algae that is chemically converted into hydroxyapatite (HA). This material is distributed worldwide as the Communauté Européenne approved material AlgiPore (Dentsply Friadent, Mannheim, Germany), as the US Food and Drug Administration approved material C GRAFT (The Clinician Preference LLC, Golden, CO), and the Russian approved material AlgOss (Unexim Co, Moscow, Russia). A total of 209 sinus grafts were performed on 118 patients who presented with a severely resorbed maxillary alveolar process with 1 to 5 mm (mean, 3.6 mm) of remaining bone. The available bone was comparable to Class D bone as described by Simion et al. After 6 months implants were placed and 6 months later the implants were loaded.

RESULTS:
From September 5, 1990, to September 1, 2004, the author performed 209 sinus grafts on 118 patients. The longest observation period of loaded implants in this study is 156 months (13 years). Implant loss was 27 out of 614 loaded implants (4.4%), showing a survival rate of 95.6%. Smokers and women over 50 are included. Although AlgiPore/C GRAFT/AlgOss (ACA) undergoes a resorption process, we found only 14% volume loss after 6.4 months compared with 49.5% after 6 months when autogenous bone was used.

CONCLUSION:
This retrospective study of over 14 years shows once again that the sinus lift procedure with grafting of the sinus floor and subsequent implant placement is a proven method. This 14-year longitudinal study shows that the marine derived HA material ACA in a mixture with approximately 10% autogenous collector bone and blood or platelet rich plasma is able to enhance enough new bone in 6 months to allow implant osseointegration after 6 more months with a high implant survival rate.

3. Narrativer Review

Demers C, Hamdy CR, Corsi K, Chellat F, Tabrizian M, Yahia L.
Natural coral exoskeleton as a bone graft substitute: a review.
Biomed Mater Eng. 2002; 12 (1): 15-35.

Natural coral graft substitutes are derived from the exoskeleton of marine madreporic corals. Researchers first started evaluating corals as potential bone graft substitutes in the early 1970s in animals and in 1979 in humans. The structure of the commonly used coral, Porites, is similar to that of cancellous bone and its initial mechanical properties resemble those of bone. The exoskeleton of these high content calcium carbonate scaffolds has since been shown to be biocompatible, osteoconductive, and biodegradable at variable rates depending on the exoskeleton porosity, the implantation site and the species. Although not osteoinductive or osteogenic, coral grafts act as an adequate carrier for growth factors and allow cell attachment, growth, spreading and differentiation. When applied appropriately and when selected to match the resorption rate with the bone formation rate of the implantation site, natural coral exoskeletons have been found to be impressive bone graft substitutes. The purpose of this article is to review and summarize all the pertinent work that has been published on natural coral as a bone graft including in vitro, animal and clinical human studies. Preliminary report of our own experiments as well as our recommendations on the use of coral are also included.

4. Fallserie

Ewers R, Schumann B, Watzinger F.
Eight year experience with algipore® on 300 patients.
International Journal of Oral and Maxillofacial Surgery. 1997; 26: 34.

Since 1989 we have used Algipore produced out of marine calcifying alges, as an osteoconductive bone substitute material. We use this material for augmentation in periodontal infrabony pockets as well as for filling defects or augmentation methods combined with or without monocortical autogenous bone grafts from the iliac crest or chin. The advantage of this material is the interconnective microporosity with a very high specific surface, half as much as natural bone. Due to this surface the material gets resorbed between 15 and 18 months and is completely replaced by natural bone. Since the material is highly porose it is not stable enough for primary loading. Therefore, this material can only be used in cavities and unloaded areas or in connection with osteosynthesis materials. The data collected show minor complications such as fistulas and wound dehiscencies. The presentation includes histological studies of human biopsies taken after 3, 6, 9, 12, 18 and 24 months showing how the material gets surrounded by natural bone and finally gets resorbed and completely replaced by natural bone

5. Fallserie

Khoury F, Keller P, Keeve PL.
Stability of Grafted Implant Placement Sites After Sinus Floor Elevation Using a Layering Technique: 10-Year Clinical and Radiographic Results.
Int J Oral Maxillofac Implants. 2017 Sep/Oct; 32 (5): 1086-1096.

PURPOSE:
To evaluate long-term survival rates and radiographic stability of sinus floor elevations carried out using a two-layer grafting technique.

MATERIALS AND METHODS:
Records were analyzed for patients treated with sinus floor elevations using a modified technique. Phycogenic hydroxyapatite (Algipore, Dentsply Sirona Implants) and autogenous bone particles harvested from intraoral sites were grafted in two distinct layers after elevation of the sinus mucosae. In this approach, the basal part of the sinus floor is grafted with autogenous bone, while the cranial part is grafted with the phycogenic hydroxyapatite. In some cases, implants were placed simultaneously, such that the entire surface of each implant was covered by autogenous bone particles. A titanium membrane was used to close the sinus window, and the implants were loaded 3 months later. In two-stage approaches, the implants were inserted 3 to 4 months after the grafting and loaded after 3 additional months. Panoramic radiographs were taken after the grafting procedure, after implant insertion, after the prosthetic restoration, and then annually for 10 years. These radiographs were used to measure the height between the implant shoulders and the top of the graft.

RESULTS:
Of the 214 sinus floor elevations performed on 129 patients using the bilayering technique, 198 procedures in 118 patients were included in the study (136 one-stage and 62 two-stage). Membrane perforations during surgery occurred in 17.9% of the procedures and were sutured and sealed with fibrin glue. A total of 487 implants were placed in the grafted areas. No severe postoperative complications occurred, but three implants were lost throughout the 10-year follow-up period. A small decrease of vertical height was observed between the grafting surgery and the stage-two surgery (mean: 1.8 mm). After that, no bone height was lost over the 10 years.

CONCLUSION:
The layer grafting technique in combination with sinus floor elevation resulted in radiographically stable vertical bone height for 10 years. This technique enabled early placement and loading of implants in the grafted areas. The survival rate obtained with this procedure is similar to that expected for implants placed in nongrafted areas.

6. Fallserie

Scarano A, Degidi M, Perrotti V, Piattelli A, Iezzi G.

Sinus augmentation with phycogene hydroxyapatite: histological and histomorphometrical results after 6 months in humans. A case series.

Oral Maxillofac Surg. 2012 Mar; 16 (1): 41-45.

BACKGROUND:
Phycogene hydroxyapatite is a biological hydroxyapatite derived from calcifying maritime algae, and is prepared by hydrothermal conversion by pyrolitical segmentation of the calcium carbonate of native algae into fluorhydroxyapatite. The aim of the present study was a histological and histomorphometrical evaluation, in humans, of specimens retrieved from sinuses augmented with phycogene hydroxyapatite, after a healing period of 6 months.

CASE SERIES:
Ten healthy patients with noncontributory past medical history (four women and six men, all nonsmokers, mean age 59 years, range 54-65 years) were included in this study. All patients were candidates for augmentation in the posterior maxilla in order to receive fixed restorations. The maxillary sinuses were filled with phycogene hydroxyapatite (Algipore(R), Dentsply Friadent, Mannheim, Germany). Twenty-three implants (XiVE(R), Dentsply Friadent, Mannheim, Germany) were placed in the augmented sinuses after a healing period of about 6 months. The bone cores were retrieved and were processed for histology. Most particles of phycogene hydroxyapatite were surrounded by a mineralized tissue, and the biomaterial particles had served as an osteoconductive scaffold. Most particles were bridged by newly formed bone characterized by the presence of large osteocytic lacunae, also around the phycogene hydroxyapatite particles, which appeared to be partially resorbed and substituted by new bone. No inflammatory cells or foreign body reaction cells were present around the biomaterial. No gaps were present at the bone-particle interface, and the bone was always in close contact with the particles. Histomorphometry showed that the percentage of newly formed bone was 35.2 +/- 3.6%, marrow spaces 35.6 +/- 2.3%, and residual grafted material 37.1 +/- 3.8%.

DISCUSSION:
In conclusion, the present results support the literature findings that phycogene hydroxyapatite can be used, successfully, for sinus augmentation procedures.

7. Fallserie

Schopper C, Moser D, Sabbas A, Lagogiannis G, Spassova E, König F, Donath K, Ewers R.

The fluorohydroxyapatite (FHA) FRIOS Algipore is a suitable biomaterial for the reconstruction of severely atrophic human maxillae.

Clin Oral Implants Res. 2003 Dec; 14 (6): 743-749.

Grafting of the maxillary sinus is an established treatment modality to provide sufficient bone for the fixation of dental implants. We stated the hypothesis that the porous fluorohydroxyapatitic (FHA) biomaterial FRIOS Algipore could be used as a suitable biomaterial for sinus grafting in severely atrophic maxillae. To investigate the accuracy of our hypothesis, 69 trephine specimens from 26 patients who received maxillary sinus grafting with FRIOS Algipore were retrieved during the installation of dental implants. The specimens were processed undecalcified and subjected to histomorphological and histomorphometrical examination. After a mean healing time of 7 months, 23.0% (+/-8.3) new bone had formed around the implanted particles. Bone formation was also evident within the pores of the particles. Statistical analysis indicated that bone formation originated from the sinus floor. Particles provided scaffolding for the promotion of newly formed bone towards apical sinus portions. Mineral dissolution from the walls of the pores was observed prior to and during bone apposition. Thereafter, portions of the particles were resorbed during bone remodeling and replaced by newly formed bone. The present investigation shows that the biomaterial FRIOS Algipore is a suitable biomaterial for sinus grafting of severely atrophic maxillae.

8. In vitro-Studie

Wanschitz F, Nell A, Patruta S, Wagner A, Ewers R.
Influence of three currently used bone replacing materials on the in vitro proliferation of human peripheral blood mononuclear cells.
Clin Oral Implants Res. 2005; 16 (5): 570-574.

OBJECTIVES:
A cell culture system for biocompatibility testing of bone grafting materials is described. We investigated the in vitro viability and proliferative response of peripheral blood mononuclear cells (PBMC) from 10 healthy donors in the presence of three materials currently used for bone grafting: Algipore, Bio-Oss and Bone Source, for immunologic biocompatibility testing.

MATERIAL AND METHODS:
PBMC isolated from venous blood from 10 healthy donors were incubated for 4 days with each bone replacing material, in the presence and absence of interleukin-2 (IL-2). After 4 days, H3-thymidine was added for 18 h and the incorporated radioactivity was measured with a beta-plate counter.

RESULTS:
Basal PBMC counts were 152.9+/-66.2 counts per minute (c.p.m.) (mean+/-SD), in the presence of 0.4 U IL-2/well 206.5+/-83 c.p.m. were measured. With Algipore and Bio-Oss, which are deproteinized bone replacing materials, the proliferation rate of PBMC with IL-2 was not significantly modified: for Algipore 151+/-51 c.p.m./+IL-2 188.8+/-62 c.p.m., for Bio-Oss 144.5+/-64.9 c.p.m./+IL-2 176.3+/-71.23 c.p.m. For Bone Source 164.2+/-80.4/+IL-2 188.3+/-81 c.p.m. were measured.

CONCLUSION:
This in vitro experiment indicates, that the investigated bone replacing materials are not acting as specific antigens/haptens and are not generating increased proliferative responses of human PBMC from healthy donors. Even with IL-2, that induces proliferation of T lymphocytes, which encountered their specific antigen, the proliferation rate of PBMC from healthy donors was not increased after incubation with this bone grafting materials.

9. Kontrollierte klinische Studie

Iezzi G, Degidi M, Piattelli A, et al.
Comparative histological results of different biomaterials used in sinus augmentation procedures: a human study at 6 months.
Clin Oral Implants Res. 2012; 23 (12): 1369-1376.

OBJECTIVES:
Various grafts or combination of graft materials have been used in sinus floor augmentations, and human histological reports on their performance are available, although limited in number. Histological analysis of the regenerated tissues will provide useful information regarding the nature and amount of newly formed bone. Aim of the present study was a histological and histomorphometric evaluation, in humans, of specimens retrieved from sinuses augmented with phycogene hydroxyapatite, biphasic calcium phosphate ceramics, calcium carbonate, porcine bone and anorganic bovine bone, after a healing period of 6 months.

MATERIALS AND METHODS:
A total of 15 patients, undergoing 30 sinus augmentation procedures with five different biomaterials, participated in this study. A total of 82 titanium dental implants were inserted in the augmented sinuses after a healing period of 6 months. A total of 60 bone cores, 2 for each augmented sinus, 12 for every biomaterial, were retrieved and all were stored immediately in 10% buffered formalin and processed to obtain thin ground sections.

RESULTS:
In all biomaterials, many grafted particles were lined and, sometimes, bridged by newly formed bone. Some biomaterials particles appeared to be partially resorbed and substituted by newly formed bone. Histomorphometry showed that, in all biomaterials, newly formed bone and residual grafted material particles represented about 30%.

CONCLUSIONS:
Longer term histological and histomorphometric studies will be necessary to understand better the resorption times of all these biomaterials. The high interconnecting microporosity allowed, in all the present biomaterials, the ingrowth of newly formed bone and vessels in the pores of the partially resorbed particles. In conclusion, within the limitations of the present study, the data provided support the fact that all these biomaterials can be used, successfully, in sinus augmentation procedures.

10. Kontrollierte klinische Studie

Moeintaghavi A, Ghanbari H, Sargolzaie N, Foroozanfar A, Dadpoor Y.
Comparative Study of Algipore and Decalcified Freeze-Dried Bone Allograft In Open Maxillary Sinus Elevation Using Piezoelectric Surgery.
Journal of Periodontology & Implant Dentistry. 2013; 5 (1): 1-6.

BACKGROUND AND AIM:
Vertical and horizontal bone resorption of the alveolar ridge are common in edentulous jaws. In the distal area of the maxilla, an adequate bone volume is often lacking because of the proximity of the sinus cavities to crestal bone. Sinus floor augmentation is an established way of increasing the height and volume of bone in the posterior region of the maxilla, which increase the stability of dental implants. For this purpose various materials, including auto grafts, allografts, alloplasts, and xenografts have been used. The aim of this study was the radiographic and clinical comparison of Algipore with decalcified freeze-dried bone allograft (DFDBA) inthe open maxillary sinus lift technique using piezoelectric instruments.

MATERIALS AND METHODS:
A total of 20 sinus grafts were performed in 10 patients who had a severely resorbed bilateral maxillary alveolar process with a residual bone thickness of between 1 and 5 mm (mean, 3.6 mm). The operation involved an osteotomy performed on the lateral maxillary wall using piezoelectric instruments, elevation of the sinus membrane, and placement of either of the two bone graft materials in each randomly-selected side. Preoperative and postoperative standard radiographs taken at nine months of follow-up were used to compare the outcome of bone height after the maxillary sinus lifting procedure. Changes in radiographic density after sinus grafting were evaluated using densitometry.

RESULTS:
The radiographic density was 76.3% on the Algipore side and 72.4% on the DFDBA side (P >0.05). The mean height of newly formed bone in the augmented area was 12.3 mm on the Algipore side and 10.7 mm on the DFDBA side (P >0.05).

CONCLUSION:
After nine months there were no considerable clinical or radiological differences in outcome between Algipore and DFDBA and both of them were recognized as acceptable materials for sinus lift procedures.

11. Metaanalyse

Klijn RJ, Meijer GJ, Bronkhorst EM, Jansen JA.
A meta-analysis of histomorphometric results and graft healing time of various biomaterials compared to autologous bone used as sinus floor augmentation material in humans.
Tissue Eng Part B Rev. 2010; 16 (5): 493-507.

BACKGROUND:
To date, no studies have been published in which histomorphometric data from a large group of patients comparing various biomaterials for sinus floor augmentation procedures were evaluated.

MATERIALS AND METHODS:
A meta-analysis of the English literature from January 1993 till April 2009 was carried out. Out of 147 titles, according to our criteria, 64 articles were selected for analysis describing the use of autologous bone and their alternatives, such as allogenic, xenogenic, and alloplastic materials.

RESULTS:
On the basis of autologous bone grafting, a reference value for total bone volume (TBV) of 63% was found. Particulation of the bone graft resulted in a general reduction of -18% in TBV. Delayed implant placement reduced the TBV with -7%. Overall TBV was 8% or 6% higher if a biopsy was, respectively, taken before 4.5 months or after 9.0 months after initial sinus augmentation surgery. Allogenic, xenogenic, alloplastic, or combinations of graft materials all resulted in a significant lower amount of TBV compared to autologous bone grafting ranging from -7% to -26%. Inventorying the effect of "biopsy time" for autologous bone, the TBV was significantly higher before 4.5 and after 9.0 months of healing time compared to period in between. Surprisingly, no significant differences in TBV with respect to "biopsy time" for bone substitutes were found.

CONCLUSIONS:
On the basis of the aspect of TBV autologous bone still has to be considered to be the gold standard in sinus augmentation surgery. However, the consequence of the TBV for implant survival is still unraveled yet.

12. Metaanalyse

Handschel J, Simonowska M, Naujoks C, Depprich RA, Ommerborn MA, Meyer U, et al.
A histomorphometric meta-analysis of sinus elevation with various grafting materials. Head Face Med. 2009; 5: 12.

UNLABELLED:
Several grafting materials have been used in sinus augmentation procedures including autogenous bone, demineralized freeze-dried bone (DFDBA), hydroxyapatite, beta-tricalcium phosphate (beta-TCP), anorganic deproteinized bovine bone and combination of these and others. Up to now a subject of controversy in maxillofacial surgery and dentistry is, what is the most appropriate graft material for sinus floor augmentation.

PURPOSE:
The aim of this study is to provide a body of evidence-based data regarding grafting materials in external sinus floor elevation concerning the fate of the augmented material at the histomorphological level, through a meta-analysis of the available literature.

MATERIALS AND METHODS:
The literature searches were performed using the National Library of Medicine. The search covered all English and German literature from 1995 until 2006. For analyzing the amount of bone the parameter "Total Bone Volume" (TBV) was assessed. TBV is determined as the percentage of the section consisting of bone tissue. RESULTS: In a relatively early phase after implantation the autogenous bone shows the highest TBV values. Interestingly, the different TBV levels approximate during the time. After 9 months no statistically significant differences can be detected between the various grafting materials.

CONCLUSION:
From a clinical point of view, the use of autogenous bone is advantageous if a prosthetic rehabilitation (with functional loading) is expected within 9 months. In other cases the use of anorganic deproteinized bovine bone in combination with autogenous bone seems to be preferable. Donor side morbidity is ignored in this conclusion.

13. Systematischer Review, Metaanalyse

Danesh-Sani SA, Engebretson SP, Janal MN.
Histomorphometric results of different grafting materials and effect of healing time on bone maturation after sinus floor augmentation: a systematic review and meta-analysis.
J Periodontal Res. 2017 Jun; 52 (3): 301-312.

The aim of this systematic review was to evaluate histomorphometric variables, the amount of new bone (NB), residual graft (RG) particles and soft tissue (ST), related to various grafting materials and assess the effect of graft healing time on different histomorphometric outcomes. Studies that were published before October 2015 were electronically and manually searched in three databases. We included human studies that reported the amount of NB, RG and ST in the biopsies taken from the grafted sinuses. Based on the applied grafting materials, extracted data were categorized into different groups. Furthermore, extracted data were classified into three groups based on healing time: (i) ≤ 4.5 mo; (ii) 4.5-9 mo; and (iii) ≥ 9-13.5 mo. The search provided 791 titles. Full text analysis was performed for 258 articles resulting in 136 studies that met the inclusion criteria. Autogenous bone (AB) resulted in the highest amount of NB and lowest amount of RG compared to other grafting materials. Based on this meta-analysis, a significant difference was noticed in the amount of NB formation in grafts with a healing time of > 4.5 mo when compared to the grafts with less healing time. However, when comparing biopsies taken at 4.5-9 mo of healing (average = 6.22 mo) to the ones taken at ≥ 9-13.5 mo (average = 10.36 mo), no significant difference was noticed in the amount of NB formation of various grafts except allografts that resulted in a significantly higher percentage of NB at 9.5 mo of healing. Based on histomorphometric analysis, AB results in the highest amount of NB formation in comparison to the other grafting materials. Bone substitute materials (allografts, alloplastic materials and xenografts) seem to be good alternatives to autogenous bone and can be considered as grafting materials to avoid disadvantages related to AB, including morbidity rate, limited availability and high volumetric change. Combining AB with alloplastic materials and xenografts brings no significant advantages regarding NB formation.

14. RCT

Garlini G, Redemagni M, Canciani E, Dellavia C.
Maxillary sinus floor augmentation with vegetal hydroxyapatite "versus" demineralized bovine bone: A randomized clinical study with a split-mouth design. Journal of Dental Implants. July 1, 2014; 4 (2): 118-125.

PURPOSE:
The objective of this paper was to compare histologically and histomorphometrically a hydroxyapatite originated by algae (Algipore) versus demineralized bovine bone (Bio-Oss Geistlich Pharma, Wolhusen, Switzerland) utilised as bone substitutes in maxillary sinus floor elevation with a split-mouth design.

MATERIALS AND METHODS:
Five healthy patients underwent a bilateral maxillary sinus floor elevation procedure under local anesthesia. In each case, residual posterior maxillary bone height was between 2 mm and 5 mm. The original bone was augmented with a split-mouth design with 100% Algipore on the test side and 100% Bio-Oss on the contralateral control side. After a healing period of 6-8 months during the re-opening surgery biopsies were retrieved and Xive Implants (Dentsply Implants, Mannheim, Germany) were placed.

RESULTS:
At microscopic level both Bio-Oss and Algipore blocks resulted well osseointegrated, without inflammatory infiltrate, with an high level of mineralization, without gap between the bone and biomaterial interfaces that resulted indistinguishable. A close contact between the two faces was observed without the presence of slits. Histomorphometrical analysis showed that, on average, the percentage of medullary space was higher for the Bio-Oss compared with Algipore (38.61% ±8.90% vs. 29.23% ±7.89%). In contrast, the mean value of residual particles of biomaterials was higher in Algipore than in Bio-Oss specimens (42.86% ±18.61% vs. 22.30% ±6.40% respectively).

CONCLUSIONS:
The data confirmed that sinus lift carried out with Algipore performed in a similar way of that carried out with Bio-Oss and that this material is safe, predictable and without invasiveness.

15. Klinisch kontrollierte Studie

Ghanbari H, Moeintaghavi A, Sargolzaei N, Foroozanfar A, Dadpour Y.
Comparative study of algipore and decalcified freeze-dried bone allograft in open maxillary sinus elevation using piezoelectric surgery. Journal of Periodontology & Implant Dentistry. 2013; 5 (1): 1-6.

BACKGROUND AND AIM:
Vertical and horizontal bone resorption of the alveolar ridge are common in edentulous jaws. In the distal area of the maxilla, an adequate bone volume is often lacking because of the proximity of the sinus cavities to crestal bone. Sinus floor augmentation is an established way of increasing the height and volume of bone in the posterior region of the maxilla, which increase the stability of dental implants. For this purpose various materials, including auto grafts, allografts, alloplasts, and xenografts have been used. The aim of this study was the radiographic and clinical comparison of Algipore with decalcified freeze-dried bone allograft (DFDBA) inthe open maxillary sinus lift technique using piezoelectric instruments.

MATERIALS AND METHODS:
A total of 20 sinus grafts were performed in 10 patients who had a severely resorbed bilateral maxillary alveolar process with a residual bone thickness of between 1 and 5 mm (mean, 3.6 mm). The operation involved an osteotomy performed on the lateral maxillary wall using piezoelectric instruments, elevation of the sinus membrane, and placement of either of the two bone graft materials in each randomly-selected side. Preoperative and postoperative standard radiographs taken at nine months of follow-up were used to compare the outcome of bone height after the maxillary sinus lifting procedure. Changes in radiographic density after sinus grafting were evaluated using densitometry.

RESULTS:
The radiographic density was 76.3% on the Algipore side and 72.4% on the DFDBA side ($P > 0.05$). The mean height of newly formed bone in the augmented area was 12.3 mm on the Algipore side and 10.7 mm on the DFDBA side ($P > 0.05$).

CONCLUSION:
After nine months there were no considerable clinical or radiological differences in outcome between Algipore and DFDBA and both of them were recognized as acceptable materials for sinus lift procedures.

16. Klinisch kontrollierte Studie

Roos-Jansåker AM, Lindahl C, Persson GR, Renvert S.

Long-term stability of surgical bone regenerative procedures of peri-implantitis lesions in a prospective case-control study over 3 years.
J Clin Periodontol. 2011 Jun; 38 (6): 590-597.

OBJECTIVES:
To evaluate the extent of bone fill over 3 years following the surgical treatment of peri-implantitis with bone grafting with or without a membrane.

MATERIAL AND METHODS:
In a non-submerged wound-healing mode, 15 subjects with 27 implants were treated with a bone substitute (Algipore(®)) alone and 17 subjects with 29 implants were treated with the bone substitute and a resorbable membrane (Osseoquest(®)). Implants with radiographic bone loss ≥1.8 mm following the first year in function and with bleeding and/or pus on probing were included. Following surgery, subjects were given systemic antibiotics (10 days) and rinsed with chlorhexidine. After initial healing, the subjects were enrolled in a strict maintenance programme.

RESULTS:
Statistical analysis failed to demonstrate changes in bone fill between 1 and 3 years both between and within procedure groups. The mean defect fill at 3 years was 1.3 ± (SD) 1.3 mm if treated with the bone substitute alone and 1.6 ± (SD) 1.2 mm if treated with an adjunct resorbable membrane, (p=0.40). The plaque index decreased from approximately 40-10%, remaining stable during the following 2 years.

CONCLUSION:
Defect fill using a bone substitute with or without a membrane technique in the treatment of peri-implantitis can be maintained over 3 years.

17. Klinisch kontrollierte Studie

Roos-Jansåker AM, Persson GR, Lindahl C, Renvert S.

Surgical treatment of peri-implantitis using a bone substitute with or without a resorbable membrane: a 5-year follow-up.
J Clin Periodontol. 2014 Nov; 41 (11): 1108-1114.

AIM:
To compare two regenerative surgical treatments for peri-implantitis over 5 years.

MATERIAL AND METHODS:
Twenty-five individuals with peri-implantitis remained at study endpoint. They were treated with a bone substitute and a resorbable membrane (13 individuals with 23 implants) [Group 1], or with bone substitute alone (12 individuals with 22 implants) [Group 2]. All study individuals were kept on a strict maintenance programme every third month.

RESULTS:
Five-year follow-up demonstrated clinical and radiographic improvements in both groups. No implants were lost due to progression of peri-implantitis. Probing depths were reduced by 3.0 ± 2.4 mm in Group 1, and 3.3 ± 2.09 mm in Group 2 (NS). In both groups, radiographic evidence of bone gain was significant ($p < 0.001$). At year 5, the average defect fill was 1.3 mm (SD ± 1.4 mm) in Group 1 and 1.1 mm (SD ± 1.2 mm) in Group 2 (mean diff; 0.4 95% CI -0.3, 1.2, $p = 0.24$). Bleeding on probing decreased in both groups. Baseline and year 5 plaque scores did not differ between groups and was reduced from 50% to 15%.

CONCLUSION:
Both procedures resulted in stable conditions. Additional use of a membrane does not improve the outcome.

18. Metaanalyse

Faggion CM, Jr., Chambrone L, Listl S, Tu YK.
Network meta-analysis for evaluating interventions in implant dentistry: the case of peri-implantitis treatment.
Clin Implant Dent Relat Res. 2013; 15 (4): 576-588.

BACKGROUND ANDAIM:
Evidence from head-to-head comparison trials on peri-implantitis treatment is limited, and it is therefore impossible to conduct a direct meta-analysis. We propose an alternative statistical method, network meta-analysis, for evidence synthesis, which enables to compare the results of multiple treatments.

METHODS:
We searched, in triplicate, for randomized controlled trials (RCTs) and controlled trials in the PubMed, Cochrane Central Register of Controlled Trials, Clinicaltrials.gov, and Latin American and Caribbean Health Sciences Literature databases up to and including August 2010. We also conducted a manual search of the reference lists regarding published systematic reviews and searched for gray literature in OpenSIGLE. We assessed changes in clinical attachment level (CAL) and pocket probing depth (PPD) after nonsurgical and surgical treatments of peri-implantitis. The risk of bias of selected studies was determined by the use of specific criteria, and it was performed in triplicate and independently. We used multilevel mixed modeling to perform the network meta-analysis and Markov Chain Monte Carlo simulation to obtain confidence intervals for the fixed and random effects. RESULTS: Eleven studies were included in the review. All RCTs are at unclear or high risk of bias. Surgical therapy in conjunction with bone grafts and non-resorbable membranes achieved 3.52 mm greater PPD reduction than nonsurgical therapy alone, 95% high-probability density (HPD) intervals: -0.19, 6.81. Surgical treatment in conjunction with bone grafts and resorbable membranes achieved 2.80 mm greater CAL gain than nonsurgical therapy alone, 95% HPD intervals: -0.18, 5.59.

CONCLUSION:
Surgical procedures in peri-implantitis treatment achieve more PPD reduction and CAL gain than nonsurgical approaches. Nevertheless, these results should be interpreted with caution because of the limited number of studies included and their low methodological quality. Network meta-analysis is a useful statistical methodology for evidence synthesis and to summarize the strength and limitation in the current evidence.

19. Fallserie

Enislidis G, Fock N, Millesi-Schobel G, et al.
Analysis of complications following alveolar distraction osteogenesis and implant placement in the partially edentulous mandible.
Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology. 2005; 100 (1): 25-30.

OBJECTIVE:
The purpose of this retrospective study was to evaluate complications before, during, and after vertical alveolar distraction osteogenesis and to assess the survival rate of dental implants placed in distracted bone.
Study design
In a consecutive series, 37 patients with 45 alveolar ridge deficiencies of the partially edentulous mandible were treated with 14 intraosseous and 31 subperiosteal distraction devices. Seventy-two dental implants could be placed at the time of distractor removal and 21 implants at a second stage.

RESULTS:
Complications associated with the distraction procedure affected 75.7% of patients. The majority of complications were of minor nature with the exception of fractures of basal bone (n=3), fracture of transport segment (n=1), breakage of distractor (n=1), and severe mechanical problems (n=3). Eleven secondary grafting procedures were necessary to allow the placement of dental implants. Implant survival was 95.7% (mean postloading follow-up: 35.7 months).

CONCLUSION:
Vertical alveolar distraction osteogenesis is not an uncomplicated procedure; however, long-term survival of dental implants inserted into distracted areas is satisfactory.

20. Systematischer Review

De Risi V, Clementini M, Vittorini G, Mannocci A, De Sanctis M.
Alveolar ridge preservation techniques: a systematic review and meta-analysis of histological and histomorphometrical data. Clin Oral Implants Res. 2015; 26 (1): 50-68.

AIM:
The aim of this article was to systematically review histological and histomorphometrical data from literature that provide information regarding the effect of alveolar ridge preservation procedures on healing after tooth extraction in humans.

MATERIALS AND METHODS:
The MEDLINE-PubMed and the Cochrane CENTRAL databases were searched up to September 2012; 38 papers were selected from 646 founded. A meta-analysis was performed regarding the variations in the mean percentage of Bone, Connective Tissue and Residual Graft Material between three different types of Procedures.

RESULTS:
The highest value regarding bone percentages is produced at 3 months by Procedures with Allografts (54.4%), while the lowest is obtained, at 5 months, by those using Xenografts (23.6%). Referring to connective tissue, the highest and lowest values are shown at 7 months, with Allografts (67%) and Alloplasts (27.1%), respectively. Regarding residual graft material, the lowest rates are displayed by Procedures with Allografts (12.4-21.11%), while those using Xenografts and Alloplasts showed the best results at 7 months (37.14 and 37.23%). No statistical difference was found.

CONCLUSIONS:
With the limitations due to the features of the selected papers, no major histological and histomorphometrical differences arose among different procedures or when compared to spontaneous healing. Thus, it might be argued that in preserved sites it is unnecessary to wait over 3 to 4 months prior to implant insertion.

21. Kontrollierte klinische Studie

Thompson DM, Rohrer MD, Prasad HS.
Comparison of bone grafting materials in human extraction sockets: clinical, histologic, and histomorphometric evaluations. Implant Dent. 2006; 15 (1): 89-96.

PURPOSE:
Although there are a number of bone replacement graft materials that are currently available for clinical use, there are few studies that directly compare efficacy among graft treatments before implant placement. The purpose of this report was to compare 3 bone replacement graft materials (PepGen P-15 228 FLOW [DENTSPLY Friadent CeraMed, Lakewood, CO], Puros [Zimmer Dental, Carlsbad, CA], and C-Graft 228 [Clinician's Preference, Golden, CO]) for bone formation by clinical, histologic, and histomorphometric evaluation.

MATERIALS AND METHODS:
In this prospective, intraoral pilot study, 13 maxillary sockets in 2 patients (both smokers) were grafted immediately after tooth extraction with C-Graft 228, Puros, or PepGen P-15 228 FLOW (containing additional PepGen P-15 228 particles; FLOW PUTTY). After 4 months, bone cores were retrieved and analyzed histologically.

RESULTS:
PepGen P-15 228 FLOW PUTTY produced a significantly ($P < 0.01$) higher amount of vital bone than C-Graft 228 or Puros. The amount of vital bone for FLOW PUTTY was 12-fold higher than for C-Graft 228 and 4-fold higher than Puros. Of 7 FLOW PUTTY treated sites, 7 showed >14% vital bone versus 0 of 3 C-Graft 228 and 0 of 3 Puros treated sites. FLOW PUTTY treated sites showed new vital bone between particles of residual graft. C-Graft 228 treated sites showed residual particles in a background of connective tissue with very little bone. Puros treated sites showed nonvital bone particles in a background of connective tissue, with some new vital bone forming around the nonvital bone.

CONCLUSION:
PepGen P-15 228 FLOW PUTTY produced significantly greater vital bone as compared to Puros and C-Graft 228 after 4 months. A larger clinical study is required to confirm these results.

22. Kontrollierte klinische Studie

Bembi NN, Bembi S, Mago J, Baweja GK, Baweja PS.
Comparative Evaluation of Bioactive Synthetic NovaBone Putty and Calcified Algae-derived Porous Hydroxyapatite Bone Grafts for the Treatment of Intrabony Defects.
Int J Clin Pediatr Dent. 2016 Oct-Dec; 9 (4): 285-290.

INTRODUCTION:
To compare and evaluate clinically and radiographically the bone regeneration and the amount of bone fill in intrabony component of periodontal osseous defects through the osteoconductive and osteostimulative effect of bioactive synthetic NovaBone Putty - CMF and osteoconductive effect of calcified algae-derived porous hydroxyapatite Frios® Algipore® bone grafts.

MATERIALS AND METHODS:
Twenty-two sites in 11 patients, within the age range of 25 to 60 years, showing intrabony defects were selected according to split mouth design and divided into group I (Frios® Algipore®) and group II (NovaBone Putty - CMF). All the selected sites were assessed with the clinical and radiographic parameters like plaque index, gingival index (full mouth and site specific), sulcus bleeding index, probing pocket depth, clinical attachment level, gingival recession, and radiographic bone fill. All the clinical and radiographic parameter values obtained at different intervals (baseline, 3, and 6 months) were subjected to statistical analysis.

RESULTS:
A statistically significant reduction in pocket depth of 2.55 ± 0.52 mm (group I), 2.64 ± 0.67 mm (group II) and gain in clinical attachment level of 7.55 ± 1.44 mm (group I), 7.55 ± 2.38 mm (group II) were recorded at the end of the study. A slight increase in gingival recession was observed. The mean percentage change in amount of radiographic bone fill of group II (71.34%) was more than group I (61.93%).

CONCLUSION:
Both NovaBone Putty - CMF and Frios® Algipore® improve healing outcomes and lead to a reduction of probing depth, a resolution of osseous defects, and a gain in clinical attachment, but radiographic observation found better results with NovaBone Putty.

23. Fallserie

Wanschitz F, Figl M, Wagner A, Rolf E.
Measurement of volume changes after sinus floor augmentation with a phycogenic hydroxyapatite.
Int J Oral Maxillofac Implants. 2006 May-Jun; 21 (3): 433-438.

PURPOSE:
The purpose of this study was the determination of time-dependent volumetric changes of particulate sinus inlay grafts. A mixture of phycogenic hydroxyapatite (Algipore/C-Graft) and autologous bone collected from the surgical access area was used as the grafting material.

MATERIALS AND METHODS:
Thirty-three sinus floor augmentations using phycogenic hydroxyapatite combined with autologous bone collected at the augmentation site and venous blood were performed on 18 patients aged 57.4 +/- 12.5 years (mean +/- SD) with severe atrophy of the posterior maxilla. Graft volume was measured 1 to 14 days postoperatively and before the placement of dental implants 6.1 +/- 2.1 months later (mean +/- SD; range, 4 to 11 months) to evaluate the amount of time-dependent resorption of the implanted material on computerized tomographic (CT) images of the augmented region. The images were put into Digital Imaging and Communications in Medicine (DICOM) format and evaluated using the software library Analyze. The implanted bone replacement material was plotted manually on each CT slice, and the volume of the implanted material was calculated.

RESULTS:
The average volume loss of the bone replacement material during the observation period was 13.9% +/- 1.9% (mean +/- SEM). All sinus floor augmentations healed without complications except for delayed membrane exposure in 2 cases.

DISCUSSION:
The results indicate that the graft material, a mixture of Algipore, bone chips from the access area, and venous blood, exhibited a small volume loss over a period of approximately 6 months, thus providing predictable height for second-stage implant surgery.

CONCLUSION:
Further investigations are needed to evaluate long-term stability and implant success.

24. In vitro-Studie

Turhani D, Cvikl B, Watzinger E, Weissenböck M, Yerit K, Thurnher D, Lauer G, Ewers R.

In vitro growth and differentiation of osteoblast-like cells on hydroxyapatite ceramic granule calcified from red algae.
J Oral Maxillofac Surg. 2005 Jun; 63 (6): 793-799.

PURPOSE:
The purpose of this study was to analyze the interaction between osteoblast-like cells isolated from mandibular bone and hydroxyapatite ceramic bone substitute obtained from calcified red algae to assess the growth and differentiation of adherent cells on this biomaterial.

MATERIALS AND METHODS:
The macroporous ceramic material C GRAFT/Algipore (The Clinician's Preference LLC, Golden, CO) is composed of 100% hydroxyapatite and possesses specific mechanical and physiochemical properties. Osteoblast-like cells were seeded on 200 mg of biomaterial and cultured for 6 and 21 days under osteogenic differentiation conditions. Specific alkaline phosphatase activity, DNA, and protein content of the proliferating cells were analyzed. The morphology of the cells in contact with the biomaterial was examined by scanning electron microscopy. The osteoblastic phenotype of the cells was confirmed by analysis of the expression of bone-specific genes (osteocalcin, osteopontin and collagen type I) by semi-quantitative reverse transcriptase polymerase chain reaction.

RESULTS:
The DNA and protein content increased over the culture period. Scanning electron microscopy showed cells spreading on the surface of the biomaterials, covering the macropores, and colonizing the depth of the particles. The analysis of the expression patterns of bone-related genes confirmed the osteoblastic phenotype of the cultured cells.

CONCLUSION:
The results of this study showed that hydroxyapatite ceramic bone substitute obtained from calcified red algae support the proliferation and differentiation of human osteoblast-like cells on its surface in vitro and might be suitable for use as scaffolds in tissue engineering strategies in vivo.

25. In vitro-Studie

Turhani D, Watzinger E, Weissenböck M, Cvikl B, Thurnher D, Wittwer G, Yerit K, Ewers R.

Analysis of cell-seeded 3-dimensional bone constructs manufactured in vitro with hydroxyapatite granules obtained from red algae.
J Oral Maxillofac Surg. 2005 May; 63 (5): 673-681.

PURPOSE:
Bone tissue engineering is a promising approach for the treatment of defective or lost bone in the maxillofacial region. Biocompatible and biodegradable scaffolds seeded with living cells are used to create functional tissue for load-bearing bone reconstruction. The aim of this study was to manufacture cell-seeded 3-dimensional bone constructs based on hydroxyapatite ceramic granule calcified from red algae and mesenchymal cambial-layer precursor cells. The ability of these cells to grow on hydroxyapatite ceramic was quantitatively investigated to evaluate 3-dimensional bone constructs for their potential use in bone tissue engineering.

MATERIALS AND METHODS:
Mesenchymal cambial-layer precursor cells were isolated from mandibular periosteum biopsy samples of 3 patients. To manufacture 72 bone constructs, these cells and hydroxyapatite ceramic granules (C GRAFT/Algipore; Clinician's Preference LLC, Golden, CO) were cultivated under osteogenic differentiation conditions in a rotating wall vessel system. After 6 and 21 days, histologic examination and scanning electron microscopy were performed. The absolute DNA content, protein synthesis, and alkaline phosphatase activity were also quantified. The osteoblastic phenotype of the constructs was confirmed by the expression of bone-specific genes (osteocalcin, osteonectin, osteopontin, and core binding factor alpha1) using semiquantitative reverse transcription-polymerase chain reaction and Western blot analysis.

RESULTS:
Cells within the constructs showed good viability, which was evidenced by an increase in DNA content over the culture period. The decrease in alkaline phosphatase-specific activity could be an indicator of the maturation of cells and the induction of mineralization. The osteoblastic phenotype of the constructs was demonstrated on protein and at the RNA level over the entire culture period.

CONCLUSION:
We observed a positive effect of hydroxyapatite ceramic granules on mesenchymal cambial-layer precursor cell behavior in cell-seeded 3-dimensional bone constructs, indicating the potential applicability of C GRAFT/Algipore composites in bone tissue engineering.

26. Narrativer Review

Tettamanti L, Bassi MA, Trapella G, Candotto V, Tagliabue A.
Applications of biomaterials for bone augmentation of jaws: clinical outcomes and in vitro studies.
ORAL & implantology. 2017; 10 (1): 37-44.

Partially or totally edentulous jaws frequently undergoes from moderate to severe bone atrophy with problems of prosthetic rehabilitation. The inability to make a prosthetic rehabilitation on implants may led to the use of a partial or total removable denture with difficulties in eating and speech, ulcerations of the oral mucosa and loss of facial vertical dimension. These problems may be solved performing bone augmentation procedures. Bone grafts and distraction osteogenesis brought implant dentistry from an experimental practice to become a consolidate dental procedure. Bone grafts, in particular, are currently a valuable treatment modality for the prosthetic rehabilitation. Numerous biomaterials have been developed for the rehabilitation of partially or totally edentulous jaws with fixed or removable dentures. The aim of this paper is to describe biomaterials for bone augmentation. Biomaterials are gradually resorbed by the osteoclasts and replaced by new bone formed through osteoblastic activity. Many biomaterials have been studied, but the most common are as follows: Allogro®, Algipore®, Osteobiol®, Peptide-15, Engipore®, Medpore®, Osteoplant®, Calcium sulfate, Perioglass®, Bio-Oss®, Calcium phosphate.

27. Tierexperimentelle Studie

Barbeck M, Najman S, Stojanović S, Mitić Ž, Živković JM, Choukroun J, Kovačević P, Sader R, Kirkpatrick CJ, Ghanaati S.
Addition of blood to a phycogenic bone substitute leads to increased in vivo vascularization.
Biomed Mater. 2015 Sep 11; 10 (5): 055007.

The present study aimed to analyze the effects of the addition of blood to the phycogenic bone substitute Algipore(®) on the severity of in vivo tissue reaction. Initially, Fourier-transform infrared spectroscopy (FTIR) of the bone substitute was conducted to analyze its chemical composition. The subcutaneous implantation model in Balb/c mice was then applied for up to 30 d to analyze the tissue reactions on the basis of specialized histochemical, immunohistochemical, and histomorphometrical methods. The data of the FTIR analysis showed that the phycogenic bone substitute material is mainly composed of hydroxyapatite with some carbonate content. The in vivo analyses revealed that the addition of blood to Algipore(®) had a major impact on both angiogenesis and vessel maturation. The higher vascularization seemed to be based on significantly higher numbers of multinucleated TRAP-positive cells. However, mostly macrophages and a relatively low number of multinucleated giant cells were involved in the tissue reaction to Algipore(®). The presented data show that the addition of blood to a bone substitute impacts the tissue reaction to it. In particular, the immune response and the vascularization were influenced, and these are believed to have a major impact on the regenerative potential of the process of bone tissue regeneration.

28. Tierexperimentelle Studie

Scarano A, Perrotti V, Degidi M, Piattelli A, Iezzi G.
Bone regeneration with algae-derived hydroxyapatite: a pilot histologic and histomorphometric study in rabbit tibia defects.
Int J Oral Maxillofac Implants. 2012 Mar-Apr; 27 (2): 336-340.

PURPOSE:
Algipore is a biologic hydroxyapatite derived from calcifying maritime algae. The present study evaluated this material histologically and histomorphometrically after implantation in rabbit tibia defects for 4 weeks.

MATERIALS AND METHODS:
Six New Zealand rabbits were used in this study. In each rabbit tibia, two 7-mm defects were prepared. Control defects were left empty, and test defects were filled with Algipore. Twenty-four specimens (12 test and 12 control) were retrieved and processed for histology.

RESULTS:
In control sites, newly formed trabecular bone with large marrow spaces was plentiful in the most peripheral areas of the defects but sparse elsewhere. In contrast, in test sites, a large quantity of newly formed bone around the biomaterial particles was detected in the central medullary portion of the defect. In addition, in several areas, the biomaterial particles were bridged by newly formed bone. The percentage of contact between newly formed bone and biomaterial particles was 71.2% ± 9.8%. Inside the central portion of the biomaterial particles, it was possible to see newly formed bone (about 35.3% ± 4.8% in each particle). In test sites, newly formed bone represented 31.1% ± 1.9% of the material, with residual biomaterial particles occupying 33.4% ± 2.8% and marrow spaces another 34.7% ± 4.3%. In the control sites, the values were 30.2% ± 2.2% for newly formed bone and 68.7% ± 4.1% for marrow spaces. A statistically significant difference was found in the percentage of marrow space between the two groups, but no significant difference was observed in the percentage of newly formed bone.

CONCLUSIONS:
The present rabbit study confirmed the high osteoconductivity and resorbability of this biomaterial.

29. Narrativer Review

Iezzi G, Piattelli A, Giuliani A, et al.
Molecular, Cellular and Pharmaceutical Aspects of Bone Grafting Materials and Membranes During Maxillary Sinus-lift Procedures. Part 2: Detailed Characteristics of the Materials.
Curr Pharm Biotechnol. 2017; 18 (1): 33-44.

Various grafts or combination of bone substitute materials have been used in sinus lift procedures. Currently, ongoing developments in several disciplines, from molecular biology and chemistry to computer science and engineering, have contributed to the understanding of biological processes leading to bone healing after the use of bone substitute materials (BSBs) and therefore of the behavior of BSBs. The understanding of the properties of each graft enables individual treatment concepts and therefore allows shift from a simple replacement material to the modern concept of an individually created composite biomaterial. Indeed, the choice of the best BSB still remains crucial for success in maxillary sinus augmentation procedures. The present article provides an overview of most of the materials currently available for sinus lift, with a specific focus on their histological, molecular, cellular and pharmaceutical aspects.

30. In vitro-Studie

Gille J, Dorn B, Kekow J, Bruns J, Behrens P.
Bone substitutes as carriers for transforming growth factor-beta(1) (TGF-beta(1)).
Int Orthop. 2002; 26 (4): 203-206.

We studied the suitability of three different hydroxyapatite materials (Endobone, Bio-Oss and Algipore) as carriers for the bone growth promoting factor TGF-beta(1). The hydroxyapatite materials either were incubated for 24 h or directly loaded with hrTGF-beta(1) (Diagnostic Products Corporation, DPC) at a concentration of 10 ng hrTGF-beta(1)/mg. For the release experiment the hydroxyapatite materials covered with hrTGF-beta(1) were either suspended in pure phosphate buffered saline (PBS) or human serum albumin (HSA). The concentration of hrTGF-beta(1) was measured every 6 h the first day and then daily at the 2nd, 7th, 14th and 28th day. With Bio-Oss and Endobone the release of growth factor in HSA showed a two-phase kinetics. TGF-beta(1) reached a maximum concentration within the first 24 h and decreased almost linearly until day 28. With Algipore the concentration of growth factor reached a maximum after 12 h and showed a rapid decline until day 2. From day 2 the TGF-beta(1) concentrations remained low. Significantly, more TGF-beta(1) was released into HSA than into PBS. Our study suggests that the hydroxyapatite materials are suitable as TGF-beta(1) carriers.

31. Tierexperimentelle Studie

Schopper C, Moser D, Spassova E, Goriwoda W, Lagogiannis G, Hoering B, Ewers R, Redl H.
Bone regeneration using a naturally grown HA/TCP carrier loaded with rh BMP-2 is independent of barrier-membrane effects. J Biomed Mater Res A. 2008 Jun 15; 85 (4): 954-963.

The present study investigated whether bone regeneration and biomaterial replacement would be improved by loading of biogenous biphasic biomaterial scaffolds (HA/TCP ratio 30/70) with rhBMP-2, and whether the placement of three barrier membranes differing in structure and porosity (prototyped SLA Ti specimens, GORE RESOLUT Adapt specimens, and titanized TiMESH light specimens) would have a synergistic effect. A rabbit calvarial model was used for the implantation studies. Histological specimens were obtained after 12 weeks and evaluated quantitatively for differences between the various material combinations. Loading of the biomaterials with rhBMP-2 significantly enhanced the amount of regenerated bone and caused a pronounced biomaterial replacement. While BMP-induced bone had formed uniformly over the surgical defects, bone regeneration in the absence of BMP depends on bone promotion from the margins of the defects toward the center. No positive effect on bone regeneration was seen for any of the placed barrier membranes. While the present study had shown that rhBMP-2 loading significantly increases bone regeneration using the investigated biomaterial, barrier-membrane placement may be useful in predetermining the final shape of the regenerative site but provides no additional beneficial impact on the amount and quality of the bone regeneration induced by rhBMP-2.

32. Tierexperimentelle Studie

Pieri F, Lucarelli E, Corinaldesi G, et al.
Effect of mesenchymal stem cells and platelet-rich plasma on the healing of standardized bone defects in the alveolar ridge: a comparative histomorphometric study in minipigs. J Oral Maxillofac Surg. Feb 2009;67(2):265-272.

PURPOSE:
The purpose of this study was to test the effect of the combination of mesenchymal stem cells (MSCs) and platelet-rich plasma (PRP) incorporated into a fluorohydroxyapatite (FHA) scaffold on bone regeneration in cylindrical defects in the edentulous mandibular ridge of minipigs.

MATERIALS AND METHODS:
Two mandibular premolar teeth were extracted bilaterally in 8 adult minipigs. After 2 months, 4 standardized defects of 3.5 mm diameter and 8 mm depth were created in each root site. The defects were randomly grafted with autogenous mandibular bone, FHA alone, PRP-FHA, or MSCs-PRP-FHA. A resorbable collagen membrane was placed over the defect area and the flaps were sutured. The animals were sacrificed 3 months later and biopsy samples were taken from the defect sites for histologic and histomorphometric assessment.

RESULTS:
There was no evidence of inflammation or adverse tissue reaction with either treatment. MSCs-PRP-FHA-treated sites showed new vital bone between residual grafting particles. PRP-FHA- and FHA-treated sites showed residual particles in a background of marrow soft tissue with a moderate quantity of newly formed bone. Autogenous bone (46.97%) and MSCs-PRP-FHA (45.28%) produced a significantly higher amount of vital bone than PRP-FHA (37.95%), or FHA alone (36.03%). Further, the MSCs-PRP-FHA-treated defects showed a significantly higher percentage of contact between graft particles and newly formed bone compared with PRP-FHA and FHA group (59.23% vs 48.37% and 46.43%, respectively).

CONCLUSIONS:
Our results suggest that, in this animal model, the addition of MSCs to PRP-FHA enhances bone formation after 3 months.

33. Fallserie

Simunek A, Cierny M, Kopecka D, Kohout A, Bukac J, Vahalova D.
The sinus lift with phycogenic bone substitute. A histomorphometric study.
Clin Oral Implants Res. 2005 Jun; 16 (3): 342-348.

OBJECTIVES:
The aim of this histomorphometric prospective study was to ascertain the efficacy of phycogenic bone substitute in an augmented sinus. The process of graft healing, bone remodeling, and biomaterial replacement was examined.

MATERIAL AND METHODS:
The phycogenic material (fluorohydroxyapatite) made from calcium-encrusted sea algae was used for the sinus lifts. Twenty-four procedures were carried out (one-stage and two-stage equally) and 45 titanium stepped-screw implants were placed. The patients were followed for 12-23 months. In intervals of 6, 9, 12, or 15 months after the sinus lift, 24 graft specimens were taken with a trephine bur. These specimens were examined histomorphometrically.

RESULTS:
The grafting material was gradually resorbed and replaced by newly formed bone. Between the sixth and 15th month after the sinus lift, the percentage of newly formed bone grew linearly (from 15.5+/-9.6% to 40.8+/-15.3%) and the percentage of bone substitute decreased linearly (from 34.5+/-8.6% to 13+/-9.6%). After 15 months, the density of trabeculae in grafted bone corresponded to cancellous bone of good quality; however, the bone substitute was not completely resorbed during this period. No significant difference between the quality of the newly formed bone in the cases of the one- and two-stage sinus lifts was found.

CONCLUSION:
Sinus lift carried out with phycogenic bone substitute was shown to be an effective method with limited invasiveness and a high survival rate of implants (97.8%).

34. Fallserie

Velich N, Németh Z, Tóth C, Szabó G.
Long-term results with different bone substitutes used for sinus floor elevation.
J Craniofac Surg. 2004 Jan; 15 (1): 38-41.

One of the surgical procedures preceding implantation is elevation of the base of the maxillary sinus. Numerous bone substituting materials (grafts) may be used for this purpose, including autogenous bone, heterografts, xenogenous bone, and synthetic materials alone or in combination or mixed with growth factors and bone morphogenetic protein (BMP) preparations. A study of the frequencies of the failures (graft material resorption or implant loss) after sinus elevations with various graft materials or their combinations was conducted. In the 5-year period from 1996 through 2001, a follow-up investigation of 810 maxillary sinus augmentations was performed, in which the sinus elevations involved the use of autogenous bone, a calcium carbonate-coated polymer, hydroxylapatite of algal origin, calcium carbonate gel produced from coral or beta-tricalcium phosphate alone, autogenous bone mixed with these bone substitutes, or a combination of beta-tricalcium phosphate and platelet-rich plasma. The incidences of graft resorption and implant loss after the augmentations with various bone substitutes were recorded. Total resorption (disappearance) of the bone substitute material was observed in 2.7% of the cases. An essential difference was not experienced between the various bone substitutes from this aspect, with the exception of the gel-state calcium carbonate, where 40% of the grafts were resorbed. In total, 5.46% of the implants were lost; the differences between the various materials were not significant.

35. Systematischer Review, Metaanalyse

Oliveira HL, Da Rosa WLO, Cuevas-Suárez CE, Carreño NLV, da Silva AF, Guim TN, et al.
Histological Evaluation of Bone Repair with Hydroxyapatite: A Systematic Review. Calcified Tissue International. 2017; 101 (4): 341-354.

The aim of this study was to evaluate the morphological bone response in animal experiments by applying hydroxyapatite grafts in critical and non-critical size bone defects. Current report followed the guidelines established by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses. Animal experiments were selected by assessing repair of bone defects with hydroxyapatite as bone graft and with blood clot only as control. Eight articles were identified in specialized literature and included in the meta-analysis. Statistical analysis was carried out with a random-effect model ($p = 0.05$). Subgroup analyses were further performed to investigate bone repair in critical and non-critical bone defects. Comprehensive analysis of bone repair outcome showed a statistically significant difference between hydroxyapatite and blood clot control ($p < 0.05$). Subgroup analyses showed statistically significant difference for critical bone defects ($p < 0.05$). No statistically significant difference was reported in non-critical bone defects ($p > 0.05$). Although animal studies revealed a high risk of bias and results should be interpreted with caution, the literature suggests that non-critical bone defects may heal spontaneously and without the need of a bone graft. Conversely, when critical-size defects are present, the use of hydroxyapatite bone graft improves the bone repair process.

36. Klinisch kontrollierte Studie

Roos-Jansåker AM, Renvert H, Lindahl C, Renvert S.
Surgical treatment of peri-implantitis using a bone substitute with or without a resorbable membrane: a prospective cohort study. J Clin Periodontol. 2007 Jul; 34 (7): 625-632.

OBJECTIVES:
The aim of this prospective cohort study was to compare two regenerative surgical treatment modalities for peri-implantitis.

MATERIAL AND METHODS:
Thirty-six patients having a minimum of one osseointegrated implant, with a progressive loss of bone amounting to > or =3 threads (1.8 mm) following the first year of healing, combined with bleeding and/or pus on probing, were involved in this study. The patients were assigned to two different treatment strategies. After surgical exposure of the defect, granulomatous tissue was removed and the infected implant surface was treated using 3% hydrogen peroxide. The bone defects were filled with a bone substitute (Algipore). In 17 patients (Group 1), a resorbable membrane (Osseoquest) was placed over the grafted defect before suturing. In 19 patients (Group 2), the graft was used alone.

RESULTS:
One-year follow-up demonstrated clinical and radiographic improvements. Probing depths were reduced by 2.9 mm in Group 1 and by 3.4 mm in Group 2. Defect fill amounted to 1.5 and 1.4 mm, respectively. There was no significant difference between the groups.

CONCLUSION:
It is possible to treat peri-implant defects with a bone substitute, with or without a resorbable membran.