●臨床研究

# Osseointegration of hydroxyapatite-coated implants with new bone in one stage sinus floor elevation without bone substitute - A long-term animal experiment using canine frontal sinuses -

Cintia Yuki Fukuoka [1], Takao Watanabe [2], Masato Matsuo [2],
Akira Iimura [2] and Toshimitsu Okudera [2]

## Abstract

The aim of this study is to histologically compare the osseointegration of 2 types of hydroxyapatite (HA)-coated implants, a JHA implant (Kyocera Medical Ltd, Japan) and a KHA implant (Zimmer Ltd, USA), with the new bone forming in the space under the lifted membrane (SULM) in a long-term animal experiment of one stage sinus floor elevation (SFE), without bone substitutes and mechanical loading, using canine frontal sinuses. Sixteen implants, 8 JHA and 8 KHA were placed in 4 postmenopausal beagles for 3 and 6 months. Histological observations and histomorphometric measurements were carried out with light-microscopy using hematoxylin and eosin stained undecalcified specimens. Statistical significant differences were evaluated by one-way ANOVA.

The new bone formation was observed on a large area of the sinus wall and the implant surface in the SULM at 3 and 6 months in both groups. Bone implant contact rate with new bone in the SULM was 88.8±10.5% at 3 months and 77.0±7.9% at 6 months in JHA group, and 85.3±7.6 and 87.3±17.9% in KHA group, respectively. There was no statistical significant difference between the groups. It was concluded that both types of HA-coated implants have similar properties to promote a superior osseointegration with the new bone forming in the SULM. Furthermore, the new bone which osseointegrated with the HA-coated implants has a possibility to remain for a long time.

(J Bio-Integ 5 : 109 - 117, 2015.)

## 1. Introduction

SFE was first performed for implant patients by Tatum in 1975 and first published by Boyne in 1980[1]. The outline of the original SFE by Tatum[2] was one stage, lateral approach, titanium implants and autolougus bone grafting. In his SFE procedures, a part of the placed implant was positioned in the space under the lifted membrane (SULM). When the surgery finished, the SULM was filled by blood cells, but new bone was not yet present around the placed implant. Our animal experiments of one stage SFE without bone

1) Department of Biomaterials and Oral Biology, Sao Paulo University School of Dentistry, Brazil
2) Department of Oral Science, Graduate School of Dentistry, Kanagawa Dental University, Kanagawa, Japan

Accepted for publication 27 August 2015

substitutes[3] showed granulation tissue within a few days and then new bone started to form from the sinus wall a week later. At 2 months, the new bone volume reached its peak and then decreased. At 6 months, a small amount of new bone remained on the sinus wall. However, osseointegration between the machine-polished titanium implants and the new bone in the SULM was not seen[4]. The bone implant contact rate (BIC) was 2% at most. Generally, HA-coated implants show superior osseointegration with pre-existing bone than the machine-polished titanium implants[5]. The aim of this study is to histologically compare the osseointegration of 2 types of HA-coated implants, a JHA implant (Kyocera Medical Ltd, Japan) and a KHA implant (Zimmer Ltd, USA), with the newly formed bone in the SULM in an experiment of one stage SFE without bone substitutes, using canine frontal sinuses.

## 2. Materials and Methods

### 1) Animals:

After a period of acclimation 4 postmenopausal female beagle dogs with a mean body weight of 10.3kg were used. They were raised at a laboratory providing animal management facilities and fed standard commercial dry canine food and water *ad libitum*.

### 2) Implants:

A total of 16 HA-coated implants, 8 JHA implants, 55% crystalline HA-coated tapered implants (POIEX, FINATITE, 3.7mm in width and 8mm in length, Kyocera Medical Ltd, Japan) and 8 KHA implants, 95% crystalline HA-coated implants (SPLINE TWIST, 3.75mm in width and 8 mm in length, Zimmer Ltd, USA) were placed in canine frontal sinuses (Fig.1).

### 3) Surgical procedures:

An intramuscular injection of medetomidine hydrochloride (Domitor, Orion Pharma Inc., Finland) 0.05ml/kg followed by intravenous anesthesia with 0.5ml/kg of sodium pentobarbital (Nembutal, Dainippon Medical Pharma Ltd, Japan) were performed. Local anesthesia was applied to the skin with 2% lidocaine hydrochloride (Xylocain, Fujisawa Medical Corp, Japan).

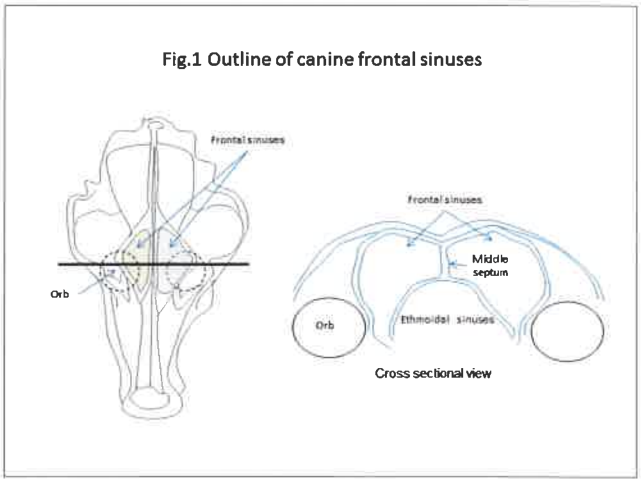


Fig. 1: Outline of canine head and frontal sinuses

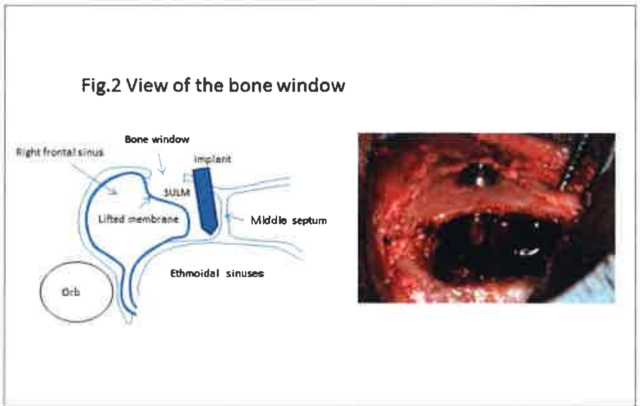


Fig. 2: View of the bone window, Blood clot and two third of the placed implant can be seen at the space under the lifted sinus membrane.

In the first surgery, a 3mm full thickness incision was made in the middle of the canine forehead. The skin flap with the periosteum was detached and a rectangular area of 10mm in length and 8 mm in width was made with a 2mm groove (Fig.2). The rectangular bone fragment was removed to open a bone window in the forehead. The sinus membrane was detached from the sinus wall and lifted through the bone window. Two holes, 3.5 ㎜ in diameter and 1.1㎜ in depth, were made beside the bone window using a cylindrical rotary instrument. The rotation was stopped right after bone penetration. One JHA and one KHA implant were placed along the middle septum with 5Ncm of torque, in each sinus. Finally, the skin flap with the periosteum was repositioned and sutured.

Three months later, the second implant surgery was performed in the right frontal sinus, following the same procedure. Three months after the second surgery, sacrifice was carried out by intramuscular injection using medetomidine hydrochloride (Domitor, Orion Pharma Inc, Finland) 0.05ml/kg and an overdose infusion of sodium pentobarbital.

### 4) Periotest analysis:

Soon after sacrifice, the skin tissue with the periosteum was removed and then the platform of the placed implant was exposed. An adapter was set into the placed implant at the forehead. The mobility of implants was checked using Periotest (Medizintechnik Gulden Ltd. Germany).

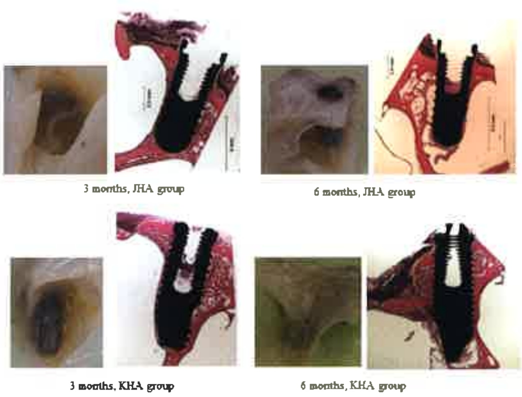


**Fig. 3:** V Visual and histological findings of, hematoxylin and eosin staining on Undecalcified section

### 5) Histological observation (Fig.3):

Bone blocks, 8㎜×25㎜×25㎜ in size, from the left and right frontal sinuses were removed and placed in 10% neutral formalin for two weeks. Afterwards, they were cut in two at the center site, dehydrated and embedded in VLC resin (MG3000, Exact Ltd, Germany). The blocks comprising the implants were cut into small 2 ㎜×20㎜×20㎜ pieces. They were adhered to an acrylic plate (TECHNOVIT7200, Exact Ltd, Germany) and sliced using a cut machine (MG4000, Exact Ltd, Germany), so that the center of the implant appeared on the specimen's surface. Then hematoxylin and eosin staining was carried out. The histological observation was performed using an E800 light microscope (Japan Optical Co, Ltd, Japan).

### 6) Histomorphometric measurement:

At the sinus wall (pre-existing bone):

(1) Sinus wall thickness; SWTw(㎜)

(2) Bone implant contact rate with pre-existing bone in the sinus wall; BICw(%)

In the SULM:

(3) New bone height from sinus wall to the top of new bone surrounding the implant; NBHs(㎜)

(4) Rate of new bone surrounding the implant surface; RNBs(%)

(5) Bone implant contact rate with new bone; BICs(%)

### 7) Statistical Analysis:

Data groups were statistically compared using variance analysis, with multiple comparison of Tukey. The level of significance was set at $p<0.05$ and $P<0.01$. Group means and standard deviation were presented.

This experiment was approved and performed in strict accordance with the Animal Care Committee guidelines of Kanagawa Dental University (No.259).

## 3. Results

### 1) Visual findings of the placed implant in the SULM (Fig.3)

A small amount of the SULM remained on the sinus wall and on the placed implant surface at 3 and 6 months after surgery in both groups. The implant, which was covered by a thin layer of whitish soft tissue, protruded from the sinus wall. No blood clot was seen.

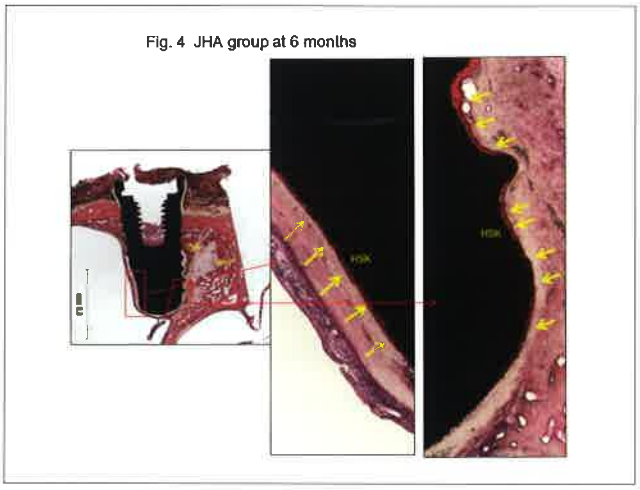


**Fig. 4**: JHA group at 6 months.
The arrows indicate a thin layer of remaining new bone (HSK) osseointegrated with the implant surface.

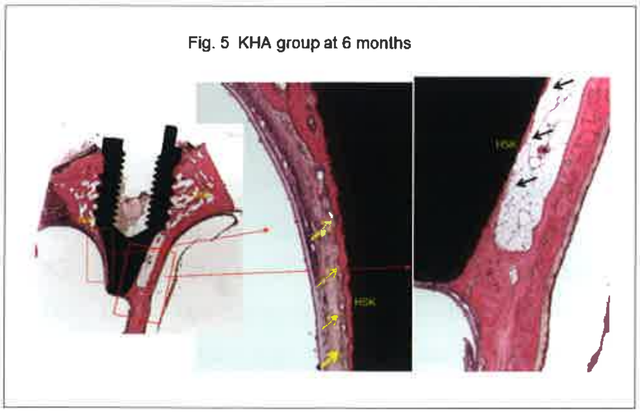


**Fig.5**: KHA group at 6 months
TSN at the implant base and NBW on the sinus wall were observed. The arrows indicate HSK osseointegrated with the implant surface. KHA group showed similar histological findings, at 3 and 6 months, to JHA group.

### 2) Histological findings, undecalcified specimens with hematoxylin and eosin staining (Fig.4, 5)

The SULM was composed of new bone and fibrous connective tissue remaining in the space between the placed implant and the sinus wall at 3 and 6 months in both groups. Under low magnification, tent-shaped new bone remaining around the base of the placed implant (TSN) and a small volume of new bone on the sinus wall at the site far from the placed implant (NBW) were observed at 3 and 6 months in both groups. They were not seen in the spaces center and under the lifted membrane. Most new bone observed in this study consisted of matured trabecular bone with lamellar structure and resorption pits. It showed static matured bone where development was already completed. Under high magnification, a thin layer of new bone (HSK), roughly 50～100$\mu$m thick was observed on the placed implant surface. HSK was also seen on the lumen side surface of the implant as well as on the wall side and continued to be visible 6months after surgery in both groups. There were no significant differences in the histological findings between the JHA and KHA groups.

### 3) Periotest analysis

Periotest analysis in JHA group revealed that the mean value increased from 1.5±0.7 at 3months to 3.6±2.1 at 6 months ($P<0.05$). The KHA group showed a value of 0.4±1.8 at 3 months and -1.0±1.1 at

**Table 1**：PERIOTEST analysis (Periotest value)

1) Sinus wall thickness: SWTw

(mm)

| Group | 3M | 6M |
|---|---|---|
| JHA | 1.1±0.2 | 1.2±0.2 |
| KHA | 1.1±0.2 | 1.2±0.3 |

(n=4)

6 months. KHA group, at 6 months, had statistically significant lower Periotest values in comparison to the JHA group ($P<0.01$). However, Periotest values in both groups were less than 10, indicating a good clinical osseointegration.

## 4) Histomorphometric measurement

(1) Sinus wall thickness (Table 1); SWTw(㎜)

SWTw in JHA group was 1.1±0.2㎜ at 3 months, and 1.2±0.2㎜ at 6 months. While in the KHA group, it was 1.1±0.2㎜ at 3 months and 1.2±0.3㎜ at 6 months. Both groups showed similar results and the average SWTw was 1.1㎜ in all groups. There were no statistical difference between them.

**Table 2** : Sinus wall thickness; SWTw (㎜)

2) Bone implant contact rate in sinus wall (pre-existing bone): BICw

(%)

| Group | 3M | 6M |
|---|---|---|
| JHA | 40.4±33.4 | 32.4±29.1 |
| KHA | 51.9±44.6 | 65.2±18.9 |

(n=4)

(2) Bone implant contact rate with pre-existing bone in the sinus wall (Table 2); BICw(%)

After 6 months, BICw ranged from 32.4±29.1% in JHA group to 65.2±18.9% in KHA group. There were no statistical difference between the groups.

**Table 3** : Bone implant contact rate with pre-existing bone in the sinus wall; BICw (%)

3) New bone height in SULM: NBHs

(㎜)

| Group | 3M | 6M |
|---|---|---|
| JHA | 5.8±2.9 | 8.8±2.7 |
| KHA | 5.8±2.2 | 6.3±2.1 |

(n=4)

(3) New bone height in the SULM (Table 3); NBHs(㎜)

NBHs ranged from 5.8±2.2㎜ at 3 months in KHA group to 8.8±2.7㎜ at 6 months in JHA group. There were no statistical NBHs differences between 3 and 6 months in both groups.

**Table 4** : New bone height in the SULM; NBHs (㎜)

4) Rate of new bone covering the implant surface in SULM: RNBs

(%)

| Group | 3M | | 6M |
|---|---|---|---|
| JHA | 70.6±21.4 | | 75.6±16.2 |
| KHA | 65.3±4.9 | P=0.028 | 78.6±11.3 |

(n=4)

(4) Rate of new bone surrounding the implant surface in the SULM (Table 4); RNBs(%)

RNBs increased from 65.3±4.9% at 3 months to 78.6±11.3% at 6 months in KHA group ($P<0.05$). There were no statistical RNBs differences between both groups.

**Table 5** : Rate of new bone surrounding the implant surface in the SULM; RNBs(%)

5) Bone implant contact rate with new bone in SULM: BICs

(%)

| Group | 3M | 6M |
|---|---|---|
| JHA | 88.8±10.5 | 77.0±7.9 |
| KHA | 85.3±7.6 | 87.3±17.0 |

(n=4)

(5) Bone implant contact rate with new bone in the SULM (Table 5); BICs(%)

The BICs in the JHA group was 88.8±10.5% at 3 months, and 77.0±7.9% after 6 months. The KHA group BICs at 3 and 6 months were 85.3±7.6 and 87.3±17.0%, respectively. Both groups showed higher BICs than BICw at 3 and 6 months. There were no statistical BIC differences between 3 and 6 months, in both groups.

## 4. Discussion

The canine frontal sinus membrane has a ciliated columnar epithelium which is histologically similar to the human maxillary sinus. The majority of implant patients are postmenopausal women, ranging from 50 to 60 years[6]. For this reason, postmenopausal dogs were used in this study. Canine frontal sinus wall has a thin cortical bone, ranging from 1.1 to 1.2㎜ in width (Table 1). Most areas of the placed implants were exposed inside the SULM (Fig.2). Various types of bone substitutes, like synthetic HA, $\beta$-TCP ($\beta$-tricalcium phosphate), sintered bovine bone granules with human growth factors, PRP and BMP have been reported to fill the SULM, to improve the new bone formation and to promote osteoconduction and osteoinduction[7-14]. In this study, no bone substitutes were used. The relationship between bone substitutes and osseointegration with the newly formed bone in the SULM should be investigated.

Concerning new bone formation in the SULM, in one stage SFE without grafting, Lai reported 2.26±0.92㎜ and 2.66±0.87㎜ at 3 and 9 months follow-up[15]. Thor showed 6.51㎜ using ITI-SLA after 1 year[16]. Chen observed 4.5㎜, ranging from 3 to 8㎜, in 47 Astra Tech implants after 2 years follow-up[17]. We found 4㎜ in height of new bone in a clinical case using a rough surface titanium implant 3 years later[18] and Nedir reported 3.0±1.4㎜ at the implant sites using ITI-SLA after 10 years[19]. This study showed sufficient NBHs, ranging from 5.8±2.2 ㎜ at 3 months in the KHA group to, 8.8±2.7㎜ at 6 months in the JHA group. The implant placed in an one stage SFE can develop sufficient new bone and remain in the SULM over a long time, even if bone substitutes are not used.

The new bone observed at 3 and 6 months in this study, consisted of matured trabecular bone with lamellar structure and resorption pits. It was considered to be a static bone, during the remodeling phase, where its development was already finished. NBW on the sinus wall and TSN at the implant base were observed at all stages, in both groups. Under high magnification, HSK covered a wide area of the placed implant surface in the SULM. Both groups showed similar histological findings at 3 and 6 months.

Ribin explained that the innate osteogenic potential of the Schneiderian membrane may be the main reason for successful formation of bone with one stage SFE, without bone substitutes[20,21]. However, new bone formation from the membrane was not observed in this study. It was in fact, fibrous connective tissue. The new bone formation in the SULM might be a reactive bone regeneration caused by surgical stimulation, such as lifting the sinus membrane and implant placement, that stimulated precursor cells in the periosteum and endosteum of the sinus wall. It does not depend on the type of grafting material used.

The original definition of osseointegration is a direct structural and functional connection between ordered living bone and the surface of a load-carrying implant[22]. In the term, there is a recognition that nonvital components are reliably and predictably incorporated into living bone, and that incorporation between them can persist under all normal conditions of loading[23]. It is used when there is no progressive relative movement between the implant and the bone with which it has direct contact[24]. Periotest analysis in this study revealed that both groups were less than 10, indicating good clinical osseointegration. BIC by histological analysis is frequently used as a parameter for evaluating osseointegration[25-27]. In canine experiments, a BIC of 60 to 67% from 4 to 8 weeks[28], 60 to 67% from 4 to 26 weeks[29] , and 30 to 60% at 11 to 12 months were reported[30]. In rabbit experiments, a ratio of 34% to 52% from 8 to 24 weeks was observed[31]. Hurzeler showed higher BIC for titanium implants with rough surface in comparison to implants with machine-polished surface, 45.8 and 35.9%, respectively. BIC in osteotome sinus floor elevation (OSFE) without grafting (40.05%) was higher than those with $\beta$-TCP grafting (23.30%) at 24 weeks, using an animal experiment, in a report by SI[32]. He concluded that spontaneous new bone formation and better bone-to-implant contact were found for OSFE without grafting, using titanium implants with rough surface. However, our previous animal experiment showed that osseointegration of machine-polished titanium implants with the new bone in the SULM was not observed[5]. The BIC was 2% at most.

Implants with HA coating were reported as achieving a high BIC of 46%[33] to 99%[34] in sinus augmentation immediately followed by implant surgery. The HA-coated implants can promote an elution of calcium ions and phosphate to favor the osteoconductivity by the higher crystallization rate of HA. KHA implants have 95% crystalline HA coating on the surface. JHA implants have 55% crystalline HA coating with about 20$\mu$m thickness, while KHA implants have HA coating with 50 to 70$\mu$m. During implant placement, in order to avoid the destruction of the HA coating when the implant causes friction with the surrounding bone, the KHA implants have a cylinder shape with the same diameter from the neck to the apex of the implant. On the other side, JHA implants have an enhanced adhesion between HA coating and the titanium surface that minimizes stress fractures. JHA implants are screw-shaped with the maximum diameter at the neck part, to promote primary fixation. This study found the BIC of both KHA and JHA implants achieved sufficient osseointegration, with more than 80% of BIC, and no differences in the histological findings and histomorphometric measurements. Periotest values also indicated sufficient clinical osseointegration. There was no difference between osseointegration with the new bone at 3 and 6 months in both groups. However, it was significantly higher than the osseointegration reported by Hidaka[4] using machine-polished implants. This study showed that both HA-coated implant groups have superior surface properties for osseointegration with the newly formed bone in the SULM. It is considered that osseointegration between the new bone and HA-coated implants can remain for a long time, at least 6 months in an one stage SFE, even if bone substitutes are not used. Generally, two stage SFE is used for cases when the available bone volume between the sinus floor and the alveolar bone crest is below 5㎜[35]. In a two-stage SFE, the new bone forms first in the SULM. The new bone is used as a pre-existing bone to place an implant in the second stage surgery. Consequently, the mechanism of osseointegration with new bone in a two-stage SFE can be understood as osseointegration with the pre-existing bone as reported by the Bränemark concept[22]. Meanwhile, the mechanism of osseointegration with the new bone in the SULM in one stage SFE is unclear. In the next study, rough surface titanium implants will be used to compare the results using HA-coated implants.

## 5. Conclusion

It was concluded that both types of HA-coated implants have similar properties to promote a superior osseointegration with the new bone forming in the SULM. Furthermore, the new bone which osseointegrated with HA-coated implants has the possibility to remain for a long time.

ACKNOWLEDGMENTS and DISCLOSURES

The authors wish to express their gratitude to the Brazilian Federal Agency for Support and Evaluation of Graduate Education –CAPES, scholarship process BEX 18807/12-7, and to the research foundation of Kyocera Medical Ltd for financial support.

This article originates from a Japanese version of 'an experimental study of maxillary sinus floor elevation following simultaneous implant placement using dog frontal sinuses' published by Yoshikazu Yamazaki, Takao Watanabe and Tsuneo Takahashi, J Kanagawa Odontol Soc, 45(2):79-89, 2010.

## References

1) Boyne PJ, James RA: Grafting of the maxillary sinus floor with autogenous marrow and bone, J Oral Surgery 38(8),613-616,1980.
2) Tatum OH: Maxillary and sinus implant reconstructions, J Dental clinics North America, 30(2),207-229,1986.
3) Shimizu H, Watanabe T, Sato J: An animal experiment using dog frontal sinuses for histological consideration of the maxillary sinus augmentation surgery for implants, J Tsurumi University Dentistry, 29,37-56,2003.
4) Hidaka T, Watanabe T, Sato J: An experimental study on maxillary sinus floor elevation and simultaneous implant placement into the frontal sinus of canine. J Tsurumi University Dentistry, 31(1),65-80,2005.
5) Buser D, Schenk RK, Steinemann S, Fiorellini JP, Fox CH, Stich H: Influence of surface characteristics on bone integration of titanium implants. A histomorphometric study in miniature pigs. J Biomedical Material Research, 25(7),889-902,1991.
6) Yajima Y: Extreme aging and dentistry, aging society, healthy life expectancy and implant treatment: J International College Dentisty, 44(1),2013.
7) Berglundh T, Lindhe J: Healing around implants placed in bone defects treated with Bio-Oss. An experimental study in the dog. Clinical oral implant research, 8(2),117-124,1997.
8) Hurzeler MB, Kirsch A, Ackermann KL, Quinones CR: Reconstruction of the severely resorbed maxilla with dental implants in the augmented maxillary sinus: a 5-year clinical investigation. International j oral maxillofacial implantology, 11(4),466-475,1996.
9) Wagner JR: A 3 1/2-year clinical evaluation of resorbable hydroxylapatite OsteoGen (HA Resorb) used for sinus lift augmentations in conjunction with the insertion of endosseous implants, J Oral Implantology, 17(2),152-164,1991.
10) Hallman M, Nordin T: Sinus floor augmentation with bovine hydroxyapatite mixed with fibrin glue and later placement of nonsubmerged implants: a retrospective study in 50 patients, Int J Oral Maxillofacial Implantology, 19(2),222-227,2004.
11) Valentini P, Abensur DJ: Maxillary sinus grafting with anorganic bovine bone: a clinical report of long-term results. Int J Oral Maxillofacial Implantology, 18(4),556-560,2003.
12) Gruber RM, Ludwig A, Merten HA, Achilles M, Poehling S, Schliephake H: Sinus floor augmentation with recombinant human growth and differentiation factor-5 (rhGDF-5): a histological and histomorphometric study in the Goettingen miniature pig. J Clinical Oral Implant Research, 19(5),522-529,2008.
13) Jodia K, Sadhwani BS, Parmar BS, Anchlia S, Sadhwani SB: Sinus elevation with an alloplastic material and simultaneous implant placement: a 1-stage procedure in severely atrophic maxillae. J Maxillofacial Oral Surgery, 13(3),271-280,2014.
14) Bortoluzzi MC , Manfro R , Fabris V , Cecconello R , Derech ED:: Comparative study of immediately inserted dental implants in sinus lift: 24 months of follow-up. Ann Maxillofacial Surgery, 4(1),30-33,2014.
15) Lai HC, Zhuang LF, Lu XF , Zhang ZY, Zhan YX g: Osteotome sinus floor elevation with or without grafting: a preliminary clinical trial. Clinical Oral Implants Research, 21(5),520-526,2010.
16) Thor A, Sennerby L, Hirsch JM, Rasmusson L: Bone formation at the maxillary sinus floor following simultaneous elevation of the mucosal lining and implant installation without graft material: an evaluation of 20 patients treated with 44 Astra Tech implants. J Oral Maxillofacial Surgery, 65(7),64-72,2007.
17) Chen TW, Chang HS, Leung KW, Lai YL, Kao SY: Implant placement immediately after the lateral approach of the trap door window procedure to create a maxillary sinus lift without bone grafting: a 2-year retrospective evaluation of 47 implants in 33 patients. J Oral Maxillofacial Surgery, 65(11),2324-2328,2007.
18) Shimizu H, Hidaka T, Watanabe T, K Iwano, Nakao I, Seto K: A case treated with subantral augmentation without grafting material; J. Japanese Society Oral Implantology, 7,30-38,1994.
19) R Nedir, N Nurdin, L Vazquez, S Abi Najm, M Bischof: Osteotome sinus floor elevation without grafting: A 10-Year prospective study. Clin Implant Dent Relat Res. 18:123-131, 2015
20) Riben C, Thor A: The maxillary sinus membrane elevation procedure: Augmentation of bone around dental implants without grafts—A review of a surgical technique. Int J Dentists, 10,1155-1164,2012.
21) Troedhan A, Kurrek A, Wainwright M: Biological principles and physiology of bone regeneration under the Schneiderian membrane after sinus lift surgery: A radiological study in 14 patients treated with the transcreastal hydrodynamic ultrasonic covitational sinus lift (intralift). Int J Dental, Article ID 576238, 12 pages 2012

22) Brånemark P-I, Hansson BO, R Adell, U Breine, J Lindström, O Hallén, A Öhman: Osseointegrated implants in the treatment of the edentulous jaw. Almqvist and Wiksell, 132, Stockholm, 1977
23) Worthington P: History, development, and current status of osseointegration as revealed by experience in craniomaxillofacial surgery. In: P-I Brånemark, BL Rydevik, R Skalak, editors. Osseointegration in skeletal reconstruction and joint replacement. Carol Stream, IL: Quintessence Publishing Co, 25-44,1997
24) Brånemark P-I: Osseointegration and its experimental studies. J Prosthetic Dentistry, 50:399-410,1983
25) Hurzeler MB, Quinones CR, Kirsch A, Gloker C, Schupbach P, Strub JR: Maxillary sinus augmentation using different grafting materials and dental implants in monkeys. Part I. Evaluation of anorganic bovine-derived bone matrix. Clinical Oral Implants Reseach, 8(6),476-486,1997.
26) Hurzeler MB, Quinones CR, Kirsch A, Schupbach P, Krausse A, Strub JR: Maxillary sinus augmentation using different grafting materials and dental implants in monkeys. Part III. Evaluation of autogenous bone combined with porous hydroxyapatite. Clinical oral implants research, 8(5),401-411,1997.
27) Quinones CR, Hurzeler MB, Schupbach P, Arnold DR, Strub JR, Caffesse RG: Maxillary sinus augmentation using different grafting materials and dental implants in monkeys. Part IV. Evaluation of hydroxyapatite-coated implants. Clinical oral implants research, 8(6),497-505,1997.
28) Cook SD, Rust-Dawicki AM: Preliminary evaluation of titanium-coated PEEK dental implants. J Oral Implantology, 21(3),176-181,1995.
29) Cook SD, Rust-Dawicki AM: In vivo evaluation of a CSTi dental implant: a healing time course study. J Oral Implantology, 21(3),82-90,1995.
30) Zubery Y, Bichacho N, Moses O, Tal H: Immediate loading of modular transitional implants: a histologic and histomorphometric study in dogs. Int J Periodontal Restorative Dentistry, 19(4),343-353,1999.
31) Rasmusson L, Meredith N, Cho IH, Sennerby L: The influence of simultaneous versus delayed placement on the stability of titanium implants in onlay bone grafts. A histologic and biomechanic study in the rabbit. Int J Oral Maxillofacial Surgery, 28(3),224-231,1999.
32) Si M, Mo JJ, Zhuang LF, Gu YX , Qiao SC, Lai HC: OSFE with and without grafting:an animal study in labrador dogs. Clinal Oral Implants Research, 26,197-203,2015.
33) Rohner D, Tay A, Chung SM, Hutmacher DW: Interface of unloaded titanium implants in the iliac crest, fibula, and scapula: a histomorphometric and biomechanical study in the pig. Int J Oral Maxillofacial Implantology, 19(1),52-58,2004.
34) Proussaefs P, Lozada J: Histologic evaluation of a 9-year-old hydroxyapatite-coated cylindric implant placed in conjunction with a subantral augmentation procedure: a case report. Int J Oral Maxillofacial Implantoloy, 16(5),737-741,2001.
35) Wetzel AC, Stich H, Caffesse RG: Bone apposition onto oral implants in the sinus area filled with different grafting materials. A histological study in beagle dogs. Clinical Oral Implants Research, 6(3),155-163,1995.