

# Performance of coralline hydroxyapatite in sinus floor augmentation: a retrospective study

Zhi-Bin Luo · Qing-Bin Zhang · Zhao-Qiang Zhang · Dan Chen · Wang-Xiang Yan · Ke-Feng Li · Yu Chen

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## Abstract

**Objective** The purpose of this study is to retrospectively explore the utilization of coralline hydroxyapatite in maxillary sinus augmentation.

**Method** One hundred and eighteen cases of sinus lift with coralline hydroxyapatite (CHA) were included in this study. In detail, simultaneous implantation was conducted in 78 patients (174 implants) and delayed implantation was done in 40 cases (82 implants) around 6 months after bone transplantation. The clinical features and X-ray radiographs after operation were analyzed to evaluate osseointegration procedures according to a planned medical follow-up. In the delayed group, around 6 months, a bone biopsy was taken just during implant placement in order to evaluate the new formed bone from a histological and histomorphometrical point of view. A further 6 months later, abutment connection

was performed, and the patients received prosthetic restoration of the missing teeth.

**Result** Clinically, the incisions healed well. No abnormal reactions were found during follow-up period. All the 174 simultaneous implants were successful after 1–5 years of medical review; Out of 82 delayed implants, 3 were found to be loose. Histologically, all the specimens showed signs of active remodeling, and all the tissues had a large amount of osteocyte at sixth month after sinus augmentation. New bone formed dramatically. Radiologically, the density of CHA gradually reduced since the beginning of the third month, and CHA may be completely resolved at about fifth year.

**Conclusion** CHA is proven an ideal bone graft material for its reliable clinical results and favorable histocompatibility in the treatment of sinus atrophy or other kinds of insufficient bone volume in this region. Moreover, CHA's signal application can achieve desired clinical effect.

**Clinical relevance** This study shows the clinic application of CHA in maxillary sinus augmentation. Compared with popular mixture of autogenous bone and grafting materials, our results show CHA's signal application can achieve ideal osseointegration interface and satisfying clinic effect.

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Authors Zhi-Bin Luo and Qing-Bin Zhang contributed equally to this paper.

Z.-B. Luo (✉)

Department of Oral Implantology, Guanghua School of Stomatology, Institute of Stomatological Research, Sun Yat-sen University, Guangzhou 510055, China  
e-mail: dentistzb@163.com

Q.-B. Zhang · Z.-Q. Zhang

Department of Oral and Maxillofacial Surgery, Key Laboratory of Stomatology, School and Hospital of Stomatology, Guangzhou Medical College, 39 Huangsha Road, Liwan District, Guangzhou, Guangdong 510140, China

D. Chen · W.-X. Yan · Y. Chen

Department of Oral and Maxillofacial Surgery, The 1st Affiliated Hospital, Sun Yat-sen University, 58 2nd Zhongshan Road, Guangzhou, Guangdong 510080, China

K.-F. Li

Department of Medicine, University of California, San Diego, CA 92103-8467, USA

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## Introduction

Inadequate alveolar bone height in the area of the maxillary sinus is a common problem encountered in the prosthetic rehabilitation of the maxilla [1, 2]. Clinically, management of the atrophic edentulous posterior maxilla with a fixed partial denture or a fixed prosthesis is a major challenge with regard to convenience and comfort. Implantology is

absolutely practical in such situations. However, implant surgical procedures in this region are often relatively difficult due to the insufficient bone volume [3]. Dental implant insertion into this region should have been a better alternative if bone volume is sufficient and bone quality is good enough. However, bone height in this region is generally limited due to the loss of the maxillary teeth and progressive pneumatization of the basal sinus with formation of caudal recesses. The lack of cortical bone and the low density of cancellous bone correlate significantly reduced implant stability and increased failure rate. In addition, implants installation is made particularly difficult by the ventilation of the maxillary sinus (increasing with age) in this region.

To solve the drawbacks of traditional implantation, many different methods have been utilized to provide adequate bone stock for osseointegrated implants [4–7]. Sinus floor elevation is probably the most widely accepted method to increase bone height by formation of new bone in the caudal section of the maxillary sinus to date. The analysis of the literature seems to demonstrate that maxillary sinus grafting is a reliable surgical technique which permits implants to be placed in the atrophic posterior maxilla with an excellent long-term prognosis. The innumerable grafting materials have been proposed and utilized for the augmentation procedure, including allografts, xenografts, alloplastic materials as well as composite grafts composed of different types of transplants and even tissue-engineered bone [8–11]. Although autogenous bone has been considered to be the gold standard for sinus augmentation procedures since the beginning, it also has some disadvantages: limited amount of bone available and second operation associated with morbidity [12] (i.e., risk of neural disturbances in case of intraoral grafts due to possible lesions of the inferior alveolar nerve branches and gait disturbances in case of harvesting from the iliac crest). There is also a tendency for the bone to undergo partial resorption [13]. The fast healing of an autograft provides a unique advantage when compared with other biomaterials even though there is a tendency for the bone to undergo partial resorption [13]. Similar results have been obtained with different grafting materials, such as autogenous bone, allografts, xenografts, alloplastic materials, and mixtures of these materials. Bone substitutes mixed with autogenous bone were used in most clinical situation (Table 1) [13–18]. However, there are few systematic studies related to single bone substitutes application for maxillary sinus augmentation. Additionally, there is a concern that some biomaterials might cause a foreign body reaction, and the current materials for sinus augmentation are still under debate to date.

Hydroxyapatite is a biocompatible alloplast and a proven alternative for augmentation of sinus, which has been used and studied for over two decades [19]. Hydroxyapatite, a calcium phosphate compound  $[\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2]$ , is the major mineral component of bone. Coralline hydroxyapatite (CHA) is a special type in the hydroxyapatite family. The

porous, coral-derived type (Interpore 200  $\mu\text{m}$ , Interpore Orthopaedics, Inc., Irvine, CA) is formed by a hydrothermal exchange reaction of marine coral through the conversion of calcium carbonate coral to hydroxyapatite, which maintains the natural porous superstructure [20, 21]. Porous hydroxyapatite for augmentation is available in both granule and block form. The granular variant is associated with more predictable results and fewer complications [22]. In addition, the granular form requires considerably less operative exposure and soft tissue dissection. Previous studies have shown that the porous type (200 nm diameter) enables fibrovascular and, in some procedures, bony in-growth [23]. Since the porous form of hydroxyapatite has been postulated to grow into bone in specific surgical procedures, although it is not osteoinductive [24], it resists infection by creating a vascularized framework through the granules.

However, CHA is not used as widely as would be expected for augmentation of sinus given its proven qualities of safety, versatility, and long-term use. A possible reason for this lack of popularity may be the absence of conclusive data regarding the long-term maintenance of the augmented volume. To evaluate the long-term fate of coral hydroxyapatite used in augmentation of sinus, this retrospective clinical study was conducted aiming to verify the function and long-term efficacy of using CHA alone in sinus lifting.

## Materials and methods

From January 2005 to January 2011, 118 patients who received sinus augmentation with complete record in our department were included in this retrospective study. The patients consisted of 33 females and 85 males (average age 39.6 years, ranging from 23 to 72 years). All patients were fully informed of any risks possibly occurring, including the minimal possibility of human immunodeficiency virus, hepatitis C virus, and hepatitis B virus transmission. The protocol was approved by the Ethics Committee of Guanghua School of Stomatology, Institute of Stomatological Research, Sun Yat-sen University, and all patients signed a written informed consent form.

### Inclusion criteria

Inclusion criteria include maxillary partial (unilateral or bilateral) edentulism involving the premolar/molar areas and the presence of less than 5 mm of crestal bone between the sinus floor and the alveolar ridge.

### General exclusion criteria

General exclusion criteria include acute myocardial infarction within the past 6 months, uncontrolled coagulation disorders,

**Table 1** Sinus augmentation using grafting materials by lateral window technique

Authors	No. of patients	No. of sinus	No. of implants	Grafting material	Healing aug(ms)	Healing impl (ms)	Follow-up (ms)	Implant survival (%)
Van den Bergh et al. (1998) [13]	42	62	161	AB	4	4	34	100
Hallman et al. (2005) [14]	20	30	79	AB + DBBM	6	6.7	36	89
Marchetti et al. (2007) [15]	30	48	140	AB + DBBM	5	5	12.0	94.9
Bornstein et al. (2008) [16]	56	59	111	AB + DBBM/AB + TCP	7.75	2	60	98
Chiapasco et al. (2008) [17]	692	952	2,037	AB	4–6	6	59	95.8

AB autogenous bone, DBBM deproteinized bovine bone mineral, TCP tricalcium phosphate

uncontrolled metabolic diseases (diabetes mellitus, bone pathologies), psychological or psychiatric problems, heavy smokers (>10 cigarettes/day), patients treated with radiotherapy to the head/neck district within the past 24 months, and patients treated with intravenous bisphosphonates.

#### Local exclusion criteria

Local exclusion criteria include maxillary sinus pathologies, oral infections, and uncontrolled periodontal disease.

All patients underwent a clinical examination. Panoramic radiographs and study models were conducted and obtained (Fig. 1). Following this, CBCT examination was performed to study the proposed implant sites as well as to evaluate the morphology of the bony walls and possible sinus pathology when necessary.

#### Surgical procedures

The surgical procedures were conducted under local anesthesia by the same surgeons. A remote buccal incision was carried out. Two vertical releasing incisions were made anteriorly and posteriorly, respectively. Next, a mucoperiosteal flap was cut and elevated, allowing good access to the lateral



**Fig. 1** The teeth located in 15,14, and 26 had been extracted for 4 months because of accidental traffic trauma. The panoramic X-ray showed the residual crest height was 2–5 mm

sinus wall. Using a Lindemann bur, a sinus window was outlined, and the osteotomy was finished with a diamond round bur under continuous cooling using sterile saline solution. As the Schneiderian membrane was detached, the infractured lateral sinus wall was rotated medially. This technique was used to lift the sinus mucosa in a cranial direction. CHA material was then transferred to fill the cavity (Fig. 2). The defect of the lateral sinus wall was covered using resorbable, collagenous membrane (China). The mucoperiosteal flap was repositioned and sutured using resorbable suture materials.

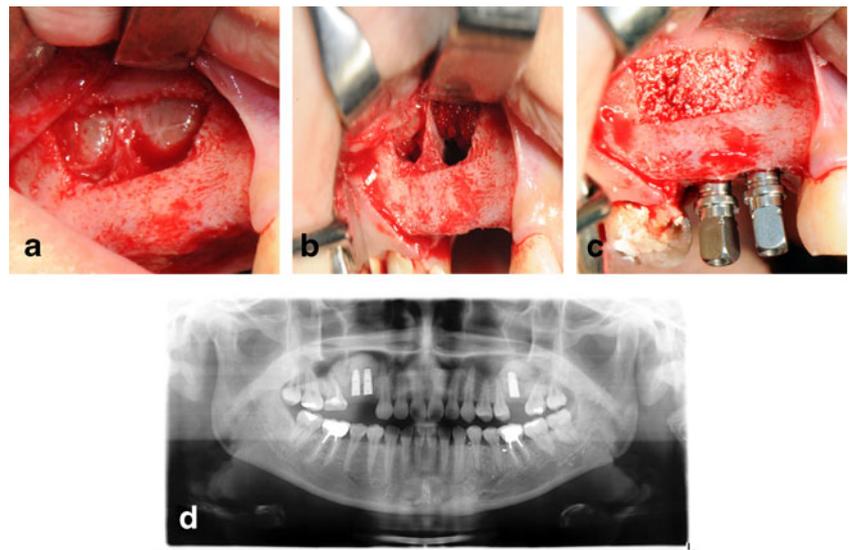
Provided there were no known allergies and no general contraindications, clindamycin at a dosage of 600 mg three times per day for 1 week and 180 mg gentamicin once daily for 3 days were given intravenously as antibiotic prophylaxis. All sutures were removed on the tenth postoperative day. Patients were not allowed to blow their nose and advised to administer decongesting nose drops (xylometazoline 0.1 %) five to six times per day in both nasal cavities over a period of 1–2 weeks. They were also instructed not to wear their maxillary prosthesis for at least 14 days.

When the crestal bone between the sinus floor and the alveolar ridge was more than 3 mm, we conducted 78 simultaneous implantation of the system of Ankylos implants (Germany); when it was less than 3 mm, we performed 40 delayed implantation after a mean healing time of 6 months (range, 4–8 months). Forty cylindrical bone biopsies from the augmented posterior maxilla had previously been taken using a trephine bur with an inner diameter of 2 mm and outer diameter 3 mm. Implants were placed in the osteotomy sites obtained from biopsy sampling. After fixation in a 3.5 % formaldehyde solution, the bone samples were forwarded to the Institute of Pathology of Sun Yat-sen University for histological and histomorphometrical examination.

#### Histology and histomorphometry

All specimens were immediately fixed in 3.5 % formaldehyde solution in 0.1 M phosphate buffer (pH 7.3) at 4 °C for

**Fig. 2** The lateral window approach of right sinus was made by piezosurgery technique under local anesthetics. The sinus membrane was intact (a). The sinus septum was high. The sinus membrane was elevated carefully from sinus floor (b). Commercial biomaterial of coralline hydroxyapatite was packed into the cavity. Two implants of Ankylos system were inserted simultaneously (c). The same procedure was made on *left side*. The postoperative panoramic radiography showed the implant and filling material (d)

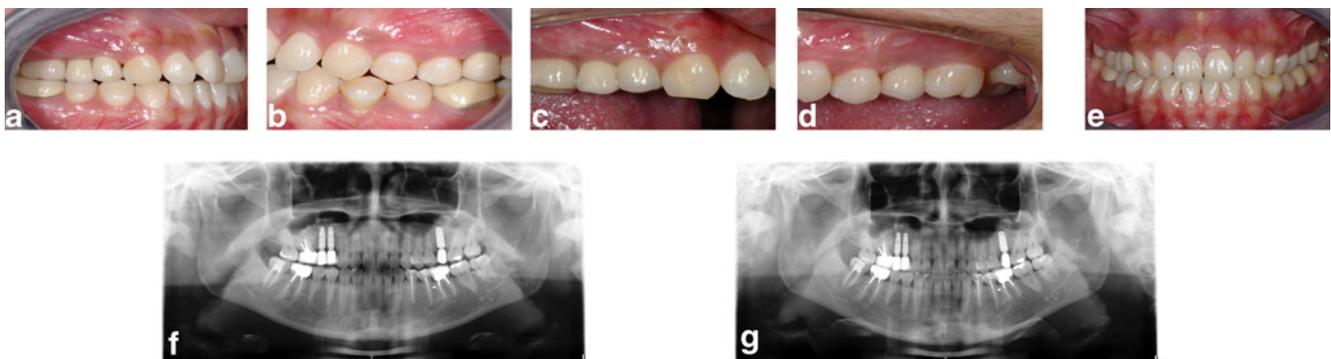


24 h. They were then rinsed three times with a 0.1 M phosphate buffer and, finally, stored in 70 % ethanol at 4 °C until ready to be embedded. All the biopsies were cold embedded in methylmethacrylate with 20 % plastoid. Undecalcified 5-mm-thick sections were made along the axis of the biopsy using a Jung K microtome. All specimens were stained with hematoxylin and eosin. The measurements were performed with decalcified specimens using a personal computer-based image analysis system (Image-Pro Plus, Media Cybernetics, Silver Springs, MD, USA). Four randomly selected sections from the serial sections collected from each sample were analyzed manually. The newly formed bone (NFB, woven type) trabecula and coralline hydroxyapatite (CHA) particles (i.e., the percentage of newly formed bone area in the elevated area observed) were recorded.

## Results

### Clinical findings

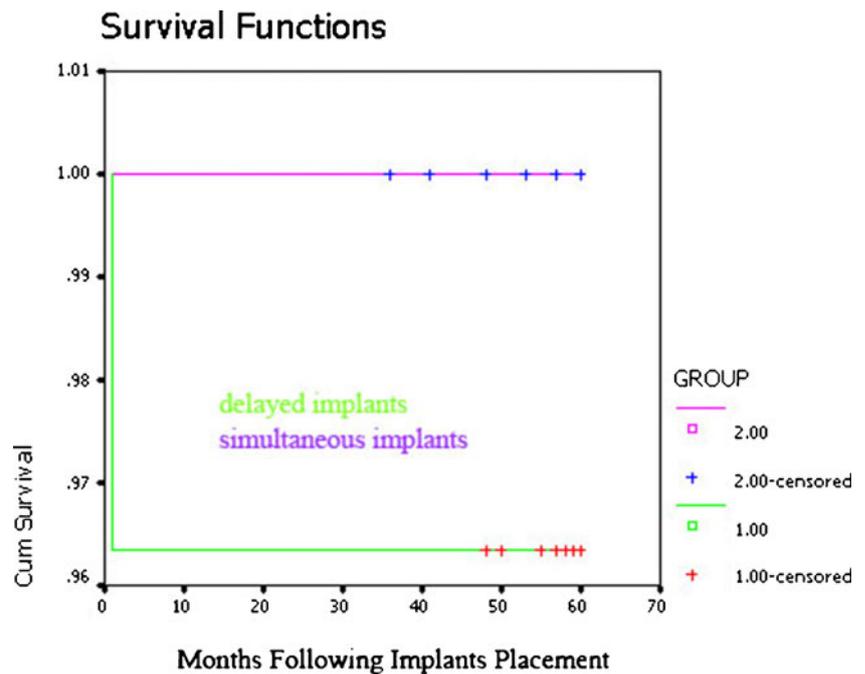
None of the 118 patients had complications. A total of 253 implants were stable, and x-ray examination showed dense bone around the implants (Fig. 3). All 174 simultaneous implants were found successful in the following-up period (1 to 5 years). For the 82 delayed implants, 3 implants failed before preparation of the definitive prosthetics and occlusal loading. The other 79 implants performed functional loading well during the follow-up period (1 to 5 years). The implants' survival rates were listed by using Kaplan–Meier curves in Fig. 4.



**Fig. 3** The prosthetic procedure began 6 months after operation. Permanent restorations of 15, 14 on *right side* were installed (a). Permanent restorations of 26 on *left side* were installed (b). The panoramic radiography after prosthetics (f). Permanent restorations after 3 years on *right side* (c). Permanent restorations after 3 years on

*left side* (d). Panoramic radiography after 3 years of observation term showed stable bone level of implant neck, even in narrow gap between two implants of 14 and 15 (g). Restorations supported by Ankylos implant had undertaken functional loading for 3 years. The soft tissue of peri-implant surrounding was healthy (e)

**Fig. 4** Kaplan–Meier curves for simultaneous/delayed implants survival



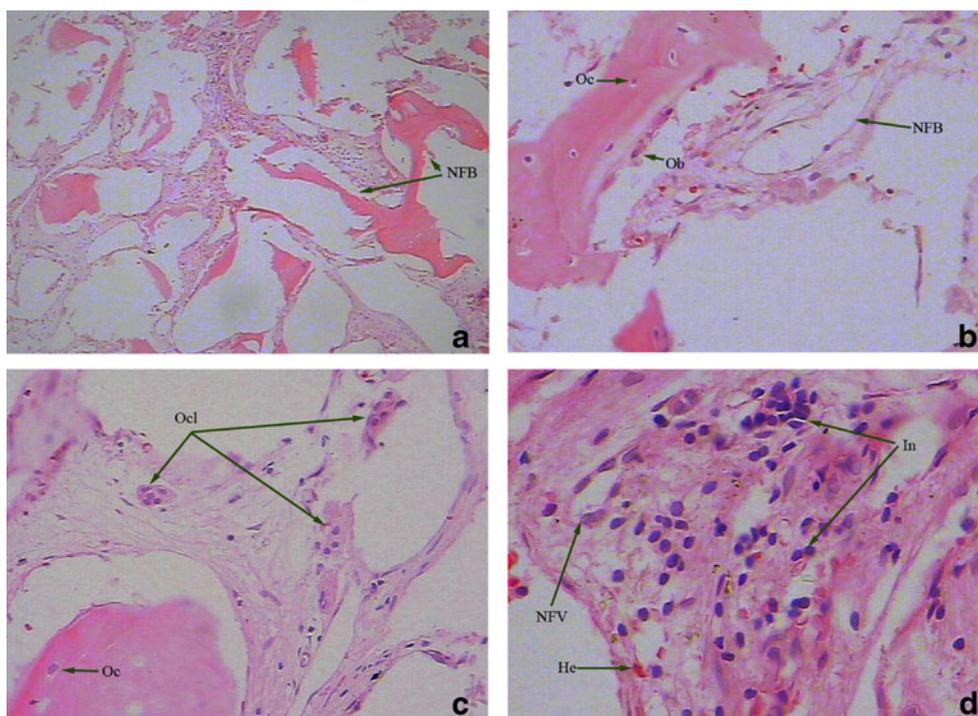
#### Histological and histomorphometrical findings

Histological view of maxillary sinus site grafted with CHA after a healing period of 6 months: (1) All the specimens exhibited a large amount of NFB (woven type, immature bone), while CHA particles had been almost completely resorbed (Fig. 5a). NFB presented features of numerous small osteocytic lacunae and had abundant medullary space filled with loose connective tissue and abundant small newly formed vessels (NFV), indicating intense angiogenesis, sign of rapid revascularization of the recipient site (Fig. 5b). (2) Many osteocytes (Oc) trapped in osteocytic lacunae and osteoblasts (Ob) were in an active status located on NFB surfaces (Fig. 5b). (3) Fiber tissue was poorly represented. (4) All the specimens showed signs of active remodeling, and many osteoclasts (Ocl) can be observed indicating active bone remodeling (Fig. 5c). (5) A marked inflammatory reaction to the CHA, and this inflammatory reaction comprised some histologic markers of inflammation (mainly lymphocytes, In). Obviously, well-formed granulomas and acute inflammation response were absent. Moreover, hematid (He) was also mixed into specimens in the process of drawing materials (Fig. 5d). In some areas, small capillaries were observed in the marrow spaces located between the CHA particles. In addition, the data of the histomorphometric study are shown in Table 2.

#### Discussion

Rehabilitation of the edentulous posterior maxilla with dental implants may be hindered because of the insufficient

bone volume produced by bucco-lingual and/or apico-occlusal atrophy of the edentulous alveolar crestal bone and pneumatization of the maxillary sinus [25]. Under this anatomical situation, it could be very difficult to obtain primary implant stability because of the absence of an optimistic quantity of cortical bone and for the loose structure of type IV spongy bone. Several methods have been tried to restore the bone height, width, and thickness in 3-D space. The maxillary sinus augmentation was proved to be an effective treatment option [26]. Clinically sinus floor elevation was an established method of harvesting sufficient vertical bone from the posterior region of the maxilla to achieve good primary stability ahead of implant insertion [27]. Even though this method has become routine with patients having too small a bone supply, the question as to which augmentation material is optimum has not been finally resolved [28]. Clinically and histologically, the use of autogenous iliac crest bone provides the best results, but the side effects and complications involved in surgery to the iliac crest cannot be ignored [29]. An ideal bone substitute material should incorporate into the host bone as well as autogenous bone [30], but, unlike autogenous bone, be available in unlimited quantities, either because synthetically manufactured or produced naturally. In recent years, bone substitute materials as an alternative to autogenous bone grafting have been enjoying growing popularity in connection with sinus floor elevation surgery [31, 32]. Several studies have been performed to compare these substitute materials with autogenous bone with regard to different aspects [33]. Sinus floor elevation using mixture of xenograft and autogeneous bone has been successful in animal-



**Fig. 5** Histological view of maxillary sinus site grafted with CHA after a healing period of 6 months. At low magnification, **a** showing a large amount of newly formed bone (NFB, woven type) trabecula and coralline hydroxyapatite (CHA) particles which are almost completely resorbed (hematoxylin and eosin, original magnification,  $\times 50$ ). At high magnification, **b** showing the presence of NFB with full osteocyte lacunae (Oc), small NFBV, and Ob which are in an active status located

on NFB surfaces, **c** showing the presence of Ocl indicating the progress of bone remodeling (hematoxylin and eosin, original magnification,  $\times 200$ ). At a higher magnification, **d** showing inflammatory cell (mainly lymphocytes, In) and He which mixed into specimens in the process of drawing materials (hematoxylin and eosin, original magnification,  $\times 400$ )

based research work and in therapeutic applications in humans [34]. In recent years, we have observed an increase in the number of studies of tests relating to the use of hydroxylapatite, obtained synthetically or from basis materials such as coral, algae, and bovine bone [35, 36], especially the application for coral hydroxylapatite. However, in these studies, the vast majority of grafting material was used of mixture of autogenous bone and grafting materials compared with very few single grafting materials application of sinus floor elevation, also lack of large-scale samples and a long-term clinical tracking reports [37, 38].

In our department, coral hydroxyapatite (CHA) was widely applied in patients in the past 7 years. CHA kept the coral nature and characteristics with physical structure and inorganic compositions similar to human bone. The characteristics are as follows: (1) CHA was made from *Goniopora* of South Pacific Ocean without any kind of contaminations. Its porosity reached 70 % and consists of macropore ( average pore size, 500  $\mu\text{l}$ ) and micropore (

average pore size, 100–120  $\mu\text{l}$ ). (2) Mineral compositions were similar to human bone. Coral crystal size and arrangement were similar to those of human bone. (3) Excellent bone biological activity was verified in animal research. (4) Controlled absorption time, thickness of hydroxyapatite could be controlled to adjust the absorption time. (5) Excellent hydrophilicity was tested in basic research. In our department, 118 patients have been treated with CHA alone. Seventy-eight patients received simultaneous implantation, and 40 cases delayed implantation. All the simultaneous implants were successful, while 3 implants failed in the 82 delayed implants. The reason behind the failure was that we made soft lining for his temporary denture to cushion the occlusion force; however, when he returned hometown, the soft lining dropped, and when he went to a dental clinic, the dentist ignored this point and directly made denture for him without any cushion lining. After 4 weeks of implants placement, the implants loosened.

**Table 2** Data of the histomorphometric study

Time	NFB (%)	Residual CHA particles (%)	NFB/residual CHA particles
6 months	49.2 $\pm$ 12.2 %	24.4 $\pm$ 4.8 %	2.02 $\pm$ 2.5 %

The degree of osseous integration is determined by the biological processes at the surface of the implant. Therefore, the success of a maxillary sinus augmentation can be assessed by examining the histological status of the bone at sinus cavity. The extent of osseous penetration of CHA depends on its properties of osteoconduction, i.e., the ability to act as a spacer and conducting structure for newly forming bone. This arises from an interconnecting pore system and physical and chemical properties similar to those of human cancellous bone. The porosity of the material provides an excellent basis for vascularization and penetration of associated cells which integration of the substitute material requires, sufficient vascularization being an absolute precondition to the osteogenic process. The pore system of CHA is architecturally structured to allow vascularization of new bone. High stability in the augmented region is achieved through the integration of CHA granulate into the new bone formations. The healing response of individual patients appeared to have a much greater effect on new bone formation than the resting time of the CHA. Resorption is a further factor affecting the successful osseous penetration of the bone substitute material. This so-called biodegradation should take place at a time appropriate to activation of new bone formation, so that the integrity of the conducting structure is not put at risk. Radiographic examination has been able to identify the presence of CHA granulate even after a resting time of up to 5 years. However, a quantitative evaluation was not possible since the initial percentage occupation by substitute material after sinus elevation was not known. It should be remembered that because of the limited quality and quantity of bone in the maxilla, the implant success rate is considerably lower than for the mandible. In a long-term study of osseointegrated oral implants, it remains to be determined whether these results for sinus regions augmented using CHA alone can also be achieved long term after implants have been subjected to prosthetic loading. By our retrospective study, we can conclude that single application of CHA, as one type of bone filling substitute of maxillary sinus augmentation, implant can achieve ideal osseointegration interface and satisfying clinic effect with both simultaneous and delayed implantation.

**Ethics** The study was approved by the Ethics Committee of Guanghua School of Stomatology, Sun Yat-sen University.

**Conflict of interest** There is no conflict of interest. This paper was financially supported by grant A2008225 of the Medical Research Foundation Program of Guangdong Province and grant 2008B030301087 of Science and Technology Plan Program of Guangdong Province Department of Science and Technology.

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