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## CONTENTS

# EFFICACY OF THE ANDRESEN ACTIVATOR BEFORE PEAK GROWTH IN CLASS II PATIENTS

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**Andresen activator (AA) is a functional appliance used to correct Class II malocclusion in growing patients. It corrects the malocclusion stimulating mandibular growth and determining a palatoversion of the upper incisors and a vestibularization of the lower incisors. The aim of this study was to analyze the treatment efficacy of class II malocclusion due to mandibular hypodevelopment before peak growth. Fourteen subjects with class II relationship of the skeletal bases and cervical vertebrae maturation stage 1 or 2 were enrolled in the study. Cephalometric analyses were carried out using landmarks derived from the analyses of Pancherz, Ricketts, Tweed and Steiner. A significant decrease (P <0.05) in ANB angle was found (-2.29±3.05°) after treatment, which was expression of an improvement in maxillo-mandibular sagittal skeletal relationships. There was also a significant reduction of OJ after treatment (-4.44±2.36 mm; P <0.001), indicating a vestibularization of the mandibular incisors and a palatoversion of the maxillary incisors, and a correction of the molar relationship. The favorable effects of the Andresen activator for the correction of the mandibular defect can be found even prior to peak growth; the achieved class I relationship maintains a correct mandible position in time, ensuring a proper skeletal growth.**

Class II malocclusion in growing patients can be treated using the Andresen activator (AA). It consists of a resin plate with anteriorly and laterally inclined planes, a passive anterior vestibular arch and two Adams clasps on the upper molars. The correction of the malocclusion is due to skeletal effects consisting in a further growth of the mandible by stimulating the condylar cartilage, and dental effects resulting in a palatoversion of the upper incisors and a vestibularization of the lower incisors (1-3). Adult patients, who have not undergone an orthopedic-orthodontic treatment, have to undertake orthognathic surgery to correct the malocclusion (4-10). The aim of this study was to analyze the efficacy of the treatment before peak growth of class II malocclusion due to mandibular hypodevelopment with the AA and to compare the results with the ones obtained in the literature from treatments performed during peak growth. In particular, the following effects were evaluated: maxillo-mandibular skeletal

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changes on the sagittal plane between the beginning (T0) and the end (T1) of the treatment; dento-alveolar changes between T0 and T1.

## MATERIALS AND METHODS

Fourteen subjects (7 females and 7 males) with the following characteristics were randomly selected: bilateral class II molar relationship (MR); class II relationship of the skeletal bases (ANB >4°); mandibular retrusion (SNB <78°); overjet (OJ) 5mm; Cervical Vertebral Maturation Stage 1 (CS1) or 2 (CS2). The documentation included study models, orthopantomography, a lateral cephalograms at T0 and T1, extraoral and intraoral photographs at T0 and T1 (11). Class II malocclusion was diagnosed by clinical examination, lateral photographs, initial lateral cephalograms and Frankel maneuver (12-13).

The skeletal ages of the subjects were calculated from the initial lateral cephalogram according to Baccetti (14). The mean age was 9±1.97 years for females and 11±1.63 years for males at T0, and it was 12±1.97 years for females and 13±2.05 years for males at T1 (Table I). Records were randomly obtained for patients who met the inclusion/exclusion criteria. The cephalometric analyses were carried out using landmarks derived from the analyses of Pancherz, Ricketts, Tweed and Steiner to collect the majority of the landmarks regarding the functional treatment of class II malocclusions (15). Analyses were performed by a first operator (OP1) and verified by a second one (OP2) using Dolphin Imaging 11.5 software (Dolphin Imaging & Management Solutions; Chatsworth, CA, USA).

The reference landmarks were: A point: ANS (anterior nasal spine); B point: Ba (Basion); Co: (Condyle); Gn: (Gnathion); Go: (Gonion); Me: (Menton); N: (Nasion); Or: (Orbitale); Pg: (Pogonion); PNS: (posterior nasal spine); Po: (Porion); S: (Sella). The reference lines and angles were: ANB angle; FMA angle; OLp (Occlusal Line perpendicular, passing through S point); SN (line connecting S and N); SNA angle; SNB angle. The linear distances measured were: A/OLp (sagittal position of the maxilla); Pg/OLp (sagittal position of the mandible); Co/OLp (position of the condylar head); Pg/OLp plus Co/OLp (sagittal mandibular length). The following parameters were measured to evaluate the dento-alveolar modifications: overjet (OJ); overbite (OB); molar relationship (MR; measured as the distance between the distal surface of the first upper molar and the distal surface of the first inferior molar on the occlusal plane. A value of -3±3 mm is for Angle's class I (MR); interincisal angle (IA).

About statistical analysis, mean and standard deviation (SD) were calculated for all cephalometric variables at T0 and T1. The statistical significance of the changes occurred during the treatment with AA was evaluated by means of the Student *t*-test with two tails for paired data and Wilcoxon test for paired data. Significance was for $P < 0.05$. All the analyses were performed using SPSS 21.0 software (IBM; Armonk, NY, USA) (16).

## RESULTS

Patients underwent AA therapy for an average of 30 months (Table I). The results regarding the comparison of the sagittal and vertical maxillo-mandibular skeletal variables between T0 and T1 are reported in Table II. No significant differences were found for SNA and SNB angles between T0 and T1: the decrease in SNA angle was -1.54±3.05° ($P>0.05$), while the increase in SNB angle was 0.63±2.74° ($P>0.05$).

During the treatment, a significant decrease ($P <0.05$) in ANB angle was found (- 2.29±3.05°), which was expression of an improvement in maxillo-mandibular sagittal skeletal relationships. No statistically significant differences were found in FMA values between T0 and T1: FMA decreased of -0.35±3.68° ($P>0.05$). The sagittal position of the maxilla did not change significantly during treatment time. The difference in the distance A point-OLp between T0 and T1 was 0.78±13.35 mm ($P>0.05$). Pg-OLp increased of 5.02±13.86 mm ($P\leq0.05$), a value close to significance, indicating that an advancement in the sagittal position of the mandible was found between T0 and T1.

The position of the condylar head (Co/OLp) did not undergo significant changes during treatment: at T1, the condylar head was not farther than OLp, as should be expected following a mandibular advancement. The difference in Co/OLp value between T0 and T1 was -0.65±2.83 mm ($P>0.05$). No significant differences were found in

the length of the mandible before and after treatment with AA (-0.97±14.90 mm; P>0.05).

The results concerning the dento-alveolar variables are shown in Table III. There was a significant reduction of OJ after treatment (-4.44±2.36 mm; P<0.001), indicating a vestibularization of the mandibular incisors and a palatoversion of the maxillary incisors. Furthermore, there was a decrease

**Table I.** *Sample of the study: age before (**T0**) and after treatment (**T1**).*

| | Patients | Age T0 (years) | Age T1 (years) | Treatment period (months) |
|---|---|---|---|---|
| Females | 7 | 9±1.97 | 12±1.97 | 27±9 |
| Males | 7 | 11±1.63 | 13±2.05 | 32±21 |

*Treatment times are reported as mean±standard deviation.*

**Table II.** *Statistical analysis of the skeletal variables before (**T0**) and after treatment (**T1**).*

| | T0 | T1 | ΔT1-T0 | *p-value* |
|---|---|---|---|---|
| SNA (°) | 81.81±4,62 | 80.26±3.38 | -1.54±3.05 | 0.0681 |
| SNB (°) | 76.56±4.40 | 77.19±3.01 | 0.63±2.74 | 0.2958 |
| ANB (°) | 5.26±2.34 | 2.96±1.66 | -2.29±3.05 | 0.0085 * |
| FMA (°) | 23.26±3.71 | 22.91±4.92 | -0.35±3.68 | 0.9164 |
| A/OLP (mm) | 75.12±15.44 | 75.91±6.31 | 0.78±13.35 | 0.3258 |
| Pg/OLP (mm) | 80.31±14.42 | 85.33±9.34 | 5.02±13.86 | 0.0580 |
| Co/OLP (mm) | 4.62±3.20 | 3.97±1.79 | -0.65±2.83 | 0.6144 |
| Pg/OLP+ Co/OLP (mm) | 87.41±12.88 | 86.44±11.93 | -0.97±14.90 | 0.5830 |

*Statistical significance is for p<0.05 (*).*

**Table III.** *Statistical analysis of the dentoalveolar variables before (**T0**) and after treatment (**T1**).*

| | T0 | T1 | ΔT1-T0 | *p-value* |
|---|---|---|---|---|
| Overjet (mm) | 7.43±2.48 | 2.99±1.10 | -4.44±2.36 | 0.0001* |
| Overbite (mm) | 2.13±3.13 | 1.75±1.86 | -0.38±3.04 | 0.5016 |
| Molar relation | 2.08±1.77 | -2.28±1.79 | -4.37±2.25 | 0.0001 * |
| IA (°) | 122.1±13.14 | 123.0±9.42 | 0.95±5.95 | 0.7031 |

*Statistical significance is for p<0.05 (*).*

in OB at the end of treatment (-0.38±3.04 mm), but it was not statistically significant (P>0.05). Regarding MR, if at T0 the relationship at the level of the first maxillary and mandibular molars had a value higher than 0, indicating a molar ratio of Class II, at T1 this variable was reduced significant (P<0.01) in all patients, approaching the ideal value of -3±3 mm, representative of a molar class I: the difference was -4.37±2.25 mm. IA increased (0,95±5,95°; P>0.05) after treatment, indicating a change in the incisor inclinations.

## DISCUSSION

Although several studies have been conducted on effects and timing of treatments with functional appliances, there are not data regarding the efficacy of functional therapy in subjects with Class II malocclusion before peak growth (17-19). Based on our results, it can be asserted that, in a premature stage of skeletal maturation (CS1 or CS2), treatment with AA leads to an improvement in the maxillo-mandibular sagittal relationship: it was evidenced by a reduction of the ANB angle (-2.29±3.05°; P<0.05), in agreement with Basciftci (20).

According to Hashim and Varjervik the change in the position of the bony bases during peak growth is substantially associated with an advancement of the mandible and a minor maxillary growth inhibition (21, 22). Also in our sample, a relative inhibition of the growth of the maxilla was highlighted by a slight reduction in SNA angle. The vertical growth of the mandible (angle FMA) did not change during treatment. Greco et al. supported the hypothesis that brachyfacial types could favorably influence the effects of functional therapy in patients with a mandibular hypodevelopment (23). The present study did not consider the major or minor effect that AA may have on the subject's facial type, anyway, no significant changes in mandibular vertical growth were observed.

Among the other skeletal effects of AA, there was the modification of the mandibular growth model in order to obtain a correction of the malocclusion. As stated by Almeida, Toth, Marsico and Ruf the advancement of the mandible at the end of the functional treatment is due to an increase in its length: in our study, there was an increase close to the significance for Pg/OLP (85.33±9.34 at T1 vs 80.31±14.42 at T0) (24-27). In fact, AA keeping the mandibular bone base protruded, stimulates condylar growth (28).

Regarding the increase in mandibular length following functional therapy, Cozza et al. found an amount of extra growth of more than 2 mm on average only for those treated during the pubertal growth peak (29). The condylar modifications following functional treatment showed no statistically significant changes, which means there was no movement of the condylar head away from the reference plane OLP. This effect could occur because, as documented in animal and human studies, condylar growth in response to a maintained mandibular protruded position has generally been seen in the superoposterior direction for bone apposition posterior to the condylar head therefore, the advanced position of the mandible is not positional, and it is not associated with an antero-reposition of the condyle (30-34).

Using as a reference plane the perpendicular to the occlusal line passing through S, a posterior displacement of the condyle head from OLp with respect to T0 has not been found. The second objective of the study was the evaluation of dento-alveolar effects of AA therapy. AA proved to be effective in correcting OJ and MR. As discussed by Franchi et al., the reduction of the overjet is certainly given by the retroinclination of the upper incisors and by the proclination of the inferior, even if in some studies this variable was not significant (35).

There was a statistically significant decrease in OJ (-4.44±2.36 mm, P<0.05). Baccetti et al. compared the dento-alveolar changes in patients treated with Twin-block before and during peak growth: the correction of OJ and MR was significant only in the patients treated at the time of the pubertal peak (17). On the other hand, in addition to a significant reduction of the OJ, a statistically significant improvement in MR (-2.28±1.79 mm at T1 vs 2.08±1.77 mm at T0; P <0.05) was also obtained in our study. The class I MR is obtained even in absence of an effective mandibular growth;

this occlusion keeps the position stable over time and ensures a correct mandibular growth (36). Therefore, the AA, thanks to the morphology of its anterior and lateral inclined planes, determines an advancement of the mandible (that is the main contribution to the improvement of MR), a correction of the OJ (through the passive vestibular arch that maintains a retroinclination of the upper incisors and through a proclination of the lower incisors).

At the end of orthopedical phase and when dental replacement is completed, a second step is possible with multibrackets treatment followed by a fixed retainer (37, 38). We should also consider the positive effects of removable functional appliance in term of oral hygiene, especially in patients affected by oral diseases, compared to fixed functional devices. (39-40).

Our orientation is to start the orthodontic treatment with functional appliances as early as possible (i.e. in CS1 or CS2), since we found a reduced compliance of the adolescent patient. Although in a phase prior to peak growth, the results of this work have highlighted the favorable effects of AA. We could underline the correction of the mandibular defect; a statistically significant improvement in maxillo-mandibular sagittal relationship at the end of functional treatment; dento-alveolar changes favorable for the correction of malocclusion represented by a significant correction of OJ and MR; the achieved class I relationship maintains the correct mandible position in time, ensuring proper skeletal growth.

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# EVALUATION OF PAIN, SWELLING AND TRISMUS AFTER EXTRACTION OF IMPACTED THIRD MOLARS RELATIVE TO THE USE OF BETAMETHASONE IN SUBMUCUSAL INFILTRATION

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**The aim of this study was to evaluate the anti-inflammatory effect of a single 4 mg injection of submucosal betamethasone after extraction of impacted third molars. Single-centre, single-blinded, parallel group study; Forty-three patients were submitted to impacted third molar extraction. In this study, 4 mg single-dose submucosal betamethasone was injected in the interventional group, while in the control group nothing was injected. Postoperative measurement included pain via the VAS scale, swelling and trismus with facial measurements and maximum mouth openings, and finally nerve sensitivity. There was a significant difference between the two groups regarding trismic pain and edema. The use of a single 4 mg submucosal betamethasone injection leads to a reduction of oedema, trismus and pain in patients undergoing impacted third molar extraction.**

The most common postoperative complications of impacted third molar extraction are pain, trismus and edema. Non-steroidal anti-inflammatory drugs (NSAIDs) are the most commonly used ones for these outpatient procedures (1, 2). However some patients need additional drugs to control postoperative pain and swelling. The anti-inflammatory action of corticosteroids reduces postoperative morbidity (3). Betamethasone is a synthetic corticosteroid with an intense anti-inflammatory activity. In the organism, the disodium betamethasone phosphate is hydrolyzed in the biologically active form of betamethasone alcohol and the blood peak is reached in 60 min.

In oral and maxillofacial surgery it is widely used as it inhibits vasodilation, fluid exudation and thus edema formation, cell exudates and fibrin deposits around inflamed areas. It is able to reduce postoperative complications and to improve the clinical course of outpatient surgery interventions such as included third molar avulsion. The disodium betamethasone phosphate is contraindicated in the presence of systemic infections, ongoing immunization with

*Key words: third molar extraction, betamethasone, corticosteroids*

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attenuated viruses, hypersensitivity to bisulfites and matabisulphites, pregnancy and lactation (4). In the presence of other systemic treatments due to oral diseases, it is recommended not to interfere with other drugs (5). The aim of this trial was to evaluate the efficacy of a single submucosal injection of 4mg betamethasone on swelling, pain and trismus after lower third molars surgical extraction.

## MATERIALS AND METHODS

*Experimental Design*

A single-centre, single-blind, parallel group study was set up to evaluate the efficacy of disodium betamethasone phosphate in submucosal infiltration in the control of inflammation following the impacted third molar excision, in terms of postoperative complication reduction and in their influence on the post-operative clinical course. On the basis of the inclusion and exclusion criteria, patients have been recruited from January 2010 to December 2014 for oral surgery as outpatients at the Department of Dentistry and Maxillo-Facial Surgery of the University Hospital Integrated Trust (AOUI) of Verona and Private Practice.

This study was approved by the Verona Hospital IRB and all participants signed an informed consent agreement. This study followed the Declaration of Helsinki on medical protocol and ethics and the regional Ethical Review Board of Verona approved the study. Patient age, gender and oral status were taken into consideration (6, 7).

Inclusion criteria were: patients with clinical and radiographic diagnosis of disodontiasis of impacted third molars, programmed for outpatient surgical extraction, patients with healthy periodontium without signs of acute pericoronitis at the time of surgery, third molars had to belong to classes B or C and in position II or III according to the radiographic classification of Pell & Gregory (8, 9).

The following exclusion criteria were defined: systemic infectious diseases (including HIV, HBV or HCV infections), heart and vascular diseases, coagulation disorders, hepatopathies, haematological diseases, diabetes, autoimmune and neoplastic diseases, psychiatric disorders or alterations of mental abilities with inability to the fulfill the follow-up program, recent anti-inflammatory therapy or chronic drug intake (antihistamines, antidepressants or steroids) that may influence the inflammatory response, conditions that may contraindicate oral surgery (10-12).

In case of implant surgery, the presence of the third molar could harm the success (13-16). In addition, other conditions could determine patient exclusion: patients that for various reasons did not perform the operation; did not present to one of the control appointments; are in orthodontic therapy; patients who have to undergo orthognathic or maxillofacial surgery; reported the use of other anti-inflammatory drugs at the postoperative controls on his/her own discretion (17-23). Nevertheless, third molars do not interfere with orthodontic therapy or even aggravate the stability of final retainers (24-26). They were divided into two groups: the “test group” with infiltration of submucosal Betamethasone and the “control group” without infiltration of submucosal Betamethasone.

*Surgical Protocol*

The same surgical protocol was used for all patients. This provided truncal anesthesia to the inferior alveolar nerve with 1.8 ml of Mepivacaine 4% hydrochloride with adrenaline in a ratio of 1:100000, local-regional plural anesthesia injections into the oral vestibule with 1.8 ml of Mepivacaine 4% hydrochloride with Adrenaline in ratio 1: 100000, mouth rinse with chlorhexidine mouthwash 0.20%, the preparation of a triangular flap using a scalpel blade No. 15 mounted on Bard-Parker handle No. 3 and detachment of a muco-periosteum flap to total thickness in order to obtain the skeletonization of the area and the exposure of the cortical bone, the osteotomy with tungsten carbide rosette cutter, the exposure of the crown of the dental element and the creation of leverage points.

Coronal and root odontotomy with Lindemann’s drill mounted on straight handpiece (depending on the type of dental inclusion) were performed, so as for the luxation with straight and angled lever and the extraction of the dental element, the curettage of the alveolar cavity with alveolar spoon, osteoplasty and alveoloplasty, accurate hemostasis and absorbable suture (Polysorb ®), the submucosal infiltration of Betamethasone sodium phosphate (Bentelan ®) 4mg \ 2ml (only for patients in the test group, no infiltration was performed in the control group). Surgical times were also recorded, starting from the flap preparation to the end of the suture.

*Post-operative management*

After the operation, the patient was given some

indications for postoperative management: ice packs on the cheek skin, above the mandibular angle, to be maintained continuously in the first 2 hours after the operation. A soft and cold diet was recommended for the first two post-operative days. A specific post-operative, antibiotic and pain-relieving pharmacotherapy was also prescribed for each patient, for the prevention of post-operative local infections. The antibiotic of choice was Amoxicillin + Clavulanic Acid (Augmentin®) with a dosing schedule of 2g/day, 1g every 12 h for 5 days. If the patient had a history of Penicillin allergy, the second choice was Azithromycin (Zitromax®) 500 mg/day for 3 days.

An analgesic therapy for immediate post-operative pain included Paracetamol + Codeine phosphate (Tachidol®) 1 tablet (500mg + 30mg) at 1 h and 8 h after surgery. The choice fell on this drug because of its analgesic activity without any anti-inflammatory effect. The patient was seen for postoperative control the day after the intervention (T1), the oral-facial parameters of edema and trismus, the intensity of pain, the post-operative course of the surgical wound were evaluated and the sensitivity of patient mandibular region was analyzed.

At a distance of three (T2) and twelve days (T3) from the surgical extraction, the patient was reviewed for control and the oral-facial parameters, the intensity of pain and the post-operative course of the surgical wound were re-evaluated. Sensitivity of the mandibular region was also re-examined. The measurements necessary for evaluating the edema were performed at T0, T1, T2 and T3, respectively.

The measurement method used to quantify postoperative edema was the "linear method" (27, 28). This technique implies the calculation of the extent of the oedema by means of measurements, i.e., the distance between labial and tragus commissures (measure between the labial commissure and the tragus -MCT) and the distance between the lateral canton of the eye and the angle of the jaw. the prominence of the cheek (measure between the angle of the mandible and the lateral canton of the eye -MAC) was also measured. The measurements were made on the side where the avulsion occurred. The measurements were then added together and the difference between the ones before and after the surgery at the different controls, expresses the extent of facial deformation. The formula used is as follows: Edema = (MCT + MAC) at T1\2\3 - (MCT + MAC) at T0.

In order to evaluate the trismus, the distance between the incisal edge of the upper central incisors and the lower central incisors was taken as reference; the maximum inter-incisal distance (MID) that can be detected placing the patient in maximum oral opening. Measurements were made with a rigid ruler, preoperatively (T0) and postoperative at T1 T2 and T3. The measurements were repeated 3 times, and the average of the 3 measurements was then used as the kept value. Subsequently the difference between the postoperative measurements and the preoperative measurement was calculated according to the following formula: Trismus = MDI to T1\2\3 - MDI to T0.

The pain extent was measured using the Visual Analogue Scale (VAS). The VAS scale is a straight line of 10 cm with two ends corresponding to "no pain" and the "worst possible pain". It is a one-dimensional tool that quantifies what the patient subjectively perceives as pain, or as relief. The patient is asked to mark with a cross a point between the two ends of the line. Then the distance between the cross drawn by the patient and the end corresponding to "no pain" is measured with a ruler. The pain measured by the VAS scale is expressed with a 2-digit value that is the distance in millimeters between the two previously mentioned findings.

The general sensitivity of the skin of the face and of the lips is evaluated by touching the affected areas with the tip of a probe. Some useful questions are also asked to describe the eventual alteration of the sensibility. Operative times were recorded to evaluate their influence on the clinical course, in particular on the extent of oedema and of postoperative trismus. To test the effectiveness of treatment between the two groups, a statistical model represented by the t test for independent data was used. Statistical significance was assumed for a value of $p < 0.05$. All statistical analysis was conducted using SPSS software (SPSS for Windows version 11, SPSS Inc., Chicago, IL, USA).

## RESULTS

Forty-three patients were considered suitable for this study. They were divided into two groups: the test group made of 21 patients and the control group made of 22 patients. Three patients were excluded from the study because they did not show up for

one or more check-ups. Ultimately, data from 40 patients, 20 in the control group and 20 in the test group were analyzed. In the control group, the age range was between 15 and 41 years with an average of 24.6 years while in the test group the age range was between 18 and 34 years with an average of 26.7 years. In addition, the male/female ratio was 12/8 in the control group, and 11/9 in the test group.

*Post-operative edema*

At the first check the extent of the edema was significantly lower (p=0.0018) in the test group than in the control group, reporting values of 2.2±0.7 cm for the control group and 1.3±0.5 cm for the test group. At day 3, facial edema was significantly reduced in both groups but to a greater extent in the test group, 1.2±0.3 cm for the control group and 0.5±0.3 cm for the test group, respectively; also in this case the difference was statistically significant (p=0.0001). At the removal of sutures, facial edema had normalized in both groups, in fact no significant differences were found (p=0.0739). The submucosal infiltration of betamethasone significantly reduced facial edema on the first day of 58% and on the third day after surgery of 26.5% (Table I-II).

*Post-operative trismus*

The trismus extent detected on the first post-operative day was of considerable magnitude in both groups but to a greater extent in the control group, 1.7±0.8 cm in the control group and 1±0.7 cm in the test group, respectively. On the third day, there was a reduction of trismus in both groups; its extent was considerable in the control group, while in the test group the reduction was much less marked. Despite this, the magnitude of trismus on the third day was on average lower in the test group than in the control group, 1±0.7 cm in the controls and 0.8±0.7 in the tests, respectively, even if this difference was not statistically significant (p=0.1041). At final inspection, the trismus had disappeared in both groups (Table III-IV).

*Post-operative pain*

We found a statistically significant reduction (p=0.0001) of pain that the patients felt in the test group compared to the control one. It was significantly lower on both the first and third post-operative days. At the final check, no patients experienced any kind of pain (Table V-VI).

*Neurological examination*

Mild and transient alterations in sensitivity in the area of innervation of the inferior alveolar nerve were detected in 3 patients, 2 belonging to the control group and 1 to the test group, in the immediate postoperative period on day 1 and day 3. All patients regained normal sensitivity at the final control.

*Evaluation of surgical times*

There was no significant difference in operative times in the two groups examined. However, a significant increase in oedema and trismus were found with increasing operating times (Table VII).

## DISCUSSION

The application of a rigorous surgical protocol combined with a correct post-operative management allowed to reduce complications and improve the clinical course of patients treated for every surgical treatment, included third molar avulsion also (29-31). Surgical trauma cannot be eliminated, as it is related to the necessary intervention steps such as osteotomy for exposure of the dental elements.

In this study, we sought to reduce surgical trauma complications by using corticosteroids, specifically, by 4mg-betamethasone submucosal infiltration. The administration of corticosteroids in different dosages and by different intake methods is effective for pain, oedema and trismus control. In fact, corticosteroids, by inhibiting the mediators of inflammation, reduce the vascular exudate and the consequent edema. They also have some analgesic effects derived from their anti-inflammatory action and prostaglandins inhibition.

Although corticosteroid intake was more effective within the first 24 h after surgery, their benefit was also detectable within the first 3 postoperative days. Baxendale et al. demonstrated the efficacy of oral administration of 8 mg dexamethasone prior to surgery in 50 patients, reporting a significant

**Table I.** *Effects of submucosal infiltration of betamethasone on the edema on the first day and on the third day after surgery*

| Variable | Group Control | Group Test | Value P |
|---|---|---|---|
| **Edema** | | | |
| Day 1 | 2.2 ± 0.7 | 1.3 ± 0.5 | 0.0018 |
| Day 3 | 1.2 ± 0.3 | 0.5 ± 0.3 | 0.0001 |
| Suture removal | 0.1 ± 0.1 | 0 | 0.0739 |

**Table II.** *Bar graph showing the effects of submucosal infiltration of betamethasone on the edema on the first day and on the third day after surgery*

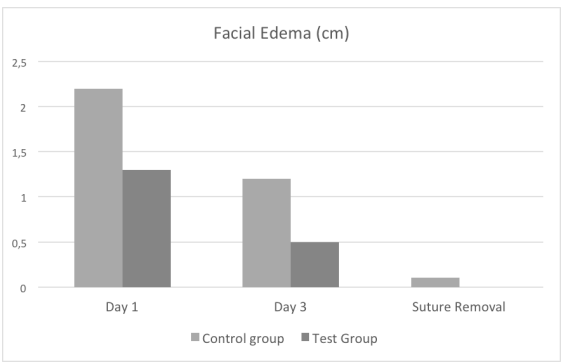


**Table III.** *Effects of submucosal infiltration of betamethasone on the trismus on the first day and on the third day after surgery*

| Variable | Control Group | Test Group | Value P |
|---|---|---|---|
| **Trismus** | | | |
| Day 1 | 1.7 ± 0.8 | 1 ± 0.7 | 0.0468 |
| Day 3 | 1 ± 0.7 | 0.8 ± 0.7 | 0.1041 |
| Suture Removal | 0.1 ± 0.1 | 0 ± 0.1 | |

**Table IV.** *Bar graph showing the effects of submucosal infiltration of betamethasone on the trismus on the first day and on the third day after surgery*

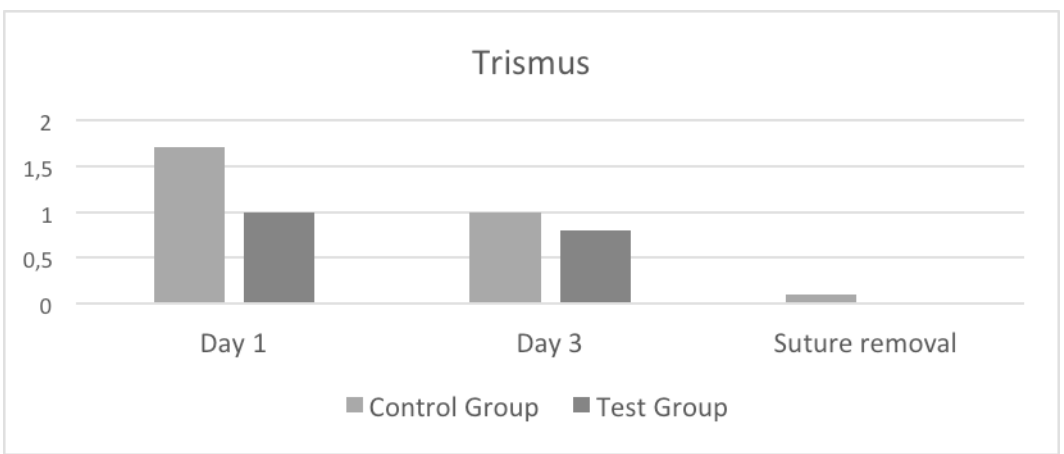

**Table V.** *Effects of submucosal infiltration of betamethasone on the pain on the first day and on the third day after surgery*

| Variable | Control Group | Test Group | Value P |
|---|---|---|---|
| **Pain** | | | |
| Day 1 | 6.4 | 4.1 | 0.0001 |
| Day 3 | 4.8 | 2.3 | |
| Suture Removal | 0 | 0 | N.D. |

**Table VI.** *Line graph showing the effects of submucosal infiltration of betamethasone on the pain on the first day and on the third day after surgery*

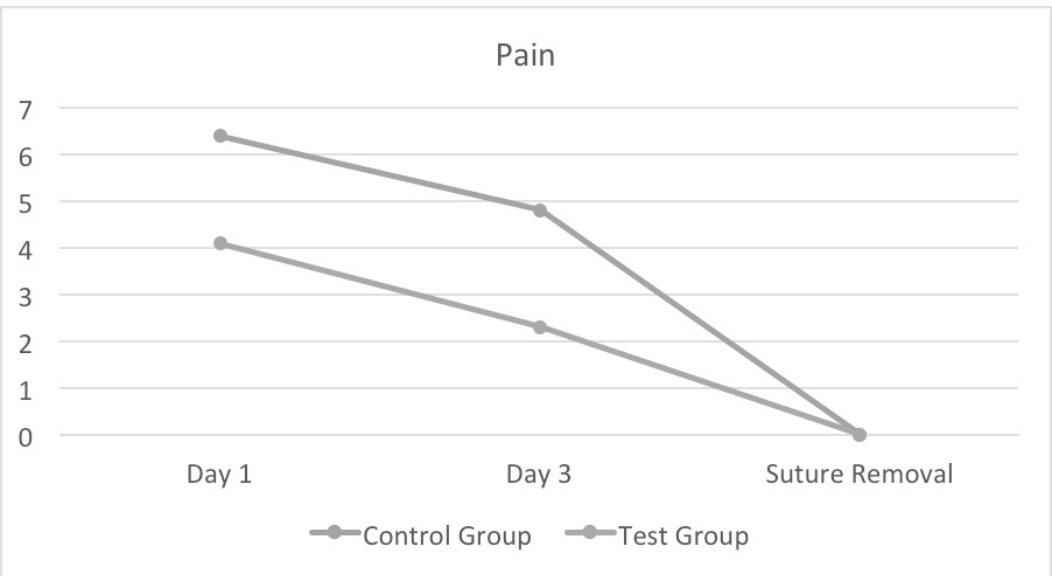


**Table VII.** *Surgical times in the two groups examined*

| | Control Group | Test Group | Value P |
|---|---|---|---|
| Surgical Time | 21.8 ± 10.6 | 20.5 ± 12.6 | 0.69 |

decrease in pain and oedema, but without significant changes on trismus (32). Beirne and Hollander found that pre-surgical intravenous injection of 125 mg methylprednisolone did not significantly reduce trismus but led to a significant pain reduction on the first postoperative day compared to placebo and an important edema reduction up to 3 days after the surgery (33).

Milles and Desjardins confirm that methylprednisolone was effective in reducing oedema compared to placebo at 24 and 48 h after surgery, but no significant effects on pain and trismus reduction were observed (34). Pedersen et al detected a 50% reduction in trismus and oedema and a 30% reduction in pain with intramuscular preoperative 4 mg dexamethasone administration in the masseter muscle (35). Neupert et al. reported a significant reduction in pain and trismus with 4 mg dexamethasone intravenous injection but this did not significantly improve the degree of oedema compared to placebo (36).

A recent meta-analysis by Markiewicz et al. that considered 12 articles, confirmed the corticosteroids powerful effects in reducing trismus and oedema in the postoperative period but found no significant reduction in pain (37). Many authors have associated the administration of corticosteroids and non-steroidal anti-inflammatory drugs (NSAIDs), showing greater efficacy in reducing swelling and pain. In a clinical study on 45 patients, Buyukkurt et al. reduced trismus and pain by combining diclofenac intake with intramuscular infiltration of prednisolone, but they did not observe any significant reduction in edema (38). Lin et al. reported an improvement in postoperative oedema following the combination of 50 mg diclofenac with 10 mg of oral prednisolone (39). Tiigimae-Saar et al. associated 120 mg of etoricoxib and 30 mg of prednisolone taken orally after surgery, reporting a greater improvement in pain and oedema and a greater reduction in trismus compared to the administration of etoricoxib alone (40).

This study showed that a single administration of submucosal 4mg-dose betamethasone reduced oedema by 58% on day 1 and 26.5% on day 3; the trismic reduction was 5.2 mm on the first postoperative day, but the difference was not significant on day 3. The pharmacological treatment was associated with less pain on day 1, but this difference disappeared by day 3. There are no significant differences in sensitivity in the two groups. New technologies help us in surgical procedures to be less invasive towards the patient (41-44).

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# TOOTH AGENESIS: PART 1. INCIDENCE AND DIAGNOSIS IN ORTHODONTICS

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**Dental agenesis has a great clinical significance due to its frequency during daily practice and the therapeutic problems that can arise from it. This paper will explore the incidence of dental agenesis, its diagnosis and how this anomaly affects the teeth differently. The second subsequent paper will look at its treatment and management.**

*Incidence of tooth agenesis*

Dental agenesis is a very common developmental anomaly in humans, which can lead to important clinical problems (1). In the last decades, the clinicians have observed a significant increase in the cases of agenesis. It is not clear whether this observation is the result of a real evolutionary trend or it is the result of more advanced screening and diagnosis procedures for dental anomalies (2,3). Considering the most recent works in the literature, a greater frequency of agenesis can be observed in the European population rather than in the Asian, American and African populations, combined or not with other skeletal changes (4-6). The incidence of agenesis of permanent teeth ranged from 2.6% to 11.3%, depending on the different demographic and geographical profiles, except for the third molars, which are absent in 9-30% of the population (7).

In most cases of agenesis (80%) there is a lack of development of one or few teeth (hypodontia), while the prevalence of severe forms of agenesis gradually becomes more rare (8). The agenesis of three or more permanent teeth was observed in 1% of the population, while the agenesis of six teeth or more teeth (oligodontia) in 0.1% (14). The incidence of agenesis in primary dentition is considerably lower; it is 0.4-0.9% in the European and Brazilian population, and about 2.4% in the Japanese population. The absence of a single deciduous tooth was detected in 60% of cases of agenesis, while the

*Key words: tooth agenesis, dental agenesis, hypodontia, oligodontia, orthodontics, diagnosis*

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absence of more than two deciduous teeth can be found in 8% of children with deciduous hypodontia.

Specific patterns of agenesis in the permanent dentition have been investigated: unilateral agenesis was found to be more frequent than bilateral, whereas the absence of the third molars and of the second premolars usually affects all quadrants and it is often found in combination with these two types of agenesis and a lack of development of the incisors (9). The possible relationship between the agenesis of primary dentition and the presence/absence of succedaneums dental elements remains controversial; several Authors argue that the failure of development of a deciduous tooth is closely associated with an increase in the prevalence of agenesis of the corresponding permanent element (10).

The overall frequency of agenesis is similar between the right and the left side and, in permanent dentition, between the maxilla and the mandible, although the frequency differs in the two jaws when considering individual dental typologies. Although no preference in side is shown, the upper left incisor is more frequently absent than the right one, probably because the unilateral palatine cleft, which often associates with the growth of that tooth germ, affects more frequently the left hemiface (11). Some studies also reported a more frequent localization of ageneses in the posterior part of the jaws, followed by the frontal region of the maxilla, the middle part of the maxillary and mandible, and finally the mandibular anterior region (12). The prevalence of agenesis in both dentitions is significantly higher in females than males, with a male: female ratio of 2:3 for white and 1:2 for black people.

To date, it is not established nor accepted by the scientific community an etiological theory that justifies this specific and recurrent distribution of agenesis. From these data emerges that the tooth that is more subjected to numerical variations is the most distal of each morphological class.

In the Caucasian population, the teeth that are most frequently affected by agenesis are the third molars, followed by the lower second premolars, the lateral incisors and the upper second premolars, by the lower central incisors and by the maxillary and mandibular first premolars (10, 13, 14). Some studies found that the agenesis of the lateral incisor, both inferior and superior, is more frequent that the agenesis of the second premolar. In the primary dentition, the teeth that are most affected by agenesis are the upper lateral incisors followed by the lower central and lateral incisors. The upper central incisors, the first molars and the lower canines are the most stable permanent elements, showing rarely a lack of development. Unlike dental agenesis, the prevalence of supernumerary teeth varies between 1.5%-3.5%, and in 80% of the cases there is a single additional element, frequently located between the upper incisors (mesiodens) (12, 15).

Dental agenesis usually occurs as isolated anomalies, but may also be a typical appearance of many malformative syndromes such as cleft palate and lip. When associated with clefts, the agenesis is mainly due to dental elements located in the oral region within the cleft (mostly lateral incisors); it has also been observed that in patients with this problem, a lack of teeth in other parts of the mouth is more common than in the general population, presumably due to the common etiology at the base of the two developmental alterations.

The origin of syndromic agenesis is commonly found in the alteration of some genes, whose functions are critical to the development of various organs (16,17). Syndromes in which congenital absence of dental elements can be detected are, among other things, ectodermal dysplasia and Down syndrome. In many syndromes, a typical agenesis pattern has been observed and in some cases, there is a significant difference from the overall population. A sizable portion of severe dental agenesis is part of more complex syndromes, meanwhile in several syndromes such as the Down syndrome, dental agenesis resembles common hypodontia and can only be observed in a subgroup of patients (18,19).

Therapeutic problems are aggravated by the fact that the diagnosis of the disease is much more delayed: it is possible to establish malocclusions that are secondary to the migration of the dental elements adjacent to the site of agenesis (20). Orthodontic play a fundamental role due to create or close spaces (21). At the end of the treatment, fixed retainers are used to maintain the result and avoid relapses (22-24).

*Diagnosis of tooth agenesis*

The diagnosis of dental agenesis is usually made at an early age, at the time of the transition from deciduous to permanent dentition, when there is a delay in the eruption of one or more dental elements. Only an X-ray examination allows establishing a certain diagnosis of congenital absence of a dental element. This is different from dental impaction (retention), which is a failure in dental eruption: the tooth does not appear in the oral cavity although its time of eruption has passed.

It should be kept in mind that the radiographic identification of a tooth is not possible until the tooth germ has started its calcification, which may occur at different ages. A radiographic examination of the dental arches (orthopantomography) performed at six years old should show the presence of the tooth germs of all permanent teeth, except for the third molars and sometimes for the second premolars which may begin their calcification process even at the age of eight (25). An accurate medical history allows us to identify if it is a true agenesis or if the missing teeth have not been earlier removed due to destructive caries, severe periodontal disease, traumas or orthognathic surgery (26-28). In this case, the missing tooth is replaced by implant surgery (29-34). Finally, in the presence of oligodontia or anodontia, more complex and severe syndromic conditions (e.g. hypohidrotic ectodermal dysplasia) have to be investigated, submitting the patient to accurate medical history and specialized medical examinations (35).

## CONCLUSION

The incidence of dental agenesis is 2.6-11.3% in the general population, except for the third molars (36). Tooth agenesis affects more frequently females and Caucasian population. Unilateral and less severe forms are more frequent than the bilateral ones. Permanent teeth are more affected than the deciduous one. Dental agenesis can be associated with many malformative syndromes (37). A panoramic radiography should be performed at the age of six to diagnose the absence of any permanent teeth (38).

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# TOOTH AGENESIS: PART 2. ORTHODONTIC TREATMENT AND PROSTHETIC POSSIBILITIES

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**Dental agenesis has a great clinical significance due to its frequency during daily practice and the therapeutic problems that can arise from it. This paper will explore all the aspects to consider in order creating a proper multidisciplinary treatment plan: in particular, orthodontic, prosthetic and implantologic therapeutic alternatives are described for the rehabilitation of the different areas of the dental arches. In fact, dental agenesis is a problem that often requires the intervention of specialists from the different fields of dentistry and its treatment must meet aesthetics needs, stomatognathic function and patient satisfaction.**

*Treatment of tooth agenesis*

In most cases of dental agenesis, the treatment is multidisciplinary; the branches mainly involved in the resolution of agenesis are orthodontics, preventive and conservative dentistry, dental prosthesis and oral surgery (1-4). The mainly therapeutic choices valid for all agenesis situations are:

- No therapy at all: when the space left by a missing tooth closed spontaneously without deviations of the median lines nor interferences; in absence of the permanent tooth, if the deciduous tooth is healthy and without any sign of root resorption.
- Orthodontic space closure and alignment of the teeth that are adjacent to the gap: its goal is to keep the patient's natural dentition avoiding prosthetic rehabilitation but it involves premature orthodontic intervention, long-term retention and coronoplasties in the aesthetic region (1, 5-7).
- Orthodontic reopening or maintenance of spaces: it's performed for a subsequent prosthetic or implant-prosthetic rehabilitation; in growing patients it's suitable using removable or adhesive partial prostheses until the right time for positioning implant (8, 9).

For therapeutic purposes it is useful to classify dental agenesis on the base of their position in the dental arch, as follows (7):

- Agenesis in the anterior zone: when the missing tooth belongs to the morphological groups of the

*Key words: Tooth agenesis, dental agenesis, hypodontia, oligodontia, orthodontics*

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incisors and the canines.

- Agenesis in the middle zone: when the missing element is part of the lateral-posterior area which includes premolars and first molar.
- Agenesis in the posterior zone: when the agenesis affects the second and/or third molars (10).
- Combined Agenesis: when the agenesis affects simultaneously more than one of the above mentioned sites.

*Treatment of hypodontia in the anterior zone*

In the anterior region, the permanent teeth most affected by agenesis are the upper lateral incisors, followed by the lower central and lateral incisors. In case of upper lateral incisor agenesis, the first therapeutic alternative is space closure by means of mesialization of the entire unilateral sector where the agenesis is located, so that the canine will replace the lateral incisor (11).

During the orthodontic treatment it will be important to move the canine medially without tilting its root and then to slightly alter the position of the first premolar, rotating it medially and performing a vestibular root torque to recreate the canine bumps. A coronoplasty will be performed on the mesialized canine by applying composite or through indirect restorations (e.g. ceramic veneers) (12, 13). This method involves the loss of the physiological canine guide, which must be replaced by the orthodontist with a lateral group function disclusion. Even the protrusion incisor guide is altered, because of a greater buccal-palatal width of the canine than that of the root of the lateral incisor; for this reason, it will be appropriate to lightly move it in a more vestibular position (11).

In case of unilateral agenesis before performing space closure it will be necessary to carefully consider if the canine can be modified to look like the contralateral incisor: in fact there can be a considerable gap between the heights of their gingival parable. Moreover, in some cases the characteristic vestibular profile of the canine cannot be disguised because the excessive thinning of the enamel would cause dentin hypersensitivity and discoloration of the tooth. It should therefore be emphasized that the permanent upper canines of female patients, lighter and less bulky, are more aesthetically adaptable (12).

In presence of a lateral conoid, it will be a good candidate for coronoplasty. Space closure in case of bilateral agenesis can give less aesthetic problems and can be facilitated by a proper extraction of the deciduous teeth, to stimulate the eruption in a mesial position of the upper canines, which very often may remain impacted because of the absence of a mesial guide for their eruption due to the lack of the lateral incisors (14).

Space closure is indicated in biprotrused patients, in dental crowding with dentoalveolar discrepancy that requires extractions, in skeletal class II where the diminished dimensions of the teeth in the upper arch will be used to compensate for the discrepancy between the two arches, in hyperdivergents, in convex profiles with closed nose-lip angle.

The greatest benefit of closing the space is avoiding a non-prosthetic therapy and its consequent maintenance (7). In addition, the presence or absence of a Class I relationship of the canines showed no association with occlusal function or with signs and symptoms of temporomandibular disorders (15, 16). In the presence of increased overjet the closure of the space is also carried out with a more palatal movement of the central incisors.

In Class I and III malocclusion with dentomaxillary disharmony and Class II with and without crowding, the closure of the space (especially if agenesis is bilateral) is part of a global orthodontic treatment plan that often involves extraction of the first or second premolars at the mandibular arch. The second therapeutic alternative in cases of agenesis of the lateral incisors, which is the opening of the spaces with subsequent prosthesization, has the advantage of maintaining a complete occlusal joint with the possibility of obtaining correct occlusal keys and correct gnathological relationships between the arches. These are physiological and therapeutic choices which should be pursued especially in presence of a skeletal class III, of an anti-clockwise growth tendency and a brachyfacial type, of an open nose-lip angle, of a concave profile, and in absence of dental crowding (7,17,18).

The opening of the spaces in the upper lateral incisor site is obtainable with simple orthodontic

appliances and can be more or less rapid depending on the entity of the mesial migration of the canines. Osseointegrated implants can replace missing elements without any modification of the adjacent teeth and ensure, from a functional point of view, the restoration of normal canine and incisal guides.

Preliminary orthodontic preparation will have to create the appropriate space to accommodate the implant (7, 19-21). The orthodontist will have to carry out dental movements maintaining the parallelism of the roots of the teeth and also controlling periodontal health of the dental elements contiguous to the agenesis space to obtain optimal aesthetic results (22). The agenesis of the lower incisors, especially if isolated, it is not a particular functional problem and the elective treatment in these cases is the closure of the space. Space closure in the lower frontal area is facilitated by the similarity between the central and the lateral incisors, the exposure of their mesiodistal dimensions and the natural tendency to crowding in the site (7). The closure of the spaces here avoids the need for prosthesis in an area, which is not well suited to prosthetic rehabilitation with traditional methods (23).

When there is only one incisor missing, an alternative could be to close the space increasing the mesiodistal dimensions of the present incisors with composite (7). If there is the absence of two lower incisors, the indications for space closure are reduced: this therapeutic choice will be used only in case of crowding in the upper arch, combining the closure of the lower spaces with the extraction of two upper premolars (24). In fact, since the closure of the space of two incisors requires a considerable mesialization of the canines, unless the extraction of the two upper premolars is performed simultaneously, the class I ratio between the two arches is lost. The opening of the spaces in the lower frontal sector doesn't present particular difficulties in terms of biomechanic but it must be remembered that the lower intercanine diameter cannot be successfully long-term expanded because it tends to decrease spontaneously (25).

In case of three or four permanent inferior incisors agenesis, it's necessary to maintain as long as possible the deciduous incisors which often suffer from a massive abrasion that almost consumes their crowns. After growth is completed, removable or fixed prostheses will be manufactured (26,27). The agenesis of the upper central incisors poses an indisputable aesthetic problem and, by moving the median line, it causes occlusal disorders (7). Closing space would consist in mesially shifting the unilateral elements to the agenesis, transforming them aesthetically and adapting them functionally to the role of the tooth that precedes in the arch (28). Moreover, due to the high aesthetic and functional value of these teeth, it's preferred to open and/or maintain the spaces for their implant-prosthetic replacement (5,23,29).

The agenesis of the canines is very rare. If this occurs, it is better to close the spaces by means of mesialization of the premolars in class I and the distalization of the incisive group in class II subjects. Any extraction of the inferior first or second premolars depends on the presence or absence of dentomaxillary discomfort at the mandible (7).

*Treatment of hypodontia in the middle zone*

The most frequently absent tooth is the lower second premolar, followed by the upper second premolar. The ageneses of the first premolars and first molars are very rare (30). The typical patient suffering from congenital deficiency of the second premolar has a first molar and canine dental class with dental crowding, which will be reduced or absent in quadrants affected by agenesis (31). After evaluating the dentoalveolar discrepancy, it is possible to close the spaces prior to extraction of the premolar antagonists, to balance the two arches (7).

In case of agenesis of the lower premolar, in class I and III, the upper second premolars will be extracted, meanwhile in presence of class II, the upper first premolars will be extracted. If all the four-second premolars are missing, the best choice is to close the space in all types of malocclusions, except for profilometric considerations. The closure of the space can be made at the time of the fall of the second deciduous molar. Sometimes, especially in the case of a lower second premolar, it is better to extract the second deciduous molar prior to the eruption of the first permanent molar to create the most favorable conditions for spontaneous closure

of the space and to avoid undesired inclinations of the molars. This last solution is not indicated in patients with diastemas in the lower arch and/or deep bite (32).

Alternatively, it is possible to open the spaces (in case of diastemes, hypodivergence or biretruded) keeping as much as possible the second deciduous molars and intervening with traditional or implanted prosthetic solutions at the time of its loss. The agenesis of the first premolars provides indications and therapeutic modalities quite similar to those given for the agenesis of the second premolars. In the presence of agenesis of the first molars, if the second molar spontaneously migrated into a mesial position, it is recommended to upright the tooth and to close the spaces (12).

*Treatment of hypodontia in the posterior zone*

In the posterior area, the tooth most frequently affected by agenesis is the third molar. Its congenital deficiency doesn't require treatments (7). If the second permanent molar is missing, the orthodontic solution is the closure of the space by means of mesialization of the third molar, whether normally formed and correctly erupted, or in the interruption of the dental arch at the first molar, if the third molar is missing or damaged. This last solution does not affect chewing, but the antagonists of the missing tooth will extrude due to the absence of occlusal contact. In this case, the opening or maintenance of the space followed by implant restoration of the second missing molar can be a good option (33).

*Treatment of anodontia and oligodontia*

Oligodontia and anodontia often require complex and long-lasting treatments. In cases of anodontia there is the problem of an immediate restoration of the chewing function by means of traditional removable prostheses. In the formulation of the treatment plan the clinician must evaluate, the aesthetic, functional and economic needs of the patient, as well as their oral hygiene and the status of the edentulous crest. In subjects affected by anodontia, the defect in the alveolar bone makes it difficult to realize total removable prostheses with adequate retention and stability (7,34). In addition, an improper removable prosthesis may result in further aggravation of the bone defect.

An implant-fixed rehabilitation requires a sufficient amount of bone as well. Cases of oligodontia generally require a multidisciplinary treatment. A first orthodontic stage is followed by the prosthetic rehabilitation that is divided into a provisional phase, during growth, and into a subsequent definitive rehabilitation, at the end of the development.

In the provisional phase are taken into consideration the psycho-social and functional aspects of the rehabilitation of the patient and the possibility of anchorage for the movements and uprighting of the teeth in the perspective of using them as prosthetic pillars, as well as the association with maxillo-facial dysmorphism that may require the use of orthognathic surgery to solve discrepancies between the skeletal bases (7,35). In presence of large edentulous spaces, temporary removable prostheses could cause prolonged inflammation of the soft tissues and emotional discomfort in young patients and they should also be recreated from time to time to follow the growth of the jaw bone (7).

Once the orthodontic problems are solved, good static and dynamic occlusion has been obtained, and final growth is completed, definitive solution like implantology can be performed (36). Patients with oligodontia also show an increased prevalence of external root resorption associated with orthodontic treatment. This can be caused by an altered anatomy or by heavy orthodontic movements of the dental elements required in this type of patient. A radiographic follow-up is therefore recommended for 6-9 months after the end of orthodontic therapy to detect early radiographic resorption signs (7).

## DISCUSSION

The treatment of agenesis involves several fields of dentistry such as orthodontics, preventive and conservative dentistry, prosthesis and oral surgery (37-40). In the coordination of the treatment plan, the orthodontist certainly plays a major role. The choice of the best therapeutic solution must be made on the evaluation of the functional and aesthetic needs

of each individual to promote proper development, phonation and nutrition of the patient.

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# BI-LAYERED COLLAGEN NANO-STRUCTURED MEMBRANE PROTOTYPE COLLAGEN MATRIX CM-10826 FOR ORAL SOFT TISSUE REGENERATION: AN *IN VIVO* ULTRASTRUCTURAL STUDY ON 13 PATIENTS

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**A new developed collagen matrix CM-10826 (CM) of porcine origin designed to be used as oral soft tissue substitute was investigated before and after implantation by light microscopy (LM), scanning electron microscopy (SEM), and transmission electron microscopy (TEM). In a case series biopsy specimens were harvested from thirteen patients at 10, 20, 30, 43 days after abutment surgery for uncovering dental implants. The in vivo histological evaluations of each patient were performed via micro-coring of newly formed oral mucosa in the area covered by CM (test side) or left uncovered (control). Results showed that CM can be integrated in connective and epithelial tissues within 10 days, can be completely resorbed within 20 days and it is able to reduce inflammatory infiltrates and to stimulate both fibroblast/epithelial cell proliferation and neo-angiogenesis. Generally it seems to be superior in promoting soft tissue healing compared to that induced by secondary intention healing. Furthermore, it is able to act as a scaffold for soft-tissue regeneration, allowing the proliferation of keratinocytes from the wound edges and favoring neovascularization and growth of connective tissue in the mesh of porous layer. It appears that a CM might function in oral surgery as a substitute for autologous grafts and to avoid secondary intention healing in soft tissue defects.**

Keratinized gingiva (KG) is a part of oral mucosa covered with keratin or parakeratin that includes the free and attached gingiva. KG extends from the gingival margin to the muco-gingival junction. Keratinocytes account for 90% of the cell population of KG. The more undifferentiated, highly proliferating elements reside in the basal stratum, linked to each other and attached to the basal lamina by multiple adhesion receptors, including members of the integrin family. These integrins are able to recognize multiple component of the extra-cellular matrix (collagen, fibronectin, laminin) and therefore to activate intracellular signalling pathways, which regulate migration, proliferation, survival and differentiation (1-5).

Keratinocyte differentiation progresses from the

*Key words: collagen matrix, collagen membrane, gingiva, oral implant, histology*

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basal to the stratified superficial layer, where the cells, in parallel to decreasing proliferation, progressively acquire size and expression of higher molecular weight cytokeratins. This process is modulated by both intra and extracellular stimuli. The end of the differentiation pathway is the formation of keratinized or parakeratinized gingival tissue.

Some studies suggested a minimum of KG to maintain gingival health, while several others have shown that the absence of KG is compatible with the maintenance of periodontal health (6-9). Orthodontic treatment can be helpful for the periodontologist thanks to the evolution in retention and stability systems in terms of space maintenance and dental movements (10-14). It has not yet been demonstrated that in dental implants the presence of keratinized mucosa (KM), i.e. the implant counterpart of KG, is a prognostic factor for their survival (14). However, experimental studies in monkeys and humans have demonstrated that the lack of KM increases plaque accumulation around implants but the influence of this condition on the survival of the dental implants has not yet been demonstrated in humans. Besides, Zigdon & Machtei (2008) have shown that both the peri-implant width and thickness of KM may be inversely correlated with the recession of the mucosa (15).

In order to augment gingival tissue dimensions, free gingival grafts and free connective grafts have been proposed with similar clinical predictability (16,17). The use of biomaterial, like cellular dermal allografts, has also been performed to overcome the limitation of source of donor's tissue, to reduce morbidity and to allow a better colour and texture integration, but the increase of KM may be less than with an autogenous transplant (18-22). Moreover, *in vitro* analysis suggests that fibroblast seeding on a cellular dermal allograft can allow good conditions for cell adhesion and proliferation (23-25). The use of a tissue created by seeding oral keratinocytes on collagen membranes of porcine origin has also been evaluated (26-29).

More recently the use of a collagen matrix of porcine origin has proven to be as effective and predictable as the connective tissue graft for increasing the width of KG and to be associated with a significantly lower patient morbidity (30-36). A new bi-layer nanostructured collagen matrix CM-10826 (Geistlich Pharma AG, Wolhusen, Switzerland) was developed to be used as a conductor for intra-oral soft tissue regeneration. The biological principles of interaction between epithelial cells and collagen matrix CM-10826 (CM), which lead to the development of KG, has been investigated both *in vitro* and in a case report in vivo, but the biological principles and the ultra-structural *in vivo* behaviour of the matrix are still not clear (37,38).

The aim of the present study is to verify, by means of light microscopy (LM), scanning electron microscopy (SEM) and transmission electron microscopy (TEM), the *in vivo* behaviour of CM in humans, when used for grafting oral soft tissue defects.

## MATERIALS AND METHODS

The experiments were performed with the understanding and written consent of each subject and according to ethical principles, including the World Medical Association Declaration of Helsinki (2008) and was independently reviewed and approved by the General Direction of Drugs and Medical Devices of the Department of Innovation of Ministry of Health and the ethical board of the University of Verona (protocol number 10826-05).

### *Physical and chemical features of CM-10826*

CM-10826 is classified as an implantable, resorbable medical device class II, allowing permanent contact with bone and the periosteum. Cellular components and other molecules are removed with a standardized purification process, while collagen is kept in a native form. Collagen fibres are made up of 50-80 nanometre fibrils. The membrane is build up as 3D-matrix with two juxtaposed layers, formed by a compact (hard) layer on one side and a porous (soft) layer on the other one. The compact layer, formed by compact collagen fibres, which allow suturing procedures, plays a role of protection through selective exclusion against cells. On the contrary, the porous layer, formed by loose collagen fibers in which open pore sponge system is present, is organized in a 3-D network with pore diameters ranging from 40-60 μm that promotes cells infiltration. The micropores width is intended to facilitate fibroblast migration, angiogenesis and to stimulate resident keratinocytes' growth (42).

*Patient selection*

Thirteen, non-smoking volunteers (11 females and 2 male, mean age 53 years, SD=9 years) were selected among patient treated at the University of Verona for total edentulism receiving bilateral implant surgery with at least four implants for each arch, according to the standard two-stage protocol (39). All patients had a negative medical history for pathologies generally contraindicating implant surgery (40). In several cases previous pre-prosthetic surgery to restore a sufficient bone volume for implant rehabilitation of the jaws was performed. All patients had healthy oral mucosa before the surgical procedure.

*Surgical Protocol*

The reconstruction of keratinized peri-implant tissues was planned with the use of a split-thickness apically positioned flap, covering the exposed connective tissue with CM on test side and leaving the area for secondary intention healing on control side, as illustrated in Fig.1 (split mouth). A full arch para-crestal horseshoe shaped incision was made, palatal to the supposed position of the implant. This incision was performed partial thickness to avoid the risk of severing the palatal artery. A partial-thickness flap was then raised from the palatal incision towards the vestibular side to identify the implants.

After insertion of the healing caps over the implants, the elevated partial-thickness flap was firmly secured more apically on the vestibular side of the crest using simple periosteal anchored sutures, deepening the oral vestibule. The apical positioning of the palatal flap resulted in an area of extensive bleeding leading to secondary intention healing, extending the entire length of the crest.

According to the split-mouth design, Fig. 2 and Fig. 3 show how the membranes were placed randomly on the left or right side (test), leaving the opposite side for secondary intention healing (control). The membranes were properly shaped to the recipient site to cover the exposed palatal area and partially placed underneath the vestibular displaced flaps.

Particular attention was given to the complete closure and stabilization between the membrane and the soft tissue. Horizontal mattress sutures, extending from the periosteum on the vestibular side to the palatal side and passing over the graft, were placed along the whole perimeter of the surgical site. These sutures guaranteed satisfactory membrane stability minimizing the gap between CM and the underlying connective/periosteal bed. One gram of amoxicillin/clavulanate every twelve hours for 6 days was prescribed for the patient together with ibuprofen tablets. Clinical pictures were taken before and after surgery and subsequently at 3, 7, 15 and 30 days after surgery with a digital camera Canon D100, using

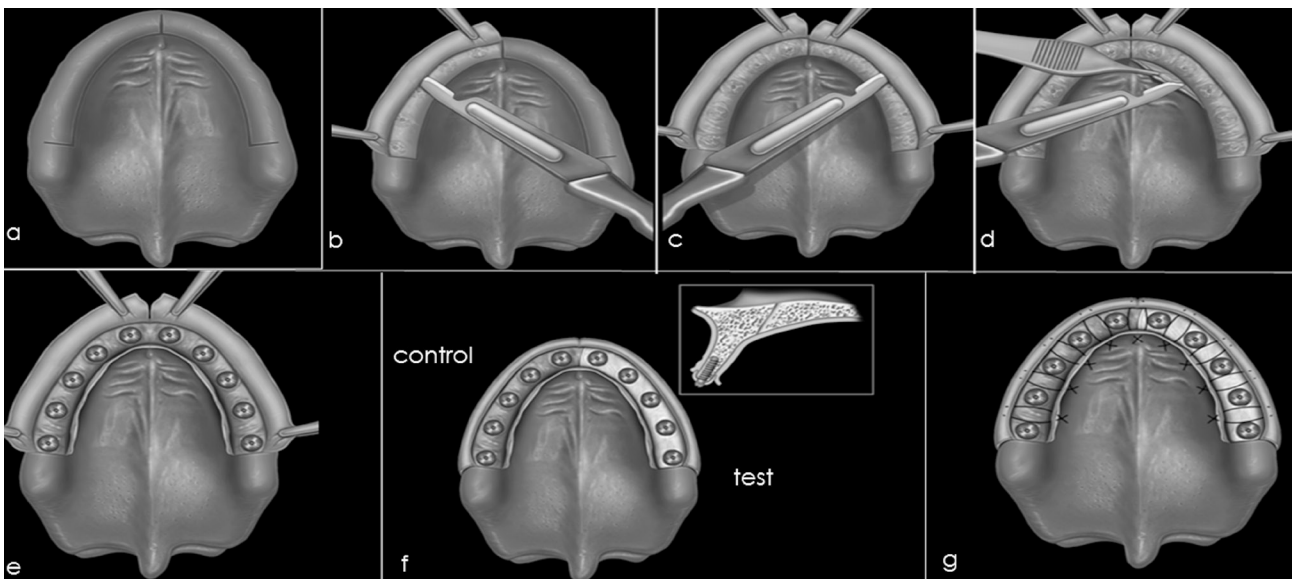


**Fig. 1**. *Edentulous ridge (**a**). Incision and partial thickness dissection (**b-d**). Insertion of transmucosal healing abutments (**e**). Matrix collagen membrane in situ (**test**) uncovered wound (**control**) (**f**). Suture (**g**).*

lens perpendicular to the alveolar ridge through the use of a mirror bite.

*Histological evaluation*

The *in vivo* histological evaluations of each patient were performed via micro-coring of newly formed oral mucosa in the area covered by CM (test side) or left uncovered (control), thus allowing to obtain a specific qualitative analysis. Biopsies were performed at different times of healing (10, 20, 30, 43 days) in different patients to follow the healing process. Samples were processed for light microscopy (LM), scanning electron microscopy (SEM) and transmission electron microscopy (TEM).

*Light Microscopy (LM)*

The samples were fixed with paraformaldehyde (4%) in phosphate buffer pH7.4, dehydrated with increasing graded ethanol, diafanized with xylene and embedded in paraffin.

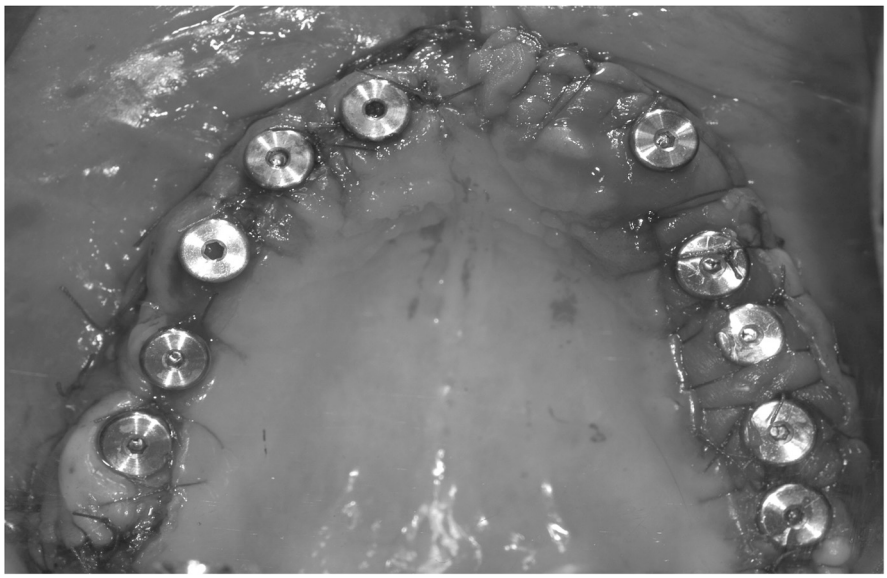

**Fig. 2**. *The right test and left control side after surgery.*

**Fig. 3**. *The healing phase after 43 days: the right test and the left control.*

The specimens were then cut with a microtome (1150 Auth, Reichert Jung, Wien, Austria) obtaining sections of 7-8 μm in thickness, stained with Gomori trichrome stain and toluidine blue. The observations were performed by a LM (Olimpus, Olympus Italia Srl, Milan, Italy).

*Scanning Electronic Microscopy (SEM)*

The fixed samples were dehydrated in acetone at increasing gradation, then dried with critical-point dried (CPD 030 -Balzers, Vaduz, Liechtenstein), fixed on stubs with colloidal silver paste and coated with Colloidal Silver and Gold by MED 010 (Balzers, Vaduz, Liechtenstein). The observations were performed with a SEM (DSM950, Zeiss, Oberkochen, Germany).

*Transmission Electronic Microscopy (TEM)*

The samples were fixed with gluteraldehyde (2%) in 0.1 M Sorensen buffer for 2 hours, post-fixed with osmium tetroxide (2%) in the same buffer for 1 hour, dehydrated in increasing grades of acetone, embedded in epoxy resin (Epon-Araldiste), and cut with a microtome (UltraCut, E-ultramicrotome, Reichert Jung, Wien, Austria). The thin sections obtained were stained with leaded citrate and uranyl acetate. The observations were performed with a TEM (Philips Morgagni, Philips, Monza, Italy).

## RESULTS

Clinical examination during follow-up demonstrated the absence of complications on the test side. Once the healing process was completed and CM membrane was completely resorbed, a normal mucosa without discoloration and irregularities was reestablished.

*Ten days from surgery*

- LM Analyses

Fig. 4a-b-c-d show photomicrographs of control samples clearly showed well preserved gingival structures, with flattening of the papillae of the *tunica propria* showing signs of inflammation and scarce neo-formation of vessels. Deeply located, in the *tunica propria,* a cleavage plane was often visible, as illustrated by the arrow in Fig. 4d, which separated the deeper layer from the superficial one.

The test samples (Fig. 4e-f-g-h) showed a normal aspect of epithelium with well developed papillae of *tunica propria*, without signs of inflammation and an abundant neo-angiogenesis. Moreover, fibroblasts, mastocytes and other inflammatory cells appeared to be present in the remnants of the collagen bundles of the membrane towards the superficial layer, as shown in Fig. 4h. No cleavage plain was present between the deeper layer and the superficial one.

- SEM Analyses

Control samples showed that the epithelial layer was always well represented and the layer of connective papillae was thinner compared to the test side with CM membrane. The reticular layer appeared to have a normal structure. SEM observations of test samples showed that the epithelial layer was well represented, with epithelial cells covering the superficial side of the membrane. The connective papillae appear well hydrated, thick and without inflammatory cells. Only scarce remnants of the membrane were present, as illustrated by the arrow in Fig. 5. The *tunica propria* had in general greater thickness on the test side compared to control side.

- TEM Analyses

Control samples showed microscopic fields with small amount of vessels. This small number of developed vessels displayed a demonstrable condition of angiopathy, displaying the lumen of capillaries partially closed (head arrow in Fig. 6c) by swollen endothelial cells (asterisks in Fig. 6b-c) arranged in a disorderly manner. Moreover, the fibroblasts seemed to be very active, as suggested by the abundant rough endoplasmic reticulum (Fig. 6a arrow-head). In the test samples the *tunica propria* was well vascularized and showed newly-formed vessels (Figure 6e-f); the fibroblasts appeared mature without signs of fibrosis as seen in Fig. 6d arrow.

*Twenty days from surgery*

- LM Analyses

Control and treated samples clearly showed a normal reconstructed epithelial layer both in the control (Fig. 7a) and test side (Fig. 7b). In the former, the fibrotic aspect of *tunica propria* was always presents. Remnants of CM were absent on the test side.

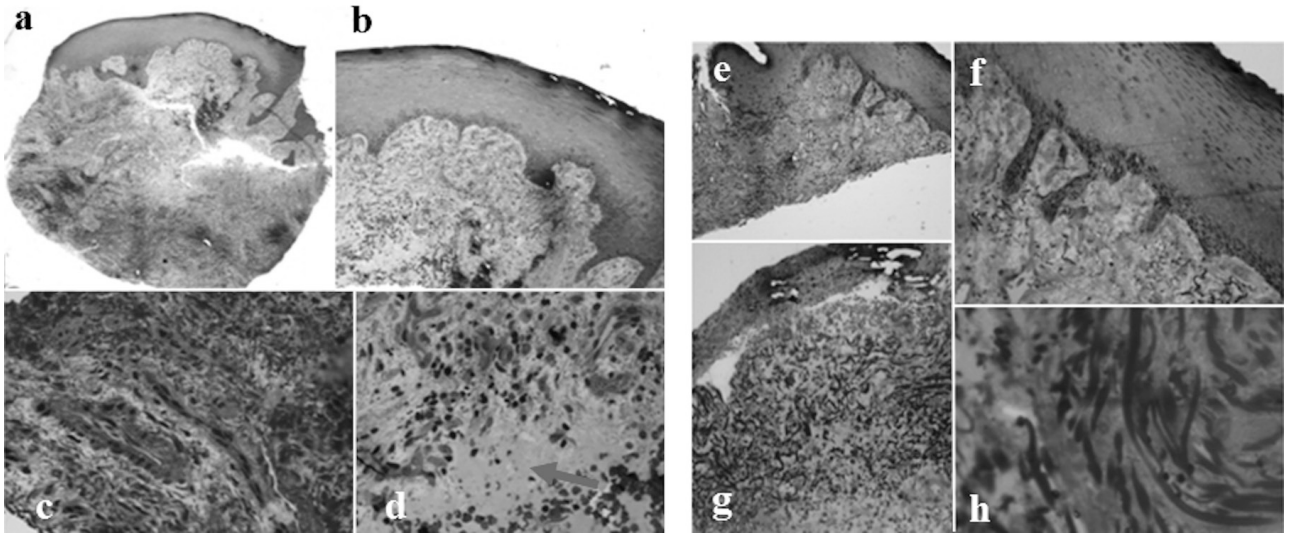


**Fig. 4**. *LM micrographs of control (**a-d**) and treated (**e-h**) oral mucosa 12 days from surgery. Toluidine blue staining. Magnifications: (**a**) x50; (**b**) x100; (**c, d**) x220; (**e**) x70; (**f**) x150; (**g**) x180; (**h**) x350.*
***Control side**: flattening of the papillae of the tunica propria showing signs of inflammation (**a, b**) and limited formation of new vessels (**c**). A cleavage plane is visible deep in the tunica propria, separating the deeper layer from the superficial one (arrow in **d**).*
***Treated side**: normal aspect of epithelium with papillae with a well-developed tunica propria (**e, f**), without signs of inflammation and evidence of abundant neo-angiogenesis (**g**). Various cells appear to invade the remnants of collagen bundles of the membrane towards the superficial layer (**h**), without any cleavage plain.*

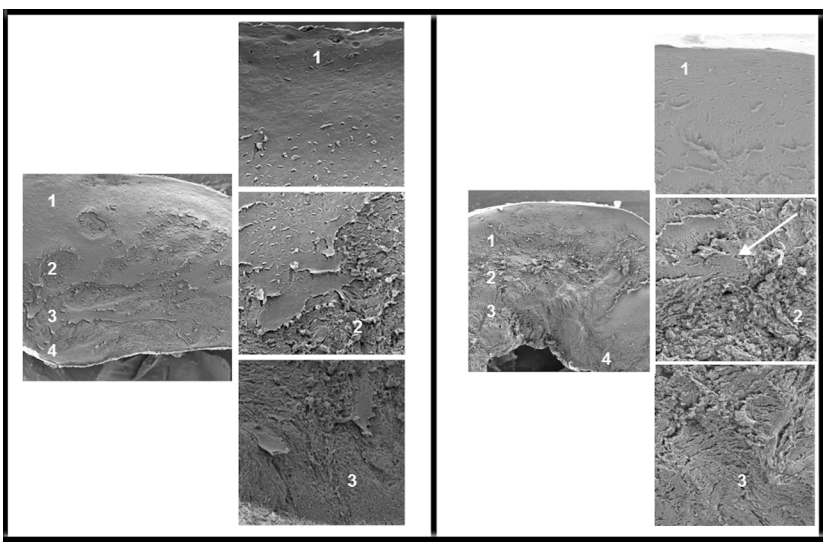


**Fig. 5**. *SEM micrographs 13 days from surgery. Magnifications: Control side (**left panel**) x100; enlargement x250. Test side (**right panel**) x70; enlargement x250.*
*Control side (**left panel**): well represented epithelial layer and thinner connective papillae compared to the test side (**right panel**); the reticular layer appears normally structured.*
*Test side (**right panel**): well represented epithelial layer with cells covering the superficial side of the membrane; clearly visible, thick connective papillae without inflammatory cells, with little visible remnants of the membrane (**right panel: arrow in 2**). **1**=Epithelium; **2**=Papillary layer; **3**=Reticular layer; **4**=Submucosa.*

- SEM Analyses

A more regular aspect was evident of the epithelial surface of the treated side (Fig. 7d) compared to the control side (Fig. 7c).

- TEM Analyses

Neo-angiogenesis was still present on the test side (Fig. 8b) but not on the control side (Fig. 8a).

*Thirty days from surgery*

- LM Analyses

A more irregular oral epithelial surface profile was present on the control side (Fig. 9a) compared to the test side (Fig. 9b). On the test side, the CM was completely resorbed (Fig. 9b).

- SEM Analyses

The LM findings were fully confirmed under SEM evaluation, as illustrated in Fig. 9 c-d, particularly as far as the superficial profile was concerned.

- TEM Analyses

TEM observations showed the absence of inflammation on the treated side where vessels were well represented (Fig. 10c).

*Forty-three days from surgery*

LM, SEM and TEM photomicrographs of control and treated samples (Fig. 11 and Fig. 12) showed features similar to those observed at 30 days from the surgery, especially concerning neo-angiogenesis (Fig. 12d).

## DISCUSSION

The present investigation was encouraged by previous observations showing the favorable biological effect of CM-10826 concerning the *in vitro* response of gingival keratinocytes in terms of IL-6 production (antiapoptosis molecule that protects the cells from their spontaneous apoptosis), cell growth and adhesion, without any toxic effect (37).

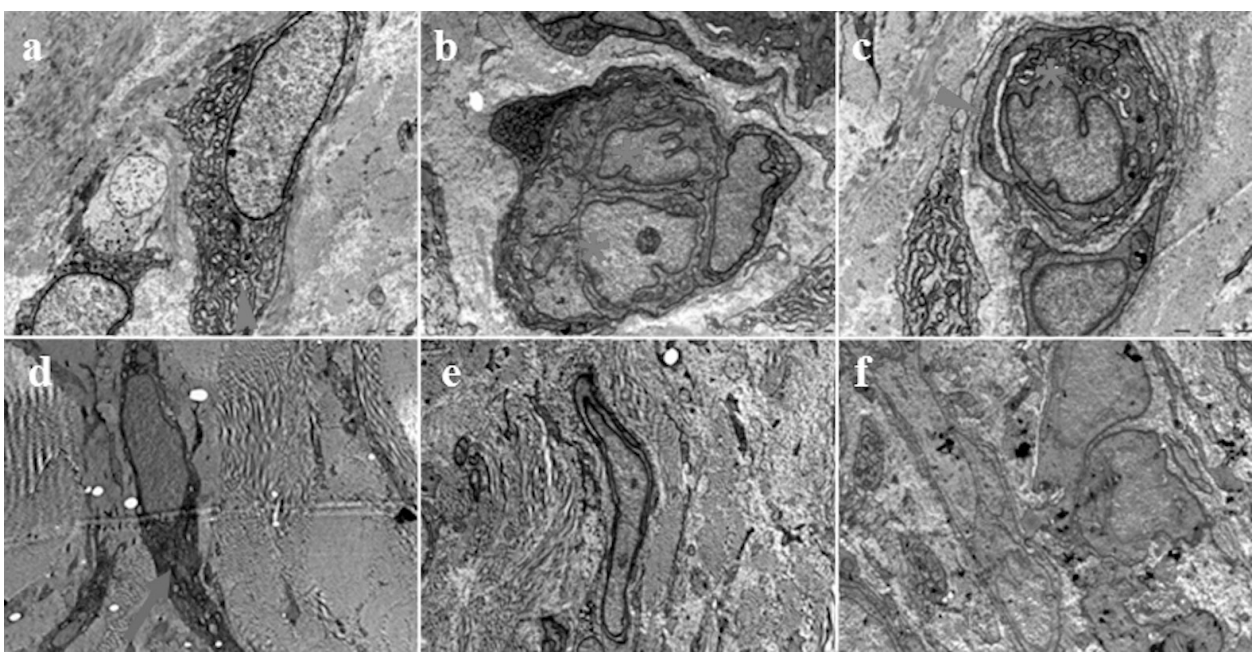


**Fig. 6**. *TEM micrographs of control (**upper row**) and treated (**lower row**) samples 13 days after surgery. Magnifications: (**a, c, f**) x5000; (**b**) x 4400; (**d, e**) x3800.*
*Control (**upper**): a small amount of vessels; the few developed vessels displaying a clear condition of angiopathy, with the lumen of the capillaries partially closed (**head arrow in c**) by swollen endothelial cells (**asterisks in b, c**) disorderly arranged. Fibroblasts appear very active with abundant rough endoplasmic reticulum (**arrowhead in a**).*
*Test (**lower**): tunica propria well vascularized with newly formed vessels (**e, f**). Fibroblasts appear mature without signs of fibrosis (**arrow in d**).*

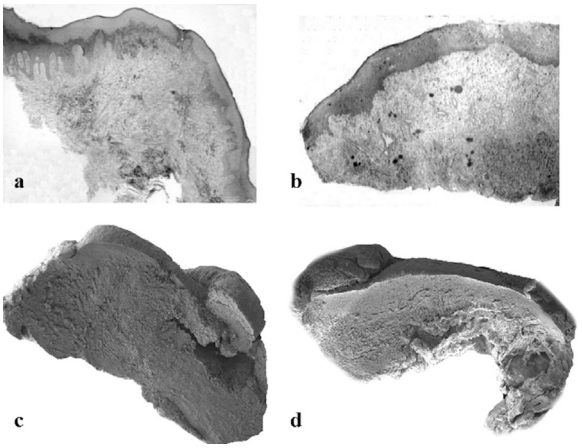


**Fig. 7**. *LM and SEM micrographs 20 days from the surgery. Magnifications: (**a-d**) x70.*
***LM**: control side (**a**) and treated side (**b**).*
***Control side**: normally developed epithelial layer, tunica propria with fibrotic aspect.*
***Treated side**: normally developed epithelial layer, remnants of the collagen membrane are no longer visible inside the connective tissue (**b**).*
***SEM**: control side (**c**) and treated side (**d**).*
*A more regular aspect to the epithelial surface of the treated side compared with the control side.*

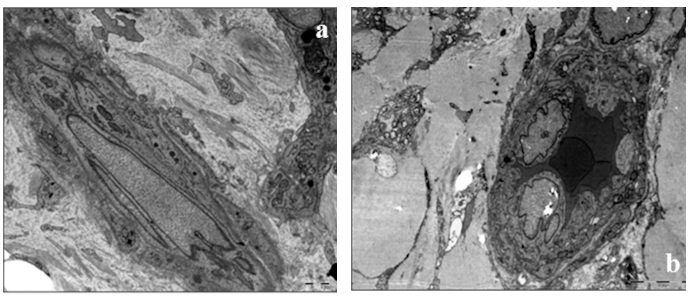


**Fig. 8**. *TEM micrographs of samples at 20 days from the surgery. Magnifications: (**a, b**) x4400. Presence of neo-angiogenesis in the treated (**b**) compared to the control side (**a**).*

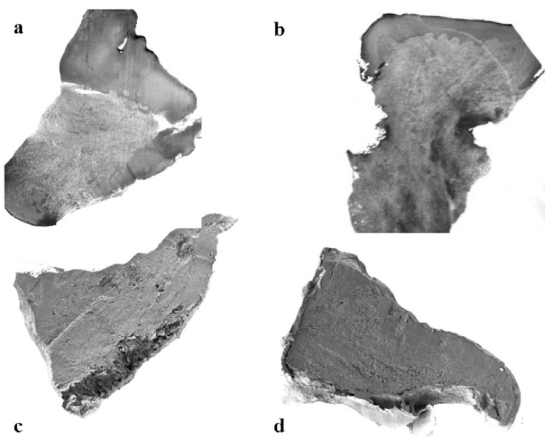


**Fig. 9**. *LM and SEM micrographs of control (**left column**) and treated (**right column**) samples at 30 days from the surgery. Magnifications: (**a-d**) x70.*
*LM (**a, b**): note the irregular profile of the oral surface in the control side (**a**) compared to the test site (**b**), in which the membrane has been completely resorbed.*
*SEM micrographs (**c, d**) show the same findings as far as superficial profile is concerned.*

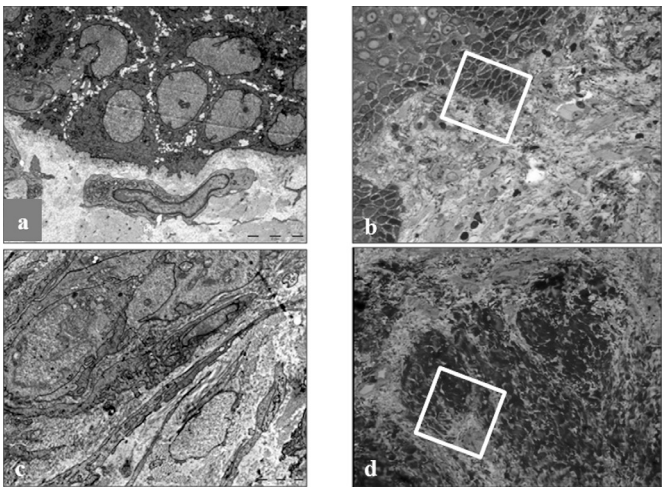


**Fig. 10**. *TEM micrographs of control (**a**) and treated (**c**) samples at 30 days from surgery showing enlargements of the squared areas in LM micrographs (**b** and **d**, respectively). Magnifications: (**a**, **c**) x 4400; (**b**) x420; (**d**) x380.*
*The absence of inflammation is confirmed in the treated site in which the vessels are well-represented (**c**).*

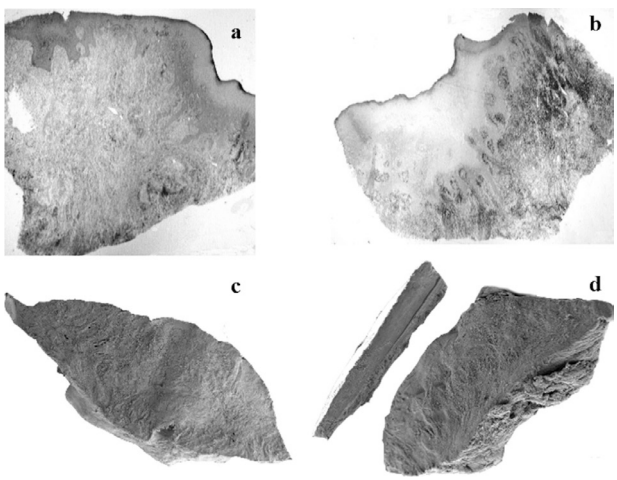


**Fig. 11**. *LM and SEM micrographs of control (**left column**) and treated (**right column**) samples at 43 days from the surgery. Magnifications: (**a-d**) x70.*
*LM (**a, b**): note the profiles of the oral surface in the control (**a**) and treated (**b**) sides, in which the membrane is completely resorbed. SEM micrographs (**c, d**) show the same findings as far as superficial profile is concerned.*

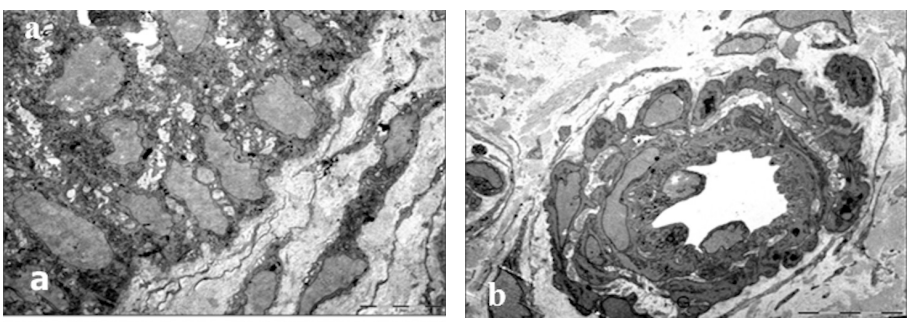


**Fig. 12.** *TEM micrographs of samples at 43 days from the surgery. Magnifications: (**a, b**) x4000. Note new angiogenesis, particularly evident in the treated (**b**) compared with the control (**a**) site.*

These findings were further confirmed by a single case report in which a patient with a bone defect resulting from an extraction of a mandibular molar and enucleation of a radicular cyst was treated with guided bone regeneration (GBR), leaving only CM to cover the GBR membrane (38). The post-extraction site was entirely healed without complications in 2 months: a biopsy of the area showed complete regeneration of the epithelium, connective tissue, and bone tissue (38). A possible use of this collagen membrane as a tissue/scaffold in oral mucosa repair was suggested (37).

In our present case series, clinical healing was excellent and the morphological findings demonstrated that CM provides a three-dimensional scaffold suitable for colonization by precursor cells and vessels and leading to the formation of a fully functional tissue. The first aspect on which to focus is the comparison of the early and late phases of healing in control *versus* treated sides. During early healing (10 days), the control side presented altered trophic zones with aspects of thinning and disappearance of the typical papillary architecture, in addition to aspects of inflammation and alterations of micro-circulation. In the late healing phase, within the oral mucosa, the *lamina propria* showed a fibrotic aspect and superficial epithelium appeared to be poorly organized. In the test side, during the early healing phase spaces delimited by the collagen fibers were filled by an inflammatory infiltrate. Our structural observations suggested that CM is actually integrated within both the connective tissue and the epithelium, potentially being a conductive material for soft tissue regeneration. This suggestion is further supported by the presence, at the surface level, of keratinocytes able to migrate towards the wound and to proliferate both on the surface and in the thickness of CM.

These findings corroborate with our previous results in the "*in vitro* model" showing that keratinocytes adhered firmly to CM-10826 and grew on its surface, spreading their large cytoplasm and interconnecting with neighboring elements (37). In fact, cell adhesion was both efficient and rapid, and occurred parallel with low mortality (37). In the present study, the greater thickness of the *lamina propria* in treated areas compared with the control side, especially evident in the reticular layer, may be interpreted as a sign of the ability of the membrane to induce proper tissue regeneration. At a deeper level, fibroblasts in proliferation were often observed. This aspect is important for the secretion of proteins for the new extracellular matrix. The presence of rich vascularization and the high level of neo angiogenesis may have created a good environment for the induction of newly formed tissue at later stage during the healing process.

During the late healing process, the positive influence of the membrane is evidenced by the normal organization of epithelium and the high-degree maturation of connective tissue of the tunica propria, where fibroblasts have an intense collagen-synthesis activity. The compact organization of collagen fibers and the presence of continuity from the *lamina propria* to overlying epithelium demonstrate the high mechanical strength of the regenerated mucosa. On the test side, excellent healing was visible both in the deep region, where the CM is located close to the periosteum, and in the more superficial region, where the CM is in contact with the surrounding gingival tissue. In our previous case report, this property was clinically very relevant. The membrane was able to recreate a healthy band of keratinized tissue even with the presence of an underlying GBR membrane (31). Furthermore, in the present study, regenerated oral mucosa appeared clinically identical to the normal mucosa showing good histological recovery, consistent with the clinical outcome. These clinical results are in agreement with other clinical studies using different collagen matrices (30, 31, 36).

We have previously shown *in vitro* that CM might function in oral surgery as a substitute for autologous grafts, thereby overcoming the limitations of autologous tissue (38). Additionally, the good *in vivo* healing response, both at macroscopic and microscopic levels as shown in this study and the maintenance of the keratinized phenotype both *in vitro* and *in vivo*, may encourage a possible use of this collagen membrane to obtain augmentation of keratinized gingiva (40-50). The histological/ultra-structural results of the present study, performed on 13 patients, indicate that a CM:

- can be integrated in connective and epithelial tissues within 10 days
- can be completely resorbed within 20 days
- is able to reduce inflammatory infiltrates and to stimulate both fibroblast/epithelial cell proliferation and neo-angiogenesis - generally it seems to be superior in promoting soft tissue healing compared to that induced by secondary intention healing
- is able to act as a scaffold for soft tissue regeneration, allowing the proliferation of keratinocytes from the wound edges and favoring neovascularization and growth of connective tissue in the mesh of porous layer.

A CM seems to be a valid solution for promoting oral soft tissue regeneration. The authors underline the validation of such a scaffold, both from the histological and clinical point of view. The membrane is completely integrated and resorbed rapidly, so that it allows the formation of an healthy newly regenerated oral mucosa. It appears that a CM might function in oral surgery as a substitute for autologous grafts or to avoid secondary intention healing in soft tissue defects.

The outcomes of this analysis will be part of a wider pre-clinical study, which is going to test the clinical efficacy of the membrane on patients. New technologies have allowed us to facilitate treatments; the experimental studies obtain more precise and predictable results, allowing us to prevent many more disease and make early diagnoses (51-54).

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# GUIDELINES FOR ACHIEVING THE BEST IMPLANTS SURVIVAL RATES IN THE REHABILITATION OF THE ATROPHIC POSTERIOR MAXILLA

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**The first option in the rehabilitation of the posterior atrophic maxilla is the sinus lift. The aim of this study is to highlight the characteristics that a sinus lift should have to maximize the subsequent implant survival rate. 33 systematic reviews regarding sinus lift procedures, implants success and survival rates were identified through scientific archives and analysed. The obtained results indicated that a heterogeneity of sinus lift procedures are described in the literature. The sinus lift should be performed through the apposition of particulate xenograft materials, in at least 4mm residual bone. Implants should have a rough surface and the patient should be non-smoker.**

The pneumatization of the maxillary sinus that occurs in the edentulous maxilla makes it difficult to have a sufficient quantity of bone structure available for performing implant positioning. The first option to overcome this problem is to perform a sinus lift. The pneumatization process, however, continues even after grafting and implants positioning as the graft is subjected to a greater pressure deriving from the sinus itself which could accelerate the resorption process and compromise implant stability (1,2). Precisely for this reason, an analysis of the behavior of the graft becomes a key factor for obtaining successful implant rehabilitations.

An overview of the literature was performed to analyze whether there were differences in implant survival in sites rehabilitated through sinus augmentation with and without grafting (3-5). Subsequently, an analysis was also performed on the difference in implant survival according to the type of bone grafting (6).

## MATERIALS AND METHODS

An initial research of systematic review abstracts was carried out through the scientific archives "PubMed" and "Cochrane Library" and the "full text articles" were downloaded in PDF. The following search terms have been selected: "xenograft sinus lift" or "graft materials sinus lift" or "sinus lift". The research was limited to the international bibliography in English from 1996 until today. Experiments on animals were excluded. From the numerous articles found, only the ones of major scientific rigour were selected for a total of 33 articles. This allowed to deepen the literature knowledge and to draw some

*Key words: implant rehabilitation, sinus lift, graft materials*

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conclusions regarding the characteristics of sinus lift.

## RESULTS

Silva et al. (2016) conducted a study to analyze the differences between implant placement contextually to the sinus lift (without grafting) and implant placement following the sinus lift plus grafting. At a 48-60 months follow up they found an implant survival of 96.00% in sites treated only with Schneider's membrane augmentation and immediate implant placement, and a 99.60% survival in sites treated with grafting positioning before implant placement (7). Despite this small difference in implant survival, the choice to perform this procedure with bone grafting is supported and motivated by a greater primary stability of the implants at the time of their positioning.

Any grafted materials placed to perform sinus lift undergo resorption, regardless of quality and type (8-10). Block et al (1998) conducted a study aimed at analyzing, through 2D radiographic investigations; the resorption of the graft positioned during sinus lifts (11). Observations were made at 5 and 10 years from sinus lift and all of them showed a reduction in height of the material. A retrospective study by Lutz et al. (2015) investigated the 5-year results on sinus lift procedures performed with autogenous bone and xenograft through the analysis of orthopantomograms. The Authors observed an implant survival rate of 95.8% at 5 years (97.1% in the autologous bone group and 94.9% in the heterologous bone group; non-statistically significant difference). 43% of the cases treated with autologous bone showed no reduction in height of the graft after 5 years from implant placement, compared to 50% of those treated with xenograft. Up to 25% resorption was observed in 47.8% of the cases treated with autologous bone and 45.8% of the cases treated with xenograft. 25-50% resorption in 8.7% of cases treated with autologous bone and 4.2% of sinuses treated with heterologous bone (12).

In 2004 Del Fabbro et al. published a review of the literature whose purpose was to investigate which graft material and which type of implant surface could guarantee the best results at 2 years of follow-up. The conclusions show how, in terms of composition of the graft, at 24 months a 96% survival of implants positioned with xenograft is observed, against the 95% survival of implants placed in heterologous and autologous bone and the 88% in autologous bone only. As far as the implant surface is concerned, implants with smooth surfaces have shown a 70% survival against a 94% survival of those with a rough surface (13).

## DISCUSSION

Data obtained from a systematic review conducted by Del Fabbro et al. (2008) show that the implant survival rate is lower in sites treated with autogenous bone (88.9%), compared to sites treated with xenograft (96.1%) or with a combination of materials (94.7%). Regarding the implant surface, better results were obtained with rough surfaces (96.7% implant survival) rather than with machined surfaces (86.3%) (13). To date, however, it is not yet clear whether sinus lift procedures performed with autogenous material are more or less effective than procedures performed with heterologous materials; long-term results found in the literature analyze follow-up up to 5 years intervention, moreover we consider systemic desease and the end of the growth (14-22).

A review of the literature conducted by Wallace and Froum (2003) show a 91.8% of implant survival rate for the rehabilitation of the posterior atrophic maxilla; implants with rough surfaces reported survival rates higher than the machined ones; implants positioned in rehabilitated sinuses with bone particulate show greater survival than implants positioned in sites treated with block grafts (23). Testori et al. (2012) show that at 5 years a 93% implant survival is observed in sites treated with xenograft insertion. 7% of failures were related to excessive cigarette consumption (over 15 per day) and a too thin bone thickness (less than 4mm) at the time of lifting, which also confirms the data already proposed by other Authors (24-31).

In many cases when it is not possible to perform the sinus lift, orthodontics can be a valid option to solve the case (32-34), followed by retention appliances (35-37).

## CONCLUSIONS

Drawing conclusions from the systematic review of the literature, it is therefore possible to define the characteristics that a sinus lift procedure should have in order to achieve the higher implant survival (38-40). The sinus lift should be performed through the apposition of particulated xenograft materials, in at least 4mm residual bone (41-47). Implants should have a rough surface and the patient should be non-smoker. Research is concentrate in diagnostic tools, with the aim to identify the best treatment for each patient (48, 49).

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# AN OVERVIEW OF GUIDED BONE REGENERATION

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**Guided bone regeneration (GBR) is a surgical procedure whose purpose is to obtain, new bone, new cementum and a new periodontal attachment around a periodontally compromised tooth. In this work, an overview of the literature was performed to analyze the state of the art concerning GBR in order to draw useful conclusions for clinical practice. Twenty-nine articles regarding GBR procedures were identified through scientific archives and analyzed. The biological rationale, the graft materials and the predictive factors were identified to help the clinicians in their practice. GBR is an effective treatment to prevent tooth loss if performed in adequate bone defects and it is also important to keep in mind predictive factors.**

A periodontal bone defect can lead to dental mobility and if left untreated, to tooth loss (1). Guided Bone Regeneration (GBR) is a surgical procedure whose purpose is to obtain new bone, new cementum and a new periodontal ligament attachment around a periodontally compromised tooth, through the use of devices such as membranes. They are used as barriers and space maintainers allowing the exclusion of epithelial growth from the site, the stabilization of the clot, and promoting osteogenesis. The bone regeneration therefore allows preventing or curing the resorption of the peri-radicular bone. A healthy periodontium and a lower risk of dental mobility are essential for the patient's general health (2). In this work, an overview of the literature was performed to analyze the state of the art concerning GBR in order to draw useful conclusions for clinical practice.

## MATERIALS AND METHODS

An initial research of the abstracts was carried out through the scientific archives "PubMed" and "Cochrane Library" and the "full text articles" were downloaded in PDF. The following search terms have been selected: "guided bone regeneration", "GBR", "guided tissue regeneration", "GTR", "xenograft GBR" o "graft materials GBR". The research was limited to the international bibliography in English from 1976 until today. From the numerous articles found, only the ones of major scientific rigour were selected for a total of 29 articles. This allowed to deepen the knowledge present in the literature and to draw some conclusions regarding GBR.

## RESULTS

Periodontitis is an infectious disease that causes the destruction of the periodontium (1, 3). If this infection is not treated, it leads to a progressive loss of attachment that can lead to premature tooth loss (4). The literature provided evidence that as in most situations, chronic periodontal diseases can

*Key words: guided bone regeneration, bone defects, implant rehabilitation*

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be successfully treated (5). There is also evidence that periodontally compromised teeth have a good chance of survival, if causal-maintenance therapy and patient compliance are adequate (6-8).

There is a wide range of treatment options available, but only a few can be truly considered regenerative procedures. According to the American Academy of Periodontology periodontal regenerations include soft tissue grafts, bone replacement grafts, root bio-modifications, GBRs and combinations (bone and soft tissue) for recessions and defects involving the furcation (9, 10).

Melcher first defined "compartmentalization", identifying the periodontal tissues were into four compartments: the lamina propria of the gingiva, the periodontal ligament, the cementum and the alveolar bone (11). The principle of GBR is based on the exclusion of the gingival cells and the connective tissue from the wound, so as to prevent the growth of these cells in the area of the defect treated with the apposition of graft (2, 12). Thanks to the use of membranes and matrices to keep away from the clot these cells, other cells with regenerative potential (periodontal ligament cells, osteoblasts and cementoblasts) can first colonize the site (13-15).

The pattern of bone formation following GBR was studied by Hämmerle et al. and Schenk et al. They found that first, a clot is formed in the defect and then it is deposited in the same zone osteoid tissue. On the other hand, a thick connective layer forms in the space underneath the membrane. All this is possible if stabilization of the material and the coagulation has been achieved, thus avoiding micro-movements that could compromise bone formation.

Studies performed by Schenk et al. reveal how neo-angiogenesis can already be seen at 2 months. Osteogenesis begins in the grafting zone in contact with the original bone where there is a random deposition of trabeculae and then continues towards the center of the defect (16, 17). The first experimental study showing the supracrestal regeneration potential of GBR was conducted on animals by Dahlin et al., while the first human study is attributed to Simion, et al. The greatest probability of implant success is obtained if the graft is left to mature for 6-9 months (18-20). Moreover, other authors argue that GBR is a more effective procedure than just open-air scaling for the treatment of intra-osseous defects and defects involving the furcation area, as GBR procedures allow a reduction of horizontal and vertical attachment levels, furcation and pocket depths (21-27). The use of biomaterials appears to be effective in considerably reducing the progression of periodontal disease and promoting the regeneration of hard and soft tissues (28-30). However, the basic problem with all filling materials is that there is no biological rationale for periodontal regeneration. In fact, a bone substitute does not have the capacity to regenerate a loss of connective attachment and the formation of a connective tissue reattachment may be absent or created in the same way that would occur during conventional open surgery.

The bone graft must be used in association with a membrane: the biomaterial acts as a scaffold for the matrix that acts as a barrier against the invasion of gingival epithelial cells in the periodontal space, preventing excessive expansion of the connective tissue, promoting the colonization of periodontal ligament cells and alveolar bone (10, 31). On an objective and radiographic examination it is possible to distinguish the prognosis of the dental elements in good-uncertain-unfavorable (32-34).

The experience leads to successfully treat by means of GBR only those dental elements whose prognosis is as good or uncertain. Setting up a correct initial therapy is of fundamental importance to eliminate plaque retentive factors before starting the regenerative therapy. This therapy must be composed of patient education to oral hygiene practices, a professional oral hygiene session every 3 months, an antibacterial therapy with 0.20 chlorhexidine mouthwashes rinses and elimination of plaque retentive factors. In doubtful cases, it is preferable to treat bone defects with regenerative therapy instead of propelling for extraction. In fact, performing the above mentioned therapeutic practices will help to reduce the underlying problems related to the host response that contribute to the progression of periodontal pathology (1).

Periodontal-compromised teeth, in a mouth with excellent oral hygiene, have the same survival rate as dental implants (35). Teeth with deep

periodontal pockets and intra-osseous defects can be successfully maintained through GBR procedures as demonstrated in several studies (35-40). However, the result of regenerative therapy depends on many factors such as patient's age, oral hygiene, nutrition, stress, concomitant therapies, and morphology of the bone defect.

A successful periodontal therapy can be expected in 2 and 3-walled infraosseous defects resulting in a reduction in the pocket depth and in a gaining of clinical attachment (26, 41-43). Autologous, allogenic bones and xenogenic materials have all been used to achieve the periodontal regeneration (28, 44, 45). Despite the surgical re-entry or the execution of radiographs that demonstrate impressive increases in volume, the actual relationship between graft material and new bone cannot be determined except through histology. In fact, as a result of GBR using non-osteoinductive bone substitutes, a bone deposition was observed only near the already existing bone, also showing fibrotic encapsulations, more present in calcium biovetri and phosphate rather than in materials of bovine derivation where they are present only occasionally (10).

## DISCUSSION

The principle of GBR is to exclude gingival cells from the treated site to promote the colonization of cells with regenerative potential. Its purpose is to reduce pocket probing and increase clinical attachment. However, the conclusions derived from the studies in the literature about the regeneration of intra-osseous periodontal defects appear to be rather controversial, varying from optimism to the fact that there are no osteoinductive effects in the materials. It is necessary to consider that there is a lack in the literature of human studies aimed at comparing regenerative procedures with the control group consisting only of maintenance therapies alone. Furthermore, it should not be forgotten that in human studies elements with a poor prognosis are sometimes included for ethical reasons but these elements have significantly lower regenerative capacities compared to elements with a discrete prognosis.

In conclusion the key elements for a successful surgery are an adequate patient selection (non smoker, motivated, compliant); an adequate defect selection (the surgery has a more favorable prognosis if the infra-bone defect is greater than 3 mm, has a narrow radiographic angle and a low baseline of the pocket depth); a performing bone graft; the use of a resorbable membrane to protect the graft; a minimal invasive surgery and professional hand skills (1-3, 25, 27). In addition, the use of new technologies can also improve the outcome of the treatment (46).

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# AN OVERVIEW OF SOCKET PRESERVATION

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**Socket preservation is a surgical procedure whose aim is to limit the physiological resorption of the alveolar ridge that occurs after a dental extraction, in order to have sufficient bone to perform an implant placement. 16 articles regarding socket preservation procedures were identified through scientific archives and analysed. The biological rationale, the graft materials and the predictive factors are identified to help the clinicians in their practice. Socket preservation is an effective treatment to prevent bone resorption if performed after an atraumatic extraction with the use of biomaterials and membranes. It is also important not to forget local and systemic predictive factors.**

Vertical and horizontal bone atrophy at a post-extraction site precludes the possibility of performing prosthetic rehabilitation on implants. From this it derives a possible discomfort given by having to resort to an alternative prosthesis such as partial mobile prosthesis or bridge between elements (1-3). Socket preservation (SP) is a surgical procedure aimed at limiting the physiological resorption of the alveolar ridge that occurs after a dental extraction, in order to have sufficient bone to perform implant placement (4-7).

In the case of multidisciplinary orthodontic-surgical-prosthetic treatments, the role of the orthodontist is in the control of orthodontic movement, in order to avoid bone resections due to rapid dental movements (8, 9, 10). Dental extractions are necessary in severe malocclusions when enamel reduction is not possible (11, 12). The aim of this work was to carry out an overview of the literature to analyze the state of the art regarding socket preservation to draw useful conclusions for the clinical practice.

## MATERIALS AND METHODS

An initial research of the abstracts was carried out through the scientific archives "PubMed" and "Cochrane Library" and the "full text articles" were downloaded in PDF. The following search terms have been selected: "socket preservation", "alveolar ridge preservation", "xenograft socket preservation" or "graft materials socket preservation". The research was limited to the international bibliography in English from 1966 to 2015. From the numerous articles found, only the ones of major scientific rigor were selected for a total of 16 articles. This allowed to deepen the knowledge present in the literature and to draw some conclusions regarding socket preservation.

*Key words: socket preservation, dental extraction, implant placement.*

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## RESULTS

After single or multiple dental extractions a remodeling of the alveolar process occurs leading to loss of vertical and horizontal bone tissue (13, 14). Typically, horizontal resorption is more conspicuous than vertical, although both occur mainly on the vestibular side (15). This double resorption inevitably leads to a narrowing and lowering of the edentulous ridge, resulting in a palatal displacement of the maxillary ridge axis, and a vestibular displacement at the mandible (16-18).

The maxillary and mandibular bones are composed of several anatomical structures, each with its own functioning, physiology and composition. In particular, they consist of: basal bone, which develops along with the skeleton, forms the body of maxilla and mandible; alveolar process, which develops after the tooth eruption and contains the dental alveolus; bundle bone, that is a bone layer that covers the alveolus, it extends coronally and it forms the bone crest at the buccal level (19-22). It is part of the periodontal structure as it encloses the exterior terminations of the Sharpey periodontal fibers. At the time of dental extraction it is the first element that resorbs (23-25).

On the other hand, the alveolar bone slowly resorbs throughout life. The remodeling process results in a crestal morphology reduced in height and thickness. Other Authors hypothesize that the alveolar resorption process takes place in two phases: during the first, the bone bundle (which almost entirely comprises the coronal vestibular portion of the bone) is rapidly resorbed and replaced by bone tissue leading to a large decrease in vertical height of the ridge. The vestibular side is subjected to greater resorption, both for the reason mentioned above, and because it is generally thinner than the palatal one (in particular, 0.8 mm at the level of the anterior teeth and 1.1 mm at the level of the premolars). During the second phase the outermost part of the alveolar bone is remodeled (26).

## DISCUSSION

Over the past 20 years, various methods have been investigated to maintain the ridge profile in post-extraction sites, minimizing its collapse. The first attempts to avoid the post-extraction resorption process were carried out by Osburn in 1974 when the need to guarantee stability of the total mobile prosthesis was associated with maintaining the initial bone volumes. Hence the idea of keeping the dental roots in place as a stabilizing scaffold.
However, this practice led to fractures of the residues of the elements left in place and infections deriving from decayed elements (27). In the 80s the concept of socket preservation began to develop while proceeding with the extraction of the dental element. This "retentive" effect of the roots could be obtained by positioning a material that mimics the root itself and limits the resorption process. This procedure significantly reduces the need to perform ancillary procedures of bone augmentation at the time of implant rehabilitation (28). Thanks to the advent of implantology the concept of "alveolar ridge preservation" (ARP) has begun to gain increasing importance in clinical practice (29).

As illustrated by Horvath et al. (2013), "alveolar ridge preservation" means "any procedure used after dental extraction aimed at minimizing external resorption, while maximizing the formation of bone within the alveolus"(30). The main objectives and clinical recommendations of socket preservation were reported in the "Osteology Consensus Report"(31): maintenance of the original hard and soft tissues; maintenance of a stable bone volume to optimize functional and esthetic outcomes; simplification of treatment procedures; placement of biomaterials for modeling the bone crest; first closure of the wound; use of materials that have a slow rate of resorption and replacement. Numerous factors can influence bone resorption: presence or absence of teeth adjacent to the extraction site, the morphotype of the subject (thin morphotypes are associated with very thin and fragile buccal bone walls), the use or not of grafting material, smoking, systemic disorders (diabetes uncontrolled, immunodeficiencies, etc.), patient compliance, the morphology of the extracted tooth (a monoradicular tooth will likely lead to greater alveolus integrity upon extraction). For the latter reason, in fact, studies aimed at evaluating

the effectiveness of biomaterials are based on monoradicular teeth. Positive outcomes in socket preservation have been recorded by different authors (32-36).

Further advantages in preserving the vestibular and the lingual heights of the alveolar crest have been found when associating grafting with the apposition of a membrane. Although it is generally assumed that flapless extractions are preferred in order not to interrupt the periosteum vascular bed and an increase in post-operative inflammation, recent clinical studies (37-41) have shown that there are no significant differences between the two techniques. Regarding the type of biomaterial that leads to the best results in the literature, xenografts seem to be the most promising material in terms of minimal alveolar resorption (38). Thanks to this procedure, surgeries like GBR and sinus lift are less frequently needed (40-43).

We can state that socket preservation by means of graft materials is an effective treatment to prevent the physiological bone resorption following dental extraction, both as regards the thickness of the bone, and as regards its vertical height. It is important that the extraction is atraumatic. However, there does not seem to be any significant difference between an extraction with or without flap (44-45). The grafting procedure for preserving the alveolar ridge is recommended, in particular of xenograft, covered by a membrane to obtain a better healing (46-48). The clinician must also take into account negative prognostic factors such as: thin periodontal morphotype, smoking, diabetes, immunodeficiencies and multiradicular tooth. Digital design technologies allows us to visualize the possible outcome before starting treatment (49).

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# AGENESIS: PILOT CASE REPORT BY 2.9 mm IMPLANT

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**The agenesis of the upper lateral incisor is one of the most frequent aesthetic-functional problems in dentistry. The reported case concerns a 49 years old male patient with bilateral agenesis of teeth 1.2-2.2 and a root stump of tooth 5.2 temporarily rehabilitated through a Maryland bridge. Without orthodontic treatment, the only solution for implant-prosthetic rehabilitation of tooth 1.2 results therefore in the use of a 2.9 mm diameter implant. The clinical and radiographic control of the implant and the gingival stability at a distance of 1 year gives a positive result both clinically and radiographically. The use of the implant with a 2.9 mm diameter is therefore indicated in extreme cases of limited bone availability.**

The agenesis of the upper lateral incisor is one of the most frequent aestehetic-functional problems in dentistry (1, 2). It is can be solved with an orthodontic/conservative/prosthetic treatment, with an orthodontic/implant-prosthetic treatment or only with an implant-prosthetic treatment (3-6). Each solution depends on patient's characteristics such as dentoalveolar discrepancy, skeletal class, gingival smile line (7-9). An accurate patient's medical history is essential: in presence of oral diseases the surgical treatment options could be altered by the systemic treatment and then turn to a conservative treatment choice (10, 11).

## MATERIALS AND METHODS

The reported case concerns a 49-years-old healthy ex-smoker male patient with the following dento-skeletal characteristics: Angle class I malocclusion, normodivergence of bone bases, bilateral agenesis of the upper lateral incisors, absence of temporomandibular joint disorders, normal movements in protrusion and laterality, altered curves of Spee and Wilson due to the lack of teeth 1.2, 2.2, 3.6, 3.7, 4.6, normal occlusal vertical dimension thanks to the preservation of tooth 4.7, midline deviation to the left, mesial migration of tooth 2.3, normal gingival smile line, slight dentoalveolar discrepancy, root stump of tooth 5.2 temporarily rehabilitated through a Maryland bridge.

The diagnostic framework and the economic conditions of the patient do not allow orthodontic treatment of the two dental arches associated with implant-prosthetic treatment of teeth 1.2-3.6-3.7-4.6 and a conservative/prosthetic treatment of tooth 2.3; so it is decided for the immediate

*Key words: agenesis, implant surgery, aestehetic rehabilitation*

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postextraction implant-prosthetic rehabilitation of tooth 1.2 also because the smile line is favorable and the dentoalveolar discrepancy of the upper arch is slight. The only problem is the mesiodistal distance of 6 mm between teeth 1.1 and 1.3 caused by the loss of interdental space following coronal fracture of tooth 5.2.

The aforementioned distance prevents the placement of an implant with a diameter of 3.3 mm. The only possible solution is to use an implant with a 2.9 mm diameter to guarantee the minimum distance of 1.5-2 mm between the implant and the dental roots (12-15).

Before the surgery, pre-treatment photos, dental casts, radiographic and occlusal analyses are performed to decide implant length and diameter and to build a surgical guide and a temporary resin crown (Methyl-methacrylate) (16-21). Perioral cutaneous (Lodopovidone 10%) and oral disinfection (Chlorhexidine 0.2%) are performed and local anesthesia of anterior maxillary teeth (Articaine 4% and Adrenaline 1/200.000) is administered. The surgical incision is performed paracrestal to preserve the interdental papillae: in particular, a split thickness flap is obtained buccally and a full thickness one palatally (surgical scalpel blade 12C). After the extraction of tooth 5.2, exploratory milling is performed using a lance-shaped bur (diameter 1.9 mm) at the center of the interdental space between teeth 1.3 and 1.1 in order to create a site of the appropriate depth (5 mm). Bone density (D3 classification of Misch) is verified using the implant probe, then the first 5 mm drilling (diameter 2.2 mm) is performed with respect to the surgical guide (22). Then the surgical guide is removed and the drilling is completed following the appropriate inclination up to 13 mm. Then a second drilling (diameter 2.8 mm) is performed for 3 mm of depth in order to prevent excessive pressure on the bone during the implant placement. Then the implant with a 2.9 mm diameter and a 12 mm length (Titanium 5 HRS Surface) is inserted up to 2 mm below the bone crest. A temporary 15°-angled abutment (Peek) is tested intraorally and then it is prepared out of the patient's mouth so it can passively receive the temporary crown. At this point, the provisional crown is relined with acrylic resin (Methyl methacrylate).

After polishing, the temporary abutment and the provisional crown are cemented (with zinc oxide-eugenol cement), placed on the implant in absence of occlusal contacts and cement or resin residues are eliminated. Then the site is sutured with poly lactic-co-glycolic acid co-polymer sutures by performing a apically repositioned flap buccally. In this way, the excess of palatal tissue obtained from the initial incision is used to favor the formation of a good quantity of buccal peri-implant mucosa (23-31).

The patient is discharged with adequate antibiotic and anti-inflammatory therapy (amoxicillin clavulanate 1g every 8 hours for six days and paracetamol with codeine 500mg + 30mg if needed). He is instructed to consume a soft diet for the first month after surgery and to maintain a good oral hygiene including chlorhexidine 0.2% rinses two times a day for a week. The suture is removed after two weeks (32-38).

## RESULTS

One month after the surgery the first clinical control of the implant and periodontal tissue stability is performed; after three months the patient is clinically and radiographically controlled again. In both cases the result is positive: the implant stability and the periodontal tissue health are optimal; furthermore, radiographically, the osseointegration appears complete. After another month, a silicon impression with the implant transfer of 3.3 mm diameter, the test of the definitive 15°-angled abutment (Titanium 5) and crown (Zirconium-Ceramics) and their placement on the implant with the aid of a prosthetic template are performed. The prosthetic template allows the perfect welding between the abutment and the implant without deterioration of the ceramic during the percussions necessary for the stabilization of the crown.

The clinical and radiographic control of the implant and gingival stability at a distance of 6 months and 1 year gave a positive result both clinically and radiographically, finding a single episode of detachment between the abutment and implant at a distance of 3 months from the cementation of the definitive crown; it was solved by removing the tangential loads on the distopalatal and distomesial surfaces of the crown of tooth 1.2.

## DISCUSSION

The use of a 2.9 mm diameter implant is indicated

in the extreme cases of limited bone availability by carefully controlling the tangential occlusal loads to the supporting crown.

Chang et al. made a comparative evaluation of crown and soft tissue dimensions between implant-supported single tooth replacements and contralateral natural tooth. Twenty patients has been treated with an implant in esthetic zone of the maxillary jaw. Authors concluded that there are only minor differences in crown form between natural tooth and implant in the esthetic zone and a median value of 96% of patients' satisfaction (39). Bernard et al evaluated the effects of an anterior tooth eruption adjacent to implant-borne restorations in both late adolescence and adult patients. They concluded that in adult patients there could be major vertical steps after anterior restoration, even if the effect of adult residual growth alterations may be small. The clinicians should keep in mind that implant behaves as an ankylosed tooth and this is the reason why in young individuals with residuous growth potential it has been shown major esthetic imairment in anterior implant-borne restorations (40).

Tooth agenesis is one of the most common developmental dental anomalies, in particular the prevalence of missing maxillary lateral incisor ranges from 1% to 3% (41-46). It is important that the clinician, who approaches agenesis of the elements in the esthetic zone knows all the factors that could influence the therapy in order to choose the best one for the patient. The innovations in the orthodontic field in terms of materials and alignment techniques allows the orthodontist to solve clinical situations of dental agenesis (47, 48).

Further experimental studies are necessary to understand if this type of solution for ageneses of the upper lateral incisors is predictable or not. Diagnostic tools and new technology could prevent and facilitate in growing patients the resolution of complex cases to the operator (49-50).

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# IMMEDIATE REHABILITATION OF THE POSTERIOR MAXILLA WITH AN AXIAL AND A TILTED POST-EXTRACTIVE IMPLANT: A TECHNICAL REPORT AND BRIEF LITERATURE REVIEW

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**The atrophic posterior ridges are usually characterized by poor bone quality and quantity: this situation requires the use of bone regenerative techniques. Other alternative surgical approaches are investigated. Nowadays the use of tilted implants offers some advantages due to its feasibility. Today, bone grafting may be practical, but depends on many factors, such as the type of bone graft used (autogenous, alloplastic, or xenograft), host response, age of the patient, various complications associated with grafting procedures, infection, and, most importantly, the time spent while the grafted material matures and is taken up by the bone. So this case report describes the feasibility of an alternative surgical technique.**

Usually, an atrophic posterior area is characterized by poor bone quality and quantity: this situation requires the use of bone regenerative techniques, such as sinus lifts or short implant insertion, or bone regeneration with vertical/horizontal crestal onlay grafts (1, 2). Today, bone grafting may be practical, but depends on many factors, such as the type of bone graft used (autogenous, alloplastic, or xenograft), host response, age of the patient, various complications associated with grafting procedures, infection, and, most importantly, the time spent while the grafted material matures and is taken up by the bone.

One review revealed that there are few studies providing data on the success rates of dental implants placed in onlay graft augmented ridges and demonstrated, on average, poor methodological quality (3). Oral diseases could compromised surgical treatment (4) and orthodontics could be a valid alternative, with the aim of preserving the remaining elements, or creating/optimizing the space for future prosthetic rehabilitation (5-7). Placement of an angulated implant, which avoids both invasive procedures such as a sinus lift, and bone augmentation procedures, may be a viable treatment option (8-10). However, some alternative techniques can also be used, such as implant placement in front of the sinus, or in the intra sinus septa, or palatal to the sinus. Thus, the same amount of bone may allow the insertion of two implants: one axial and another tilted to support a three-element prosthetic fixed unit without a cantilever (11-14). Here, we describe a case report of a maxillary immediate fixed rehabilitation, with axial and tilted implants supported in the fresh-post extractive sockets.

*Key words: tilted implants, regenerative, atrophic ridge*

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*Clinical report*

An 84-year-old woman was referred to our private clinic (Centro Medico Vesalio, V. Sorio, Padua, Italy) for rehabilitation of her upper left maxilla. Her medical history revealed only a previous episode of ischemia. Clinical observation revealed some caries-destroyed teeth and missing teeth in the upper left maxilla (Fig.1-2-3-4-5).

Given this clinical situation, a minimally invasive implant surgery was suggested to the patient to avoid bone regenerative techniques, such as a sinus lift (Fig. 6-7-8). Thus, tilted implant placement was planned to support an immediate fixed three-unit element prosthesis to restore her upper maxilla.

Her treatment goals were to reestablish lost function and esthetics with a fixed prosthesis to minimize the time period without teeth and to avoid a removable prosthesis. The patient was carefully informed about the possible treatment options: sinus floor elevation with delayed implant placement and prosthetic restoration, or an immediate fixed prosthesis supported by one axial implant and one tilted posterior implant. The patient chose the second option and signed an informed consent form. After local anesthesia had been administered, a mucoperiosteal flap was raised, exposing the facial bone of the left maxilla.

After teeth extraction, starting from the area of the first molar, the implant site was prepared with a 30° mesial inclination passing in front of the sinus cavity and proceeding in the apical portion of the bone, anterior to the sinus (Fig. 9).

A tilted implant was inserted (Win6 BioSaFin, Milan, Italy; 15 mm long and 3.8 mm in diameter). Another Win6 BioSaFin fixture (15 mm long and 4.5 mm in diameter) was inserted axially in the socket of the first premolar. Both implants reached a final insertion torque higher than 40 Ncm (Fig.10-11).

Then, two 30° multi-unit abutments (MUA) were connected over the posterior and anterior implants (Fig.12-13).

After the surgery, a three-unit composite resin interim prosthesis was relined with Combo Lign Bredent (Bz, Italy) and connected to two temporary abutments. Slight contacts in maximum intercuspation were registered and any lateral excursions were removed (Fig.14-15).

## DISCUSSION

Here, we present a technique for the immediate fixed restoration of the posterior maxilla in an elderly patient requiring surgical treatment of reduced duration. Mattsson first reported the concept of tilted implants in oral surgery to support a full-arch fixed prosthesis in patients affected by severe maxillary atrophy (15). In 2001, Aparicio applied this concept to rehabilitation, through a fixed implant-supported prosthesis of the posterior maxilla as an alternative to a sinus lift (16). In total, 25 patients received 101 implants: 59 axial implants and 42 tilted implants. After 5 years of follow-up, the success rate was 95.2% for tilted implants and 91.3% for orthogonal implants.

The marginal bone loss was, on average, 1.21 mm for the tilted implants and 0.92 mm for the axial implants. Thus, it was concluded that this surgical approach was a valid and practical alternative to a sinus lift in the rehabilitation of the atrophic maxilla (17-21). Moreover, Calandriello in 2005 conducted a study of 18 patients, treated with 60 implants supporting fixed partial/total prostheses, and reported a 96.7% success rate (mixed) and bone resorption values of 0.82 mm for axial implants and 0.34 mm for tilted implants (22). No significant difference was found between axial and tilted implants regarding the implant-related prevalence of peri-implant mucositis, peri-implantitis, or implant loss (16). Lekholm reported that a 14 mm distance between the canine bone and the distal implant allowed for rehabilitation of an atrophic maxilla with one axial and one tilted implant without a prosthetic cantilever (23).

The use of longer implants increases the bone-implant contact (BIC) in a low-quality bone region; moreover, it allows the cortical bone to be reached with increased primary stability and, consequently, it is possible to install an immediate-load fixed implant-supported prosthesis. In our case, we decided to use a tilted distal implant in the mesial-palatal direction to take advantage of the native bone. Thus, we used

**Fig. 1.** *Lateral aspect of the carie-destroyed teeth.*

**Fig. 2.** *Occlusal full arch aspect.*

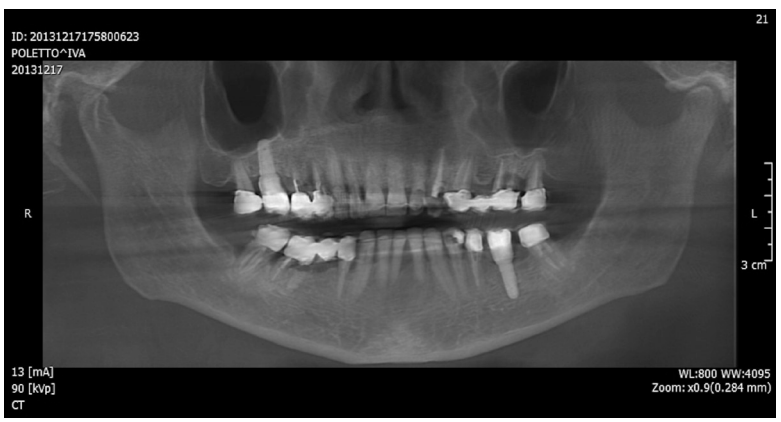


**Fig. 3.** *Initial rx OPT.*

**Fig. 4.** *Radiograph of the I left upper molar.*

**Fig. 5.** *Radiograph of the I left upper premolar.*

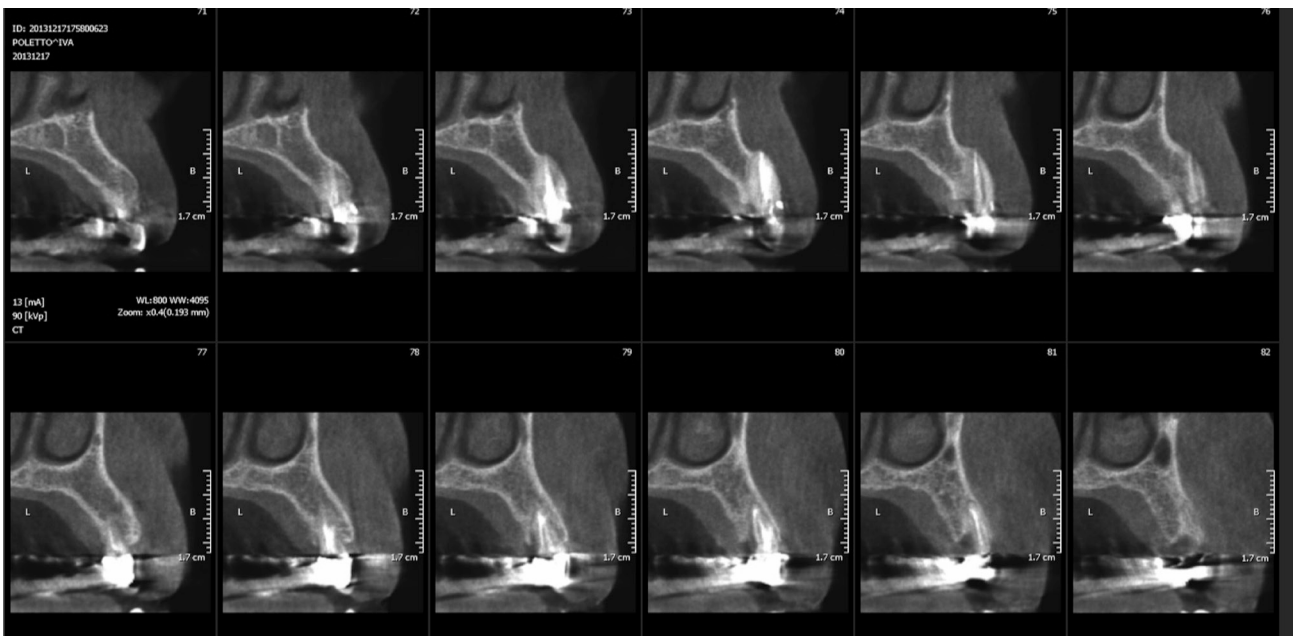


**Fig. 6.** *First screen shot of TAC.*

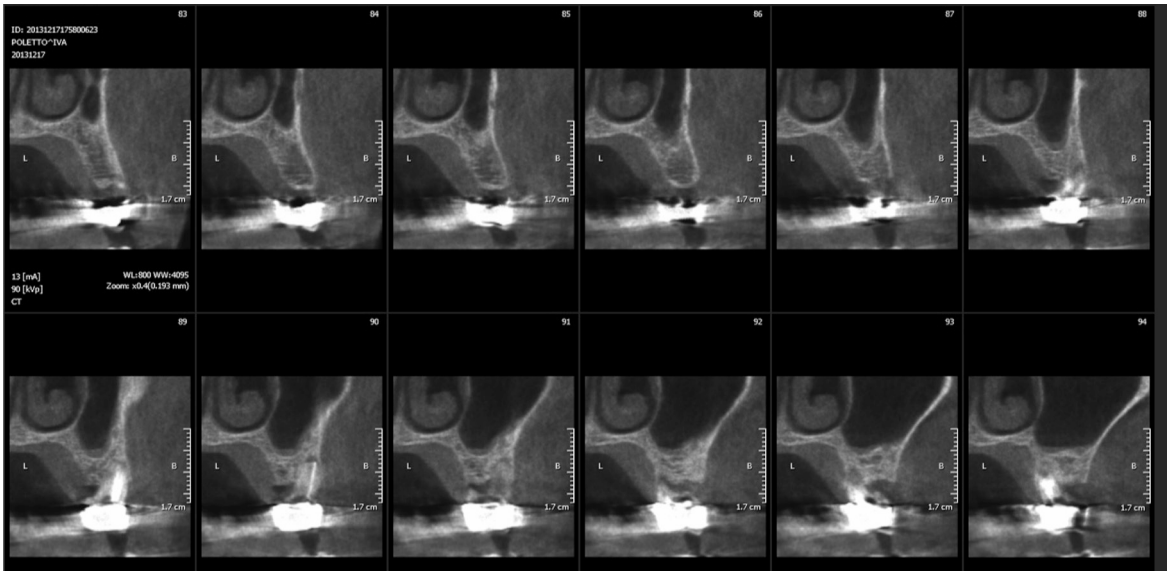


**Fig. 7.** *Second screen shot of TAC.*

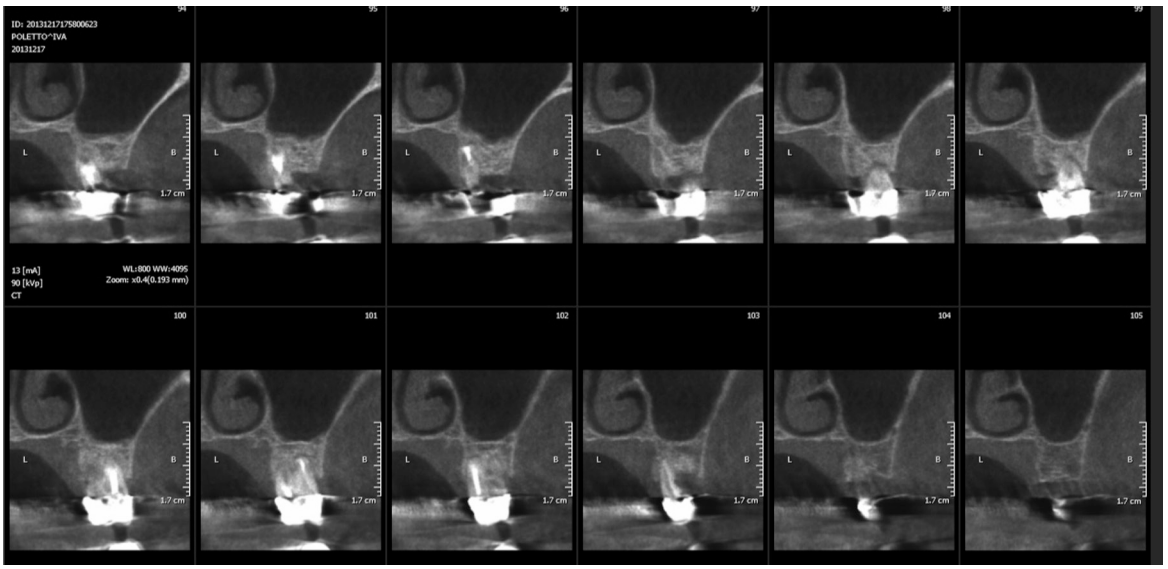


**Fig. 8.** *Third screen shot of TAC.*

**Fig. 9.** *Surgical orientation of the pins.*

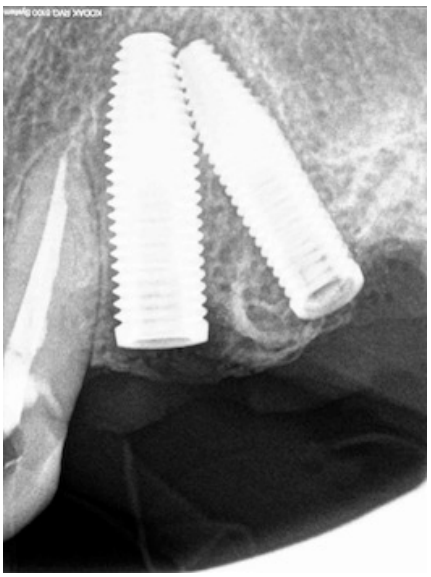

**Fig. 10.** *Radiograph after implants placement.*

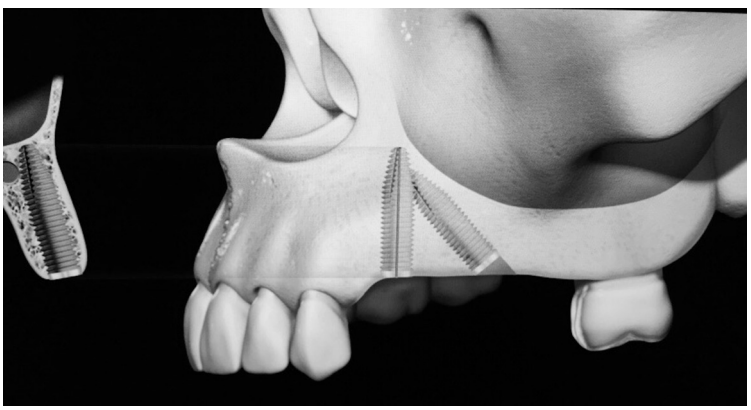

**Fig. 11.** *Virtual image representative of implants placement surgery.*

**Fig. 12.** *Angled MUA connection.*

**Fig. 13.** *Healing caps connection.*

**Fig. 14.** *Lateral aspect after immediate load implant supported prosthesis restoration.*

**Fig. 15.** *Occlusal full arch aspect after immediate load implant supported prosthesis restoration.*

two 15-mm long fixtures to reach more cortical bone.

The tilted implant impacted against the mesial sinus cortical margin with its distal surface, such that 'bicorticalism' was achieved, thereby improving primary stability and permitting an immediate load. The only risk in this procedure depends on the flexibility of the bone, which could be subjected to excessive stress due to the prosthetic components (24-26). The use of an immediate loaded full-arch prosthesis, supported by two mesial axial implants and two distal tilted implants, is a viable rehabilitation option, considering the lower rate of peri-implant mucositis and peri-implantitis compared with that reported in the literature (27-30).

This technique offers several advantages: 1) Stability even with minimum bone volume: longer implants can be used with minimum bone volume to increase BIC and reduce the requirement for vertical bone regeneration; 2) Cortical anchorage may be achieved through longer fixtures (18, 20, 25-mm long); 3) Good clinical results; 4) Avoids invasive bone regenerative techniques; 5) Can be performed in patients with various systemic conditions that are often contraindications for bone grafting; 6) Angulations allow implant placements that avoid anatomical structures; 7) There is a biomechanical advantage to using tilted distal implants rather than distal cantilever units (31); 8) Reduction of the length of cantilevers without performing bone grafting or sinus lifting; 9) Effective and safe alternative to maxillary sinus floor augmentation procedures and to a pneumatized maxillary sinus (9); 10) Distally tilted implants induced better loading transmission than vertical implants; 11) Excellent prognosis in the short-to-medium term as well as over the long term (32).

However, the technique also has some disadvantages. First, it assumes that the surgeon has biomechanical knowledge and experience in the management of prosthetic immediate loading, and is a more sensitive surgery. There are several other considerations that should be kept in mind when using this approach: the use of angulated implants should remain confined to situations of favorable bone quality (preferably greater than D3) and angulated implants should only be placed after suitable three-dimensional planning.

Greater inclinations of the implants (>30°) lead to increased force at the implant-bone and implant-abutment interfaces. Thus, extreme angulation should be avoided. We suggest an inclination between 15° and 30° (22). Cavallaro and Greenstein, after evaluating the proportion of survival and complications (biological and technical) associated with tilted abutment-supported prostheses showed that increased abutment inclination creates a greater amount of tension on the prosthesis and the surrounding bone (33-37). However, the increased tension was not associated with any significant reduction in the longevity of the prosthesis. Moreover, it was not associated with any increase in the incidence of fixation screw loosening. A trigonometric ratio was developed to estimate the two-dimensional safe distance between a tilted implant and an adjacent vertical implant (38-42). The distance or length between the fixtures can be determined by multiplying the known length of each implant by a constant derived from the sine of the insertion angle (43).

In edentulous maxillae, if the inter-implant distance is increased, the load distribution will be better. Moreover, we used an internal hexagonal connection, which offers better force dissipation. The cortical preparation is also reduced due to abutment placement: this helps with the primary stability. In addition, the internal hexagonal connection may be more coronal, which could lead to a reduction in the micro leakage of bacteria. Prosthetically, the internal hexagonal connection has some procedural disadvantages, but it offers a better implant abutment seal, fewer prosthetic complications due to lower pin fixation stress and, finally, the possibility of a better prosthetic finalization of the abutment (44-47).

The surgical approach described herein is sensitive and useful in patients with atrophic ridges. Long-term studies are required to evaluate its success rate in terms of load distribution, marginal bone loss around the implant, and prosthesis survival, although currently many practitioners are treating patients with this technique. Generally, we can state that rehabilitation using tilted implants offers many advantages versus the use of bone grafts (onlays,

sinus lift) and short implants. In particular, this type of surgery is faster, safer, more predictable, less expensive and invasive, and allows the application of an immediate load protocol when primary stability is achieved. It is helpful not forget to make an accurate clinical history, considering the possible presence of caries or malocclusions that would influence the outcome (48-50). This case report shows the feasibility of the technique in achieving clinical success, as well as surgeon and patient satisfaction.

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