

**Bone healing at implants installed in sites prepared either with
a sonic device or drills. A split-mouth histomorphometric
randomized controlled trial.**

Brief title: Bone healing at implant installed in sites prepared with either a
sonic device or drills

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Running Head: sonic device for implant site preparation

Key words: human study, histometry, morphometry, dental implants, bone, bone-to-
implant contact, bone density

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July 17th 2017

Abstract

Purpose: to evaluate histomorphometrically the early healing at implants installed in sites prepared with either a sonic device or conventional drills.

Material and methods: Sixteen volunteer patients will be recruited. Two titanium mini-implants will be installed in the distal segments of the maxilla in recipient sites prepared with either a sonic device or conventional drills. Biopsies containing the mini-implants will be retrieved after 2 weeks in eight patients, and after 6 weeks in the other eight patients. Histomorphometric analyses will be performed.

Key words: Bone-to-implant contact; bone density; dental implants; histometry; histology; sonic device.

INTRODUCTION

A systematic review with meta-analysis compared the use of a piezoelectric device and drills for implant site preparation.¹ Both technical approaches presented similar results regarding implant failure and marginal bone level changes. However, a longer time for site preparation was required for the piezoelectric device compared to the drills. was and operating time.

The healing at implants installed in sites prepared using conventional drills to sites prepared with either a piezoelectric device or a sonic device was studied in animal experiments.^{2,3} No differences in osseointegration were found in both studies. The use of piezoelectric or sonic devices has become widespread during the last years due to the precision offered during the cutting procedures of these devices, the reduced risk of damaging soft tissues, and the clear view of the surgical sites offered by this device during the preparation.⁴⁻⁶

Piezoelectric devices have been largely studied and compared with the use of drills for implant site preparation.^{7,8} In a randomized controlled clinical study,⁹ gain in implant stability was faster in sites prepared with piezosurgery compared to twist drills, while no differences in survival rate were found. As support to this finding, an experimental study in mini pigs,¹⁰ showed that sites prepared with piezosurgery presented a more advanced osteogenesis compared to those prepared with drills.

Comparatively to the piezoelectric devices, lesser amount of clinical¹¹⁻¹⁸ and experimental researches³ have been performed to evaluate the sonic devices. Nevertheless, similar advantages of the piezoelectric instruments are offered by the sonic devices in term of surgical precision, clear view of the surgical field, and low risk of possible damages of the surrounding soft tissues.³ Moreover, the sonic devices have been claimed to produce a similar increase of the temperature during the procedure of that produced by drills, and lower than that produced by piezoelectric instruments.¹⁹

Experimental histological data comparing sonic devices and conventional drills are still scarce and histological data from human are not available. Hence, the aim of the present study will be to evaluate histomorphometrically the early healing at implants installed in sites prepared with either a sonic device or conventional drills.

The hypothesis will be that the preparation of an implant recipient site using a sonic instrument might produce different osseointegration compared to a conventional site preparation using drills.

MATERIALS & METHODS

Patient selection

In the present split-mouth histomorphometric randomized controlled trial, sixteen patients will be included. The Declaration of Helsinki on medical protocols and ethics will be followed. The protocol has the approval of the Ethical Committee of the Corporación Universitaria Rafael Núñez, Cartagena de Indias, Colombia (protocol #05-2014; 8 October 2014). In the same institution will be performed all treatments. After having exhaustively illustrated the surgical procedures and the possible complications, a written informed consent will be signed by the patients. The study will be reported according to the CONSORT guidelines.

To calculate a suitable sample, data from an animal experiment in dogs performed by the same research group were used.³ In that experiment, implant site preparations was carried out either with a similar sonic device used in the present study or drills, and a difference of 7.3% in bone-to-implant contact was seen in favor of the sonic groups with an n=6. Considering a possible higher variability in humans and possible dropouts, a sample n=8 pairs of subjects is considered sufficient to reject the null hypothesis that this response difference is zero, with a power 0.8 and $\alpha=0.05$, as evaluated using PS Power and Sample Size Calculations, (William D. Dupont and Walton D. Plummer). Two groups of 8

volunteers will be randomly formed and planned for biopsies retrieval after either 2 or 6 weeks of healing.

The patients included in the present study have to satisfy the following inclusion criteria:

- (i) presence of an edentulous atrophic zone in the posterior segment of the maxilla
- (ii) height of the sinus floor ≥ 10 mm
- (iii) ≥ 25 years of age;
- (iv) smoking ≤ 10 cigarettes per day
- (v) good general health
- (vi) no contraindication for oral surgical procedures
- (vii) not being pregnant.

The following exclusion criteria will be adopted:

- (i) presence of systemic disorders
- (ii) chemotherapy or radiotherapy
- (iii) smokers > 10 cigarettes per day
- (iv) previous bone augmentation procedures in the same region.

Moreover, caries and periodontal conditions will be evaluated and, if any of these pathologies are present, they will be treated before starting the study.

Device

Titanium screw-shaped mini-implants, 4 mm long and 2.5 mm in diameter and with a ZirTi® surface (Sweden & Martina, Due Carrare, Padua, Italy) will be used. Surface features of the implants were previously reported.²⁰

Randomization and allocation concealment

Each patient will receive two mini-implants, installed in recipient sites prepared in the distal segments of the maxilla either with a sonic device or drills. The two recipient sites will be

selected prior the surgery, while the type of site preparation will be randomly decided. A researcher, neither involved in the selection of the patients nor in the surgical and prosthetic treatment, carried out electronically the randomization (randomization.com). Sealed opaque envelopes will be prepared and opened at the time of surgery and they will report the position of the sonic sites so that the surgeon will be masked about site preparation type until the surgery. The site will be indicated as mesial or distal position if the two sites will be located in the same quadrant of the maxilla, or as right or left if they will be located in opposite quadrants of the maxilla.

Clinical procedures

All surgical procedures will be performed by an expert surgeon. Local anesthesia will be provided and crestal and releasing incisions will be carried out. Full-thickness muco-periosteal flaps will be elevated, and the alveolar bone exposed. The control sites (Drills) will be prepared with a lanceolate drill (FS 230, Sweden / Martina), with a maximum diameter of 2.3 mm, while the test sites will be prepared with conical diamond inserts of increasing diameter (SFS99.000.014 to SFS99.000.024, Komet-Brasseler-GmbH, Germany) mounted on a sonic-air surgical instrument (Sonosurgery® TKD, Calenzano, Fi - Italy). The dimensions of the final drill and of the final sonic device allowed the preparation of recipient sites of similar dimensions (about 2.3-2.4 mm in the coronal aspect). The mini-implants will be subsequently installed, a cover screw will be placed on the top of the mini-implants, and the flaps will be sutured allowing a fully submerged healing.

Antibiotics (amoxicillin 875 mg/clavulanic acid 125 mg twice a day for 6 days), non-steroidal anti-inflammatory drugs as needed (Ibuprofen 400 mg), and mouth rinses with 0.12% chlorhexidine three times a day for 10 days will be prescribed. The sutures will be removed after 7 days, and the patients will be enrolled in a maintenance recall. Biopsies

including the mini-implants will be retrieved after 2 or 6 weeks of healing, paying attention to keep the implant in an eccentric position within the trephine, to reduce the dimension of the biopsy and maintaining sufficient tissue for analysis, as previously described.²¹

Histological preparation of the biopsies

The biopsies will be washed in saline solution and immediately stored in 10% buffered formalin. The histological process will be performed in the laboratory facilities at the University of Chieti-Pescara, Italy. The biopsies will be not removed from the trephine. They will be dehydrated in an ascending series of alcohol, and subsequently embedded in a glycol-methacrylate resin (Technovit® 7200 VLC; Kulzer, Wehrheim, Germany). Once the polymerization will be finalized, the biopsies will be sectioned following the longitudinal axis of the samples using precision diamond disks, and specimens of about 150 microns of width will be obtained. The specimens will be afterwards ground to about 30 µm of width and stained with acid fuchsine and toluidine blue.

Histomorphometric evaluation

The histomorphometric evaluation will be performed twice by a blinded author, and mean values will be used. A code will be reported on the histological slides so that no indications will be available on the site preparation procedures and period of healing. All histological analyses will be carried out in ARDEC Academy, Italy, using an Eclipse Ci microscope (Nikon Corporation, Tokyo, Japan) connected to a digital video camera (Digital Sight DS-2Mv, Nikon Corporation, Tokyo, Japan). To carry out measurements, the software NIS-Elements D 4.10 (Laboratory Imaging, Nikon Corporation, Tokyo, Japan) will be used. The percentages of newly formed bone (new bone), pre-existing bone (old bone), bone debris/ clot remnants (debris), and marrow spaces (soft tissue) in contact with the implant surface will be evaluated at x200 magnification from the most coronal contact of

bone to the implant surface (B) to the apical extension of osseointegration (A). The total mineralized bone will be calculated as sum of new and old bone.

Morphometric measurements (tissues density) will be performed, identifying the same tissues above indicated plus vessels, in a region included between B and A, and at a distance from the implant surface of about 0.4 mm. For this purpose, a point counting procedure will be used applying a lattice with squares of 50 microns superposed over the histological slides, using a magnification of x200.

The *interception point* for new and pre-existing bone in contact with the implant surface will be calculated and expressed in days of occurrence and bone-to-implant contact percentage, according to Botticelli et al. (2017).²²

Outcomes Measures

Healing after two weeks

Primary outcome: New bone in contact with the implant surface.

Description: The percentages of new bone in contact with the implant surface will be evaluated in the histomorphometric analysis.

Timeframe: After 2 weeks, to evaluate the early healing after surgery.

Secondary outcome: The percentage of total mineralized bone in contact with the implant surface.

Description: The total mineralized bone will be assessed as sum of new and old bone as evaluated in the histomorphometric analysis.

Timeframe: After 2 weeks, to evaluate the early healing after surgery.

Other pre-specified outcomes: pre-existing (old) bone, soft tissues (marrow spaces, Haversian canals, BMUs canals), bone debris/ clot remnants, and vessels.

Description: The percentages of pre-existing (old) bone, soft tissues (marrow spaces, Haversian canals, BMUs canals), bone debris/ clot remnants and vessels in contact with the implant surface will be evaluated in the histomorphometric analysis.

Timeframe: After 2 weeks, to evaluate the early healing after surgery.

Healing after 6 weeks

Primary outcome: New bone in contact with the implant surface.

Description: The percentages of new bone in contact with the implant surface will be evaluated in the histomorphometric analysis.

Timeframe: After 6 weeks, to evaluate the healing prior to load with a prosthesis.

Secondary outcome: The percentage of total mineralized bone in contact with the implant surface.

Description: The total mineralized bone will be assessed as sum of new and old bone as evaluated in the histomorphometric analysis.

Timeframe: After 6 weeks, to evaluate the healing prior to load with a prosthesis.

Other pre-specified outcomes: pre-existing (old) bone, soft tissues (marrow spaces, Haversian canals, BMUs canals), bone debris/ clot remnants, and vessels.

Description: The percentages of pre-existing (old) bone, soft tissues (marrow spaces, Haversian canals, BMUs canals), bone debris/ clot remnants and vessels in contact with the implant surface will be evaluated in the histomorphometric analysis.

Timeframe: After 6 weeks, to evaluate the healing prior to load with a prosthesis.

Data analysis

Mean values and standard deviations as well as 25th, 50th (median), and 75th percentiles will be calculated for each outcome variable. Means, standard deviations and 95% upper and lower confidence interval of the difference between the means of sonic and drill sites

will be calculated for each variable analyzed for both histometric and morphometric analyses.

The primary variable will be newly formed bone (new bone) in contact with the implant surface. Total mineralized bone, calculated as sum of new and old pre-existing bone, in contact with the implant surface will be considered as secondary variable.

A Wilcoxon test will be used to analyze differences between sonic and drill groups for all outcomes. The level of significance will be set at α 0.05.

With an explorative aim, a Mann-Whitney test will be used to analyze the difference in new bone and total mineralize bone between 2 and 6 weeks of healing.

ACKNOWLEDGEMENTS

This study will be economically supported by ARDEC Academy, Ariminum Odontologica Srl, Rimini, Italy.

There are no conflicts of interest with the material presented.

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