Does the Osseodensification Technique Allow for the use of a Healing Chamber with Primary Stability in Low-Density Bone? An in Vivo Study

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Abstract

This study aimed to investigate *in vivo* the hypothesis that the osseodensification technique, through a wider osteotomy, produce healing chambers at the implant-bone interface with no impact on primary stability osseointegration in low-density bone. Twenty implants (3.5 x 10 mm) presenting nanohydroxyapatite (nHA) surface were inserted in the ilium of ten sheep, after preparation of a 2.7-mm wide implant bed with conventional subtractive drilling (SCD) or a 3.8-mm wide implant bed with an osseodensification bur system (OBS) (n = 5/group/period). The final insertion torque (IT) and implant stability quotient (ISQ) evaluated the primary implant stability. After 14 and 28 days, the bone samples containing the implants were processed for histological and histomorphometric evaluation of bone implant contact (BIC) and bone area fraction occupancy (BAFO). No significant differences occurred between the implant bed preparations regarding IT and ISQ ($P > 0.05$). Histological analysis showed bone remodeling, and bone growth in all samples with no inflammatory infiltrate. BIC values were higher for SCD after 14 and 28 days ($p < 0.05$), however BAFO values were similar on both groups ($p > 0.05$). It was possible to conclude that the osseodensification technique allowed a wider implant bed preparation with no prejudice on primary stability and bone remodeling.

Introduction

The use of biomimetic surfaces was observed in the early 90s, especially with hydroxyapatite (HA) coatings[1], to improve the osteoconductive property of titanium for an enhanced connection with the bone tissue[2,3]. However, a systematic review of clinical trials showed similar long-term survival between HA-coated and uncoated titanium implants[4]. The technology of plasma spray for HA application on the titanium surface, commercially available by that time, led to unexpected failures due to peri-implantitis by the rupture of HA-titanium interfacial and the increased bacterial adhesion[5].

With the development of nanotechnology, biomimetic surfaces migrated to the nanometric level. Among new titanium coating strategies, the use of nanohydroxyapatite (nHA) coatings maintain the potential of HA to induce a chemical bond to the bone while does not present the side effects of the HA coating by plasma spray[6]. Since the deposition of bone tissue on the surface of implant devices is strongly dependent on cellular interactions with the surface[7,8], the nHA coating may accelerate osseointegration because it creates a hydrophilic surface with nanostructures, which resemble the extracellular matrix of the bone tissue concerning the size, shape, and crystallinity, and works as more substantial anchoring points at the surface for bone cells[9,10].

Dental implants inserted in low-density bone, such as the posterior maxilla region, present lower survival rates[11–13]. Although nHA coating could be an essential tool to reduce implant failures, the osseointegration process is still dependent on the implant's primary stability. In this way, the concept of osseodensification (OD) was introduced aiming to improve the primary stability of implants placed in low-density bone sites[14]. OD is a surgical instrumentation technique where the bone is compacted into

open marrow spaces during drilling, increasing implant insertion torque through preservation and densification of osteotomy site walls[14–20]. Since more bone particles will be present at the bone-implant interface when the implant bed is prepared with OD, it is expected to accelerate bone healing and, consequently, faster osseointegration[18,21].

Due to the potential of biomimetic surfaces, it is recommended to create a space between the implant surface and the bone tissue, known as a healing chamber (HC), when drilling the implant bed to facilitate the deposition of new bone at the interface[22]. It is accomplished by using a final drill with a diameter larger than the implant's core diameter, but smaller diameter than the implant thread. Consequently, at the same time that the HC moves away the necrotic bone layer created by the surgical instrumentation, it allows space for the coagulum at the interface that recruits bone cells for faster bone formation[23,24]. However, the creation of HC reduces the bone-to-implant contact (BIC) causing lower primary stability that would not recommend the use of this concept for low-density bone.

There is a lack of information in the literature if the preparation of the implant bed using OD for implants installed in low-density bone sites would allow primary stability. Thus, the present study reports an *in vivo* biomechanical, histological, and histomorphometric analysis of nHA-coated dental implants placed in a surgical bed prepared in low-density bone using OD with a final diameter that creates HC at the interface.

Materials And Methods

Animal model

This *in vivo* study was approved by the Institutional Animal Care and Use Committee from Federal Fluminense University (protocol #9531061119) following the Animal Research: Reporting of *In Vivo* Experiments (ARRIVE) and Planning Research and Experimental Procedures on Animals: Recommendations for Excellence (PREPARE) guidelines[25,26]. The animals were kept and operated at the Federal Fluminense University Farm School and were accompanied by a veterinarian with more than 20 years of experience. All the experiments occurred during the first semester of 2020.

Sample size was calculated using a priori power analysis based on a previous study's results, which evaluated BIC in a same experimental animal model to estimate the effect size[27]. Considering type 1 error of 0.05 and power of 0.95, the two-tailed t-test determined a sample size of 5 implants per group/time point. In compliance with the reduction, refinement and replacement program [28], the animals were also used for another study [27]. None of the animals were euthanized after the end of the present study.

Ten adult female Santa Ines sheep aged 2–4 years, with an average body weight of 37.05 kg (range 31–42 kg), were randomly allocated using the coin-toss method into two experimental periods (14 or 28 days of healing).

Each animal received two implants (one for each group) in the ilium, a low-density bone, with a wide bone area that simultaneously allowed the installation of multiple implants. The bone blocks can be collected without any consequence for the animals in terms of locomotion and health. The implant position was randomly defined using the sealed envelope method, a surgical map of implant positioning inserted in the selected animal, ensuring a similar distribution into bone tissue for both groups. The inter-implant distance was at least 5 mm.

Before starting the study, all animals presented good general health and physical condition after clinical examination by an experienced veterinarian. In the preoperative period, the animals received food composed of the pastures above and, during the postoperative period, in addition to the mentioned pastures, nutritional supplementation proper for sheep. Salt mineral water *ad libitum* was available during the entire experimental period. The animals were transferred from the field to the research center two weeks before the surgeries to avoid stress. The animals fasted for eight hours before the surgery.

Surgical procedure and implants installation

The animals were given 0.05 mg/kg of acepromazine intravenously (Acepran®; Vetnil, Louveira, Sao Paulo, Brazil), 0.2 mg/kg of diazepam intravenously (Teuto, Anapolis, Goias, Brazil) and 0.4 mg/kg of morphine intramuscularly (Dimorf®; Cristalia, Itapira, Sao Paulo, Brazil) for premedication. After orotracheal intubation and ventilation, 4 mg/kg of propofol intravenously (Baxter Hospitalar LTDA; São Paulo, São Paulo, Brazil) was done and sustained using 1% isoflurane (Cristalia, Itapira, Sao Paulo, Brazil). Meanwhile, 4 mg/kg of lidocaine (Xylestesin™; Cristalia, Itapira, Sao Paulo, Brazil) and 0.1 mg/kg of morphine (Dimorf®; Cristalia, Itapira, Sao Paulo, Brazil) was used to block the epidural. The edges of the iliac crests were exposed through a skin incision of 5 cm in length. The skin and fascial layers were opened separately using scalpel handle no. 3 (Bard Parker®, Aspen Surgical, Caledonia, MI, USA) and blade no. 15 (Solidor®; Lamedid, Osasco, Sao Paulo, SP, Brazil).

A total of twenty titanium dental implants (3.5 mm of diameter and 10 mm length) with a biomimetic nHA surface (Epikut Plus®, S.I.N. Implant System, Sao Paulo, SP, Brazil), which surface morphology was already characterized in previous studies[10, 27] and by Scanning Electron Microscopy (SEM) with Energy-dispersive X-ray spectroscopy (EDS) (Fig. 1). Two different instrumentation techniques for the preparation of the implantation bed were used: Control group, subtractive conventional-drilling (SCD) according to the implant manufacturer instructions for low-density bone (lance bur, 2.0 and 2.7 mm diameter tapered burs); and Experimental group, osseodensification drilling (OCD) using multi fluted tapered burs (2.0 mm pilot, and 2.5, 3.0, and 3.3 conical burs) (Densah Bur; Versah®, Jackson, MI, USA), with a final diameter larger than the implant core diameter. Drilling was performed with clockwise rotation for SCD and counterclockwise rotation for OCD group at 1200 rpm under saline irrigation for both groups.

All implants were installed with the aid of a handpiece coupled to a drilling unit (BLM 600 plus; K Driller, Sao Paulo, Brazil) under profuse 0.9% sodium chloride solution (Darrow Laboratories SA, Rio de Janeiro, RJ, Brazil) and in low rotation (24 rpm) to avoid tissue necrosis due to overheating. The final insertion torque (IT) was recorded for each implant by the drilling unit. When the IT value was higher than 50 Ncm,

an analogic wrench was used (S.I.N. Implant System, Sao Paulo, Brazil). The average (± standard deviation) of the five samples was calculated for each group. The implant stability quotient (ISQ) was determined (Osstell®, USA), simulating mesiodistal and buccolingual measurements, and the average was recorded[29]. The average (± standard deviation) of the five samples was calculated for each group.

After surgical procedures, all animals received 4 mg/kg of Tramal® (Pfizer, New York, NY, USA) and 0.5 mg/kg of the anti-inflammatory meloxicam (Meloxivet®; Duprat, Rio de Janeiro, RJ, Brazil) over five days. Also, antibiotic therapy by intramuscular injection of 0.1 mL/kg of oxytetracycline (Terramicina®; Pfizer, New York, NY, USA) was used every 24 hours for three days, including the day of the surgery. Topically, Oxytetracycline spray with hydrocortisone was used daily at the wound site (Terra-Cortril® Spray; Zoetis, Sao Paulo, SP, Brazil), and zinc oxide ointment with cresylic acid was applied (Unguento Chemitec®; Chemitec, Sao Paulo, SP, Brazil) together with silver spray (Aerocid Total®; Agener União, Araçoiaba da Serra, SP, Brazil) to support healing and prevent local infection.

Histological procedures

The sheep were submitted to anesthetic procedures after 14 and 28 days of healing. The bone blocks were collected with a 5-mm internal diameter trephine drill (S.I.N. Implant System, São Paulo, SP, Brazil). The anesthetic and surgical procedures followed the protocol reported above and all sheep were subsequently returned to the farm, where they completely recovered after the biopsies.

Immediately after the collection, the samples containing bone and implants were fixed in 4% neutral-buffered formalin solution for 48 hours. The dehydration of samples in ascending alcohol solutions of 60%, 70%, 90%, and 100% was performed under agitation and vacuuming. Thereafter, infiltration with a light-curing resin (Technovit 7200; Kulzer & Co., Wehrheim, Germany) was performed according to the manufacturer's instructions. The bone blocks were embedded in the same resin and cut in the mid-axial and apical-coronal planes using a macro-scale cutting and grinding technique (Exakt 310 CP series: Exakt Apparatebau, Norderstedt, Germany). The obtained slices were ground and polished to a final thickness of 30 to 40 μm[30]. Finally, the slices were stained with Toluidine blue to differentiate newly formed bone, and acid fuchsin were used to contrast the background. Light microscopy at 10× and 20× magnifications (Olympus BX43; Olympus Corporation, Tokyo, Japan) supported the analysis of the slices, with images acquired with the cellSens software (Olympus Corporation, Tokyo, Japan). The histological events were evaluated and are illustrated in Fig. 2.

The histomorphometric analysis was conducted from reconstructions of the implant and adjacent bone. These images were obtained from captured photomicrographs with 10× magnification in sequenced fields to scan and reconstruct. After the reconstruction of all images, the area of interest was determined and drawn, from the first thread of the implant to the fourth thread's beginning (Fig. 3A) This line delimitation (Fig. 3B) (was used to determine the BIC value, which was later transformed into a percentage (Fig. 3C). The implant-profile design was then duplicated and aligned at 270 μm in the long axis of implant, thus completing the total area of interest. Image J software (National Institutes of Health,

Bethesda, MD, USA) manually determined the bone area fraction occupancy (BAFO), which was later transformed into a percentage (Fig. 3D)[27].

One single and experienced observer has conducted the histologic and histomorphometric evaluation. All samples were coded, and the examiner has evaluated the slides blindly concerning the experimental group and end points.

Statistical analysis

The Shapiro-Wilk test was used to check data distribution. The log transformation of ISQ was used to conform to normality. Fitting a normal distribution, the groups and the healing time points were compared using the t-test considering a significance level of 0.05. All analyses were accomplished using Prism Graph Pad 8.3® software (Inc. La Jolla, California, USA).

Results

In the present research, SCD and OCD groups presented final IT values above 60 Ncm (Table 1). No significant differences were observed between the surgical techniques (P > 0.05).

Table 1
Mean (s.d.) of the final insertion torque and implant stability quotient values for the subtractive conventional-drilling (SCD) and the osseodensification drilling (OCD) groups.

Surgical technique	Final Insertion Torque / Ncm (±sd)	Implant Stability Quotient
SCD	72.0 (±7.5)	73.2 (±2.7)
OCD	76.0 (±8.0)	73.2 (±2.6)
No significant differences were identified (P > 0.05).		

The histological analyses of non-decalcified sections allowed the analysis of the biological response to the tested surgical techniques. Both groups indicated peri-implant bone regeneration (Fig. 4). After 14 days of surgical procedure, the SCD group presented newly formed bone around the thread's implants showing an evident bone-implant contact (Fig. 4A). The OCD group presented a similar reaction after 14 days, presenting new bone trabeculae islands surrounding by connective tissue permeating the implant surface (Fig. 4B). After 28 days, in both groups, newly formed bone around the implants was clearly apparent and several areas of direct BIC were observed in a time-dependent fashion. The SCD presented extensive remodeling around the implant with a larger area and advanced degree of bone maturity (Fig. 4C), when compared to previous period. The pattern of bone remodeling in OCD group also presented more organized and compact bone tissue showing larger trabeculae of newly formed bone than first period (Fig. 4D).

The evaluation of BIC and BAFO showed a time dependent increase in SCD (p = 0.002) and OCD (P = 0.006) groups (Fig. 4). However, no significant differences of BIC and BAFO were identified between the groups (P > 0.05). After 14 days of healing, BIC values were 66.09% (±13.12) and 55.97% (±9.93) for SCD

and OCD (Fig. 5A), respectively, while BAFO yield 47.96% (±5.37) and 49.99% (±6.81) (Fig. 5B). After 28 days of healing, BIC values were 82.27% (±3.38) and 74.30% (±5.08) for SCD and OCD (Fig. 5A), respectively, while BAFO yield 65.53% (±6.22) and 61.76% (±4.45) (Fig. 5B).

Discussion

The clinical approach for installation of dental implants in low-density bone, such as the posterior region of the maxilla, usually consists of an underprepared implantation site to improve the implant's primary stability so osseointegration can proceed. On the other hand, implants presenting biomimetic surfaces, which can boost itself the bone healing process, may benefited when healing chambers are present at the surface[31]. Also, when the osteotomy is performed to allow the presence of the healing chambers at the bone-implant interface, it reduces the BIC. However, there is a gap of evidence concerning the capability of the biomimetic surfaces to overcome the inadequate primary stability induced by the production of the HC. So, it is possible to enquire if a hydrophilic surface with nanostructures and associated with a wider osteotomy technique, producing healing chambers at the implant-bone interface, would produce bone enough to provide satisfactory initial implant stability.

Therefore, the present study was designed to verify if the OD technique could be a viable approach for standardization of the healing chamber in low-density bone when using dental implants with a biomimetic surface. The ilium of a sheep was used as the animal model because this region is considered as a low-density bone[18,27,32], and it was already used in other histomorphometric studies involving dental implants without the need to euthanize the animals [30]. The implants used in this study have a bioactive surface with nanostructured hydroxyapatite and the only difference between the groups was the instrumentation technique of the implantation bed.

The first prerequisite for osseointegration is adequate final insertion torque and the implant's primary stability[8,33]. Both surgical techniques in the present study demonstrated adequate primary stability in the low-density bone, reflecting the special design of the implant to boost the primary stability[34]. Comparing the surgical techniques, similar IT and ISQ were identified for both groups, demonstrating that the densification of the interface promoted by OD compensates the use of implant-implant bed- discrepancy of 0.3 mm. The improvement of primary stability when using OD was observed in previous studies[14,18,23,32,35–38], regardless of the implant's design or the implant surface[17,19,39]. Nevertheless, previous studies demonstrated that the densification of the bone interface does not guarantee adequate primary stability *ex-vivo*[15] and *in vivo*[40] because of high interfacial stresses that caused fractures and triggered a prolonged period of bone resorption. However, it was the first time that such small implant-implant bed discrepancy was evaluated, and no fibrous tissue formation was identified at the bone-implant interface.

As expected for a wider implantation bed, BIC results at 14 days indicate no statistical differences. In contrast, Pantani et al. demonstrated in an *in vivo* study in dogs that milling with a final diameter 0.2 mm narrower than the implant produces a bone-implant contact similar to subtractive conventional

osteotomy with a final diameter 0.8 mm smaller than the implant [31]. When subtractive conventional drilling is compared to OD at same final diameter, previous studies, using the same animal model, have shown that this technique improved the bone volume around dental implants[16,41,42]. In contrast, other studies did not show any healing impairment due to the instrumentation[39]. Unfortunately, in the current study design, the BIC was not assessed at the time of implant insertion to determine the histological variation in 0 to 14 days of healing.

Histomorphometric analysis of BAFO, the implant-profile design was then duplicated and aligned at 270 µm in the long axis of implant, thus completing the total area of interest, this methodology was based on previous study that used 200µm, in this study 270µm was used to enlarge the area of interest[43,44]. When BAFO is observed, it is possible to note that a faster bone healing in the OCD group again compensates for the larger osteotomy. The bone interface was furthest from the implant surface in the OCD group at the moment of implant insertion, and after 14 days of bone healing, BAFO values were similar to the SCD group. In contrast, previous data reported similar bone healing when using OCD drills in subtractive mode (clockwise rotation) and densification mode (counterclockwise rotation)[39,41]. Since it was not evaluated a 3.8mm-wide implantation bed without OCD group, it was not possible to conclude if the faster healing would be a consequence of the healing chambers at the interface, as proposed by other authors[21,41], or because there was a denser bone-implant interface.

After 28 days of healing, BIC and BAFO values were similar in both SCD and OCD groups. After the same period, a higher difference between the groups was identified in a previous study in a pig model, in which BIC results for implants inserted in beds prepared with osseodensification (62.5%) when compared to implants inserted in beds prepared by the osteotome technique (31.4%) after 28 days in the mandibular crest[37]. However, the initial interlocking due to the implant geometry was higher in the present study, which can overlap the benefit of OCD in improving bone density at the interface.

Despite the present results of wider implant bed using OCD demonstrated to be a viable approach in low-density bone, it is important to highlight that it was used only one implant geometry with the nHA surface treatment, so the extrapolation of the results of the present study to other implant systems should be done with care. Long-term analyzes for assessing bone saucerization as a function of the osteotomy technique are strongly recommended.

Conclusion

The osseodensification technique performed with a wider surgical bed provided comparable levels of initial implant stability, BIC, and BAFO compared to the conventional subtractive under-drilling procedure without impairing the osseointegration. Despite the ability of the biomimetic nHA implant surface together OD allowed acceptable primary stability, the extrapolation of the present results to other implant geometry shall be done with care and long-term analysis are required to better understand the effect of OD on the implant survival.

Declarations

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Author Contributions Statement

M.D.C-M.; F.J.B.B. and B.G..: Study design and preparation of the manuscript. M.D.C-M.; S.C.S.; M.J.G.P.U.; B.G.: Surgical Intervention and preparation and submission of the manuscript. J.A.C-M; M.D.C-M; S.C.S.: Histological and histomorphometric evaluation; P.S.; C.F.A.B.M.; R.C.M.M.: interpretation of the results and preparation of the materials. J.M.G. and M.D.C-M.: Supervision, interpretation of the results, and preparation of the manuscript. All authors have read, edited, and approved the final manuscript.

Disclosure

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Figures

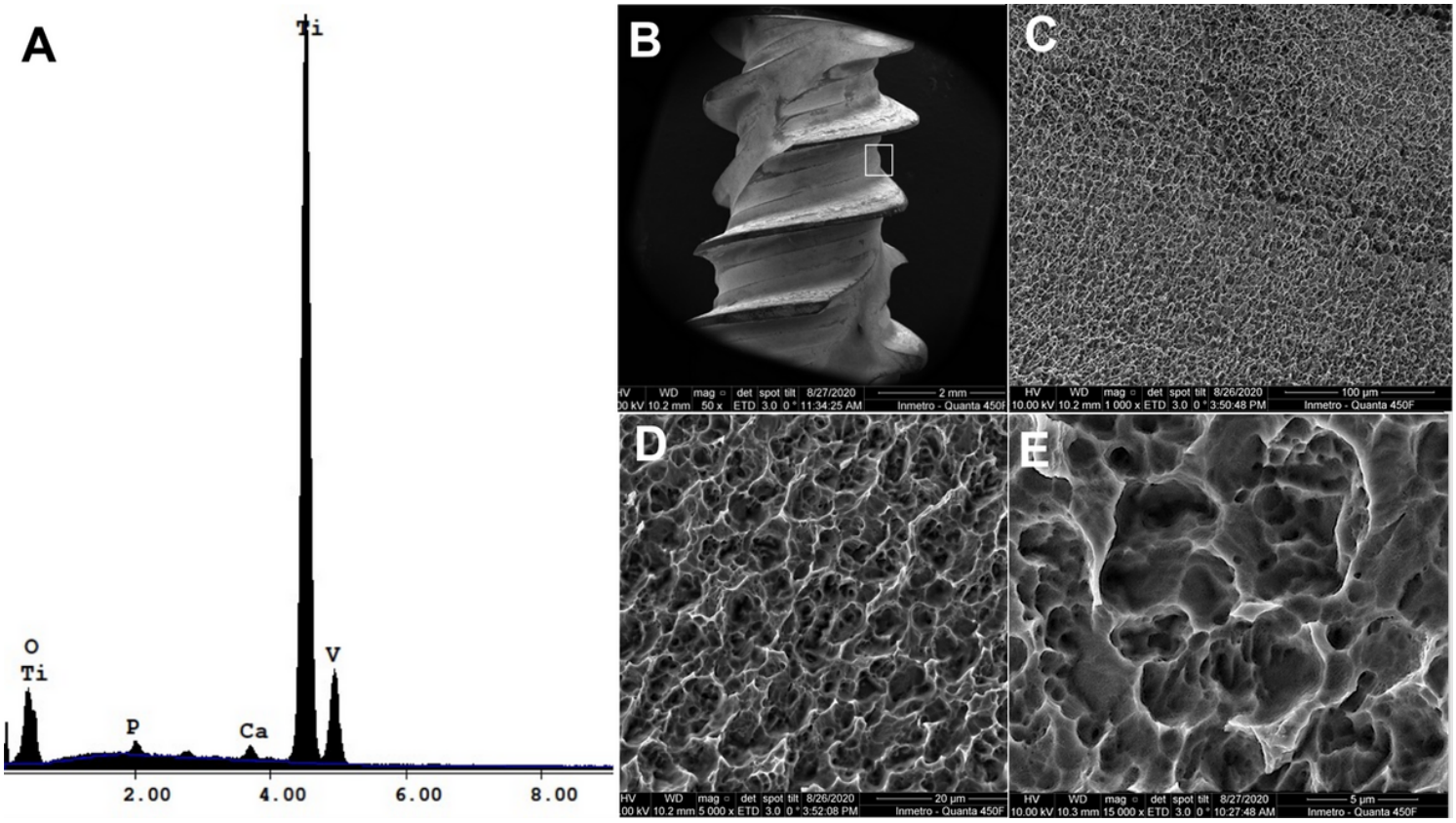

Figure 1

Scanning electron microscopy (SEM) micrographs of HAnano. A: EDS results showing the peak of Ca and P; B: implant geometry at 50x magnification (scale bar = 2 mm); C: implant surface at 1000x magnification (scale bar = 100μm); D: implant surface at 5000x magnification (scale bar = 20μm); E: implant surface at 15,000x magnification (scale bar = 5μm).

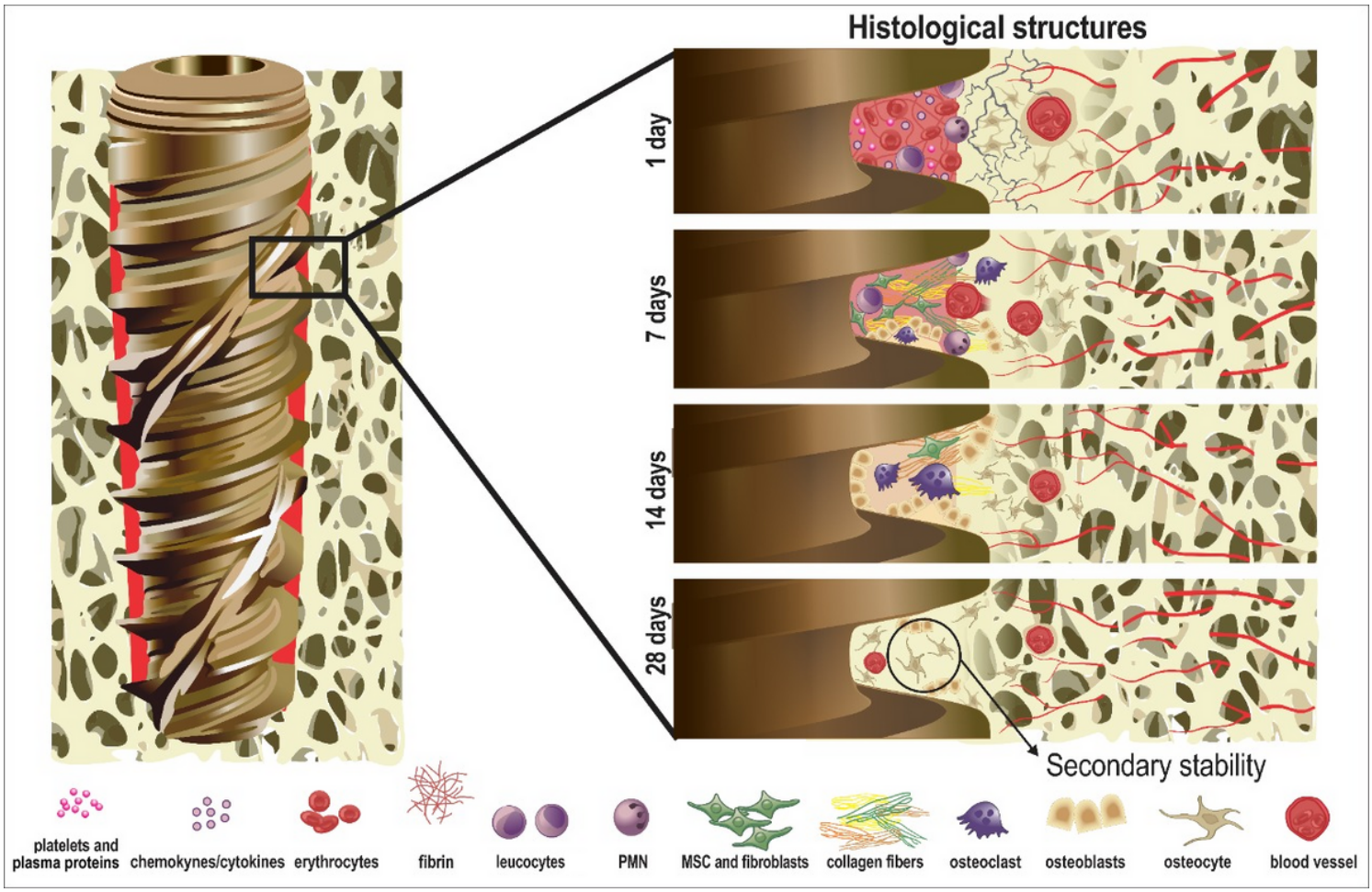

Figure 2

Graphical representation of microscopic and molecular events during osseointegration process from day 1 to 28 after implantation. It is possible to see the presence of a well-defined bone-implant interface after 28 days of implantation.

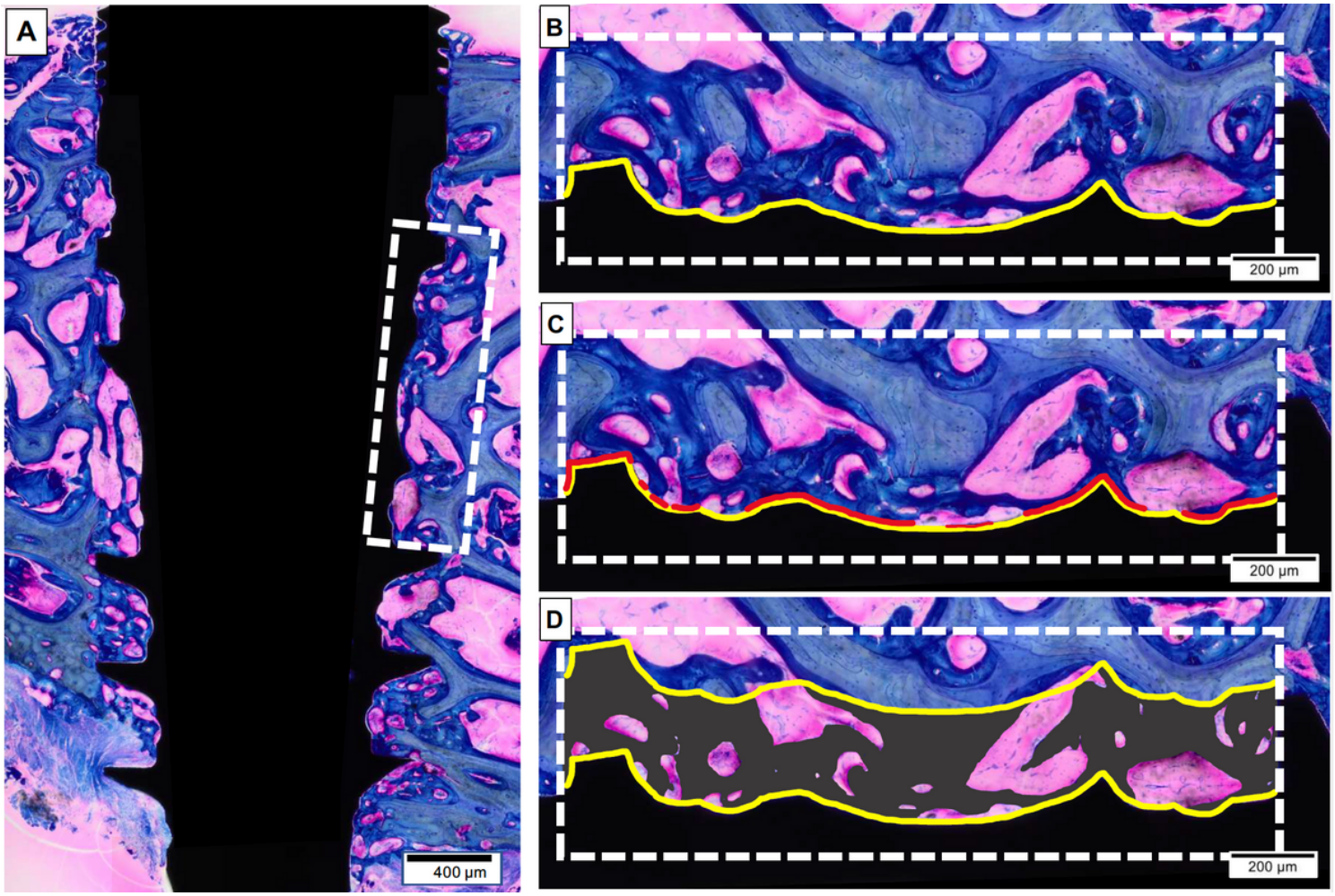

Figure 3

Illustration of histomorphometry methodology. (A) Histological reconstruction of area around the implant; (B) the line of interest considers to determinate the bone-implant contact (BIC) starts at the first thread of the implant to the beginning of the fourth thread (yellow line). (C) The red line corresponding to the BIC was measured as percentage. (D) The bone area fraction occupancy (BAFO) analysis was calculated in the same region of BIC, 270 µm from the line of implant profile design. The BAFO was manually determinates for posterior analysis (total area/BAFO) (%). Stain: Toluidine Blue and Acid Fuchsin stained. Scale bar: 200µm.

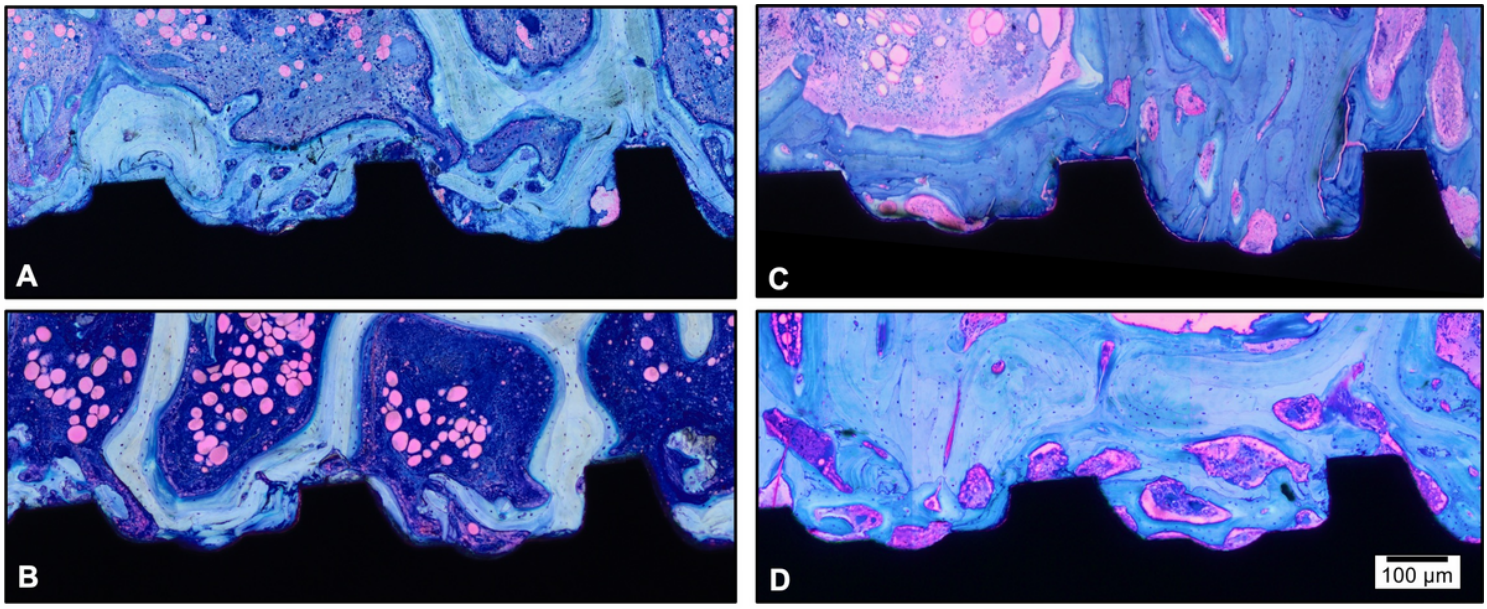

Figure 4

Representative photomicrographs of wound healing to different surgical drill technique, SCD (A and C) and OCD (B and D) 14 and 28 days after implantation, respectively. The area is corresponding to the three most coronally situated implant's threads. Stain: Toluidine Blue and Acid Fuchsin. Magnification: 20 X; Scale bar: 100 µm.

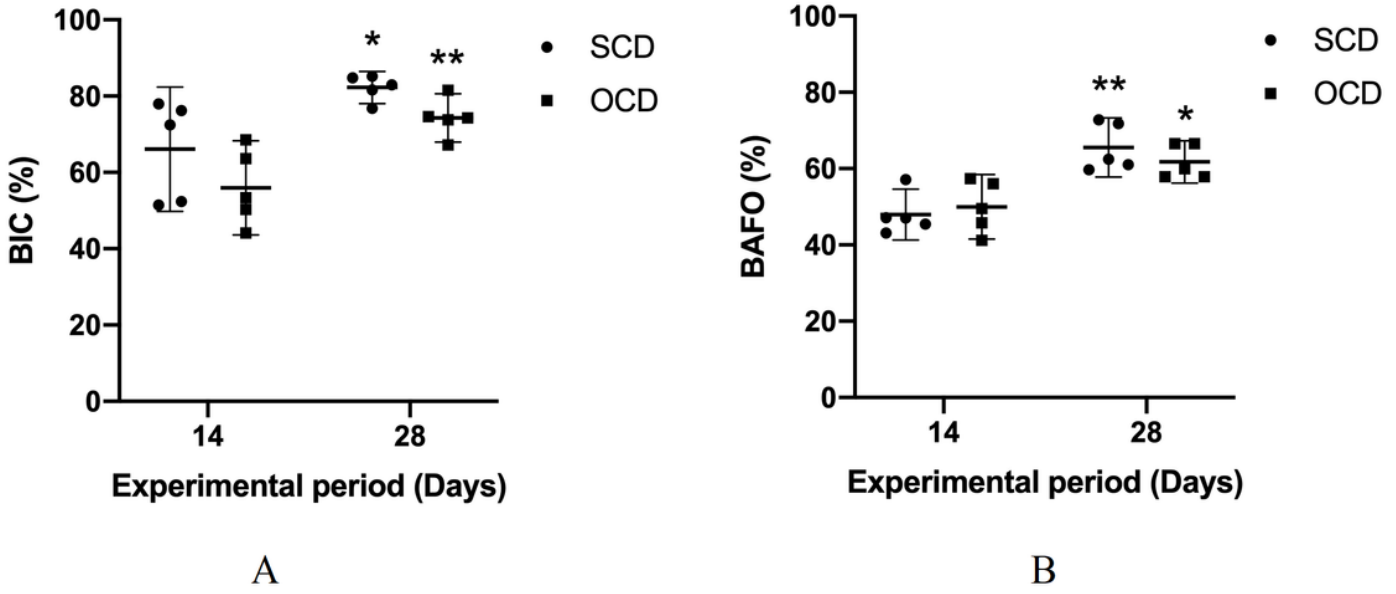

Figure 5

A. The bone-to-implant contact (BIC) and B. bone area fraction occupancy (BAFO) values of implants installed after subtractive conventional drilling (SCD) and osseodensification drilling (OCD). * and ** indicates significant difference between the evaluation period ($P<0.05$).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- STable1.pdf
- STable2.pdf
- STable3.pdf