

"Assessment Of Bone Regeneration With Dentin Graft Obtained Using The Tooth Transformer Device And Bone Quality Quantification Expressed In Hounsfield Units.

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Abstract:

Purpose: The purpose of this study is to analyze the bone quality obtained after alveolar preservation using autologous dentin graft obtained with the Tooth Transformer technology. The analysis involved assessing the Hounsfield Units (HU) within the previously regenerated implantation area. These measurements were derived from 3D images using the assistance of Blue-Sky Bio 4 Software.

Materials and Methods:

We have analyzed 67 images of regenerated alveoli using demineralized autologous dentin. From the initial cohort, 11 alveoli received an implant 6 months after the regeneration procedure, while the remaining 56 alveoli constituted the final subject of the study.

In this investigation, we examined imagery derived from an initial set of 67 regenerated alveoli treated with demineralized autologous dentin. Within this initial group 11 alveoli underwent implantation 6 months subsequent to the regeneration procedure, while the remaining alveoli formed the focal point of the study sample. The 56 patients who participated in the study, included 30 females and 26 males, aged between 21 and 81 years old, with an average age of 52.09 years (± 15.03).

They were followed up visits at 3, 6, 9, and 12 months after the alveolar preservation.

Results:

Following the 6 months visit, the alveolar regeneration with dentin, presented a 24% increase in bone density compared to the 3 month mark.

In contrast, the regenerated alveoli that did not receive an implant, had a progressive increase in Hounsfield Unit (HU) values over the course of a year, representing a 60% improvement in bone density compared to the 3 month measurement.

For the alveoli regenerated using this technique and subsequently implanted after 6 months, a highly positive correlation is observed between the Implant Stability Quotient (ISQ) measured immediately after implant insertion and the bone density expressed in Hounsfield Units (HU).

Keywords: Autologous dentin, alveolar preservation, Tooth Transformer, Hounsfield units, Blue Sky Bio 4.

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I. Introduction:

Currently, tissue and bone regeneration techniques not only rely on the clinical skill of professionals but also on their ability to integrate physiological, biochemical, immunological, and genetic concepts into their diagnosis. These factors play a significant role in establishing and ensuring the predictability of long-term oral rehabilitations through osseointegrated implants (1).

Following tooth extraction, a series of changes occur in the alveolus, both morphologically, histologically, and three-dimensionally, which deviate from the criteria of excellence in current implantology. These criteria dictate that an implant, even if osseointegrated and functionally adequate, fails to fulfill its therapeutic objective if it does not meet the patient's aesthetic demands (2).

The ideal position for an implant is where the root of the extracted tooth used to be. However, due to the process of resorption, we are compelled to seek an alternative location, compromising not only the function but also aspects such as the three-dimensional orientation of the implant in space and the aesthetics of the emergence profile (3, 4).

It is widely known that both bone and dentin originate from the same embryonic layer and share similar characteristics in terms of their organic and inorganic composition, except for their respective forming cells (5). However, the bone, due to its biomaterial nature, contributes to regeneration through bone-forming cells known as osteoblasts, making it the ideal material for this purpose. It is osteoconductive, osteoinductive and osteogenic. Nevertheless, one of its disadvantages is that it always requires a donor site. In this regard, dentin has an advantage over bone as it can be obtained either from the regenerating site itself or from donor sites that are commonly necessary to intervene, such as impacted, retained or supernumerary teeth.

Since the mid-twentieth century, specifically with the research of Urist (6) up until today, dentin has been studied as a biomaterial for bone regeneration. Over the years, the quantity and variety of studies on dentin have increased, with the majority of them establishing that it is a suitable material for this purpose (7). Additionally, dentin has the advantage of gradually and completely resorbing, taking about 8 months, which gives the bone the necessary time to regenerate "ad integrum". Moreover, due to its complete resorption, there will be no implant-biomaterial interface in the future without osseointegration (8).

Once the alveolus has been regenerated, and prior to implant insertion, the treatment plan will be largely determined by the clinical observation of the regenerated area and its radiological characteristics. The diagnosis is aided by 2D images obtained through conventional radiology and 3D images obtained through Cone Beam Computed Tomography (CBCT) (9). Analyzing these 3D images using reliable software such as Blue Sky Bio 4 allows us to determine the density of the regenerated zone, which is expressed in Hounsfield Units (HU). The HU values provide information about the density of different materials: -1000 HU represents air density, 1600 to 2400 HU for dentin, and +3000 HU for dental materials. By reading these HU values, we can assess bone density, considering that bone type IV ranges from 150 HU to 400 HU, bone type III from 400 HU to 800 HU, bone type II from 800 HU to 1200 HU, and bone type I has more than 1200 HU (3).

This study analyzed the evolution of the density in the area regenerated with autologous dentin during the year following the intervention, with radiological evaluations conducted at 3, 6, 9, and 12 months.

II. Materials and Methods:

Study Design:

This study is an "longitudinal observational case-control study" conducted at the Oral Medicine Teaching Unit in the Faculty of Medicine and Dentistry at the University of Santiago de Compostela.

The trial adhered to the principles of the Declaration of Helsinki and obtained approval from the Ethics Committee of the University of Santiago de Compostela, to ensure its alignment with ethical and governance standards.

Participants:

Those patients who were candidates for the extraction of one or more teeth from which viable dentin could be obtained and who subsequently required rehabilitation through implant-supported prostheses were selected.

The following inclusion and exclusion criteria were applied for their selection:

Inclusion Criteria:

- Healthy adult patients over 18 years of age.
- Patients in need of the extraction of one or more teeth suitable for obtaining dentin and for which clinical indications justified their extraction.
- Patients who agreed to participate in the study, signed their informed written consent, and agreed to attend follow-up visits.

- Patients without systemic issues that could influence the graft's evolution.
- Patients who understood the purpose of the study.

Exclusion Criteria:

- Patients unwilling to participate in the study.
- Patients with endocrine, metabolic, or systemic disorders that could affect alveolar preservation.
- Patients with incomplete, deficient, or abnormal dental formation.
- Pregnant patients.
- Patients with psychiatric disorders or those unwilling to commit to the study.
- Patients with pathologies that could have been exacerbated by the surgery itself or by intra or post-operative medication.
- Immunocompromised patients.
- Patients who have been treated with oral or injectable bisphosphonates.
- Patients who have undergone chemotherapy or radiotherapy within 6 months before the study.
- Patients who smoked more than 10 cigarettes per day in the last year.

Materials:

To perform both the clinical and radiological procedures, in addition to the standard instruments commonly used in regenerative surgery, we used the following technological devices:

Tooth Transformer (TT Tooth Transformer s.r.l, Milan, Italy) is a medical device specifically designed to obtain autologous dentin for use as a graft material in alveolar preservation techniques. The process involves two distinct cycles:

1. In the first cycle, lasting a maximum of 4 minutes, the tooth is triturated to obtain particles ranging between 0.4 and 0.8 mm in size.
2. The second cycle, which lasts 25 minutes, involves the use of liquids contained in single-use cartridges to demineralize, disinfect, and hydrate the dentin. This process yields autologous demineralized dentin that is suitable for use as a graft material in the alveolar preservation procedure.

Medifuge CGF Centrifuge (Silfradent s.r.l, Forlì, Italy): This centrifuge machine has a 13 minute long centrifugation cycle consisting of diverse speeds: 2700 rpm for 2 minutes, 2400 rpm for 4 minutes, 2700 rpm for 4 minutes, and finally 3000 rpm for 3 minutes. These speed variations allow the fibrin matrix to become denser, larger, and richer in growth factors. The CGF (Concentrated Growth Factors) blocks produced through this process exhibit higher stability and tensile strength, with excellent elastic behavior, making them ideal for creating membranes or mixing with biomaterial for the formation of sticky bone or sticky dentin.

CBCT 3D ProMax 3D Mid (Planmeca – Helsinki – Finland): Intelligent/Multipurpose X-ray Unit, providing panoramic and 3D digital images (CBCT).

Ostell (W&H – Bürmoos - Austria): This device uses resonance frequency analysis (in kHz) to translate Implant Stability Quotient (ISQ) into a clinically useful scale ranging from 1 to 100. ISQ values below 60 indicate low implant stability, while values between 60 and 65 indicate moderate stability, and values above 70 indicate high stability.

Clinical protocol:

Prior Protocol:

Following the completion of the medical history, a comprehensive oral examination and complete blood analysis were performed. After obtaining radiographic and tomographic images and analyzing the areas to be treated, it was ensured that all dental apices were fully formed.

Selected individuals received a vitamin therapy at least 30 days before surgery through chewable tablets containing calcium and colecalciferol (Calcium/Vitamin D3 Sandoz 1000 mg/880 IU). This therapy has been proven, especially in surgical traumatology, to enhance the quality of bone healing and reduce the healing time, in addition to preventing other fractures (10).

All patients were prescribed antibiotics, which they were required to start taking one day before the surgery.

Surgical Protocol:

- Blood extraction from the antecubital area using borosilicate tubes for obtaining CGF membranes through centrifugation. Tubes were always placed in pairs, and in the case of an odd number, one tube filled with water was included to balance the device, which has a maximum capacity of 8 tubes. After centrifugation, the tubes were left in a tube holder until the membranes were required for surgery. When necessary, the complete clot was extracted from the tube.

The clot presented two distinct zones: a lower red portion where red blood cells were trapped, and an upper yellowish portion composed mainly of fibrin, where platelets and stem cells were trapped. The red fraction

was carefully separated from the yellow upper portion using a spatula to avoid damaging the yellow fraction. The red fraction was discarded, and then, using a membrane preparation forceps, the clot was compressed to completely express the serum, forming the membrane.

- Immediately after blood extraction, the atraumatic exodontia of the dental pieces was performed, with the previous creation of a mucoperiosteal flap.
- The extracted teeth were immediately processed: Using frustoconical diamond burs, deposits of tartar and periodontal tissue adhered to the root of the extracted teeth were cleaned. Any remaining amalgams, composites, gutta-percha or restorations present on the teeth were removed, along with a small margin of additional tissue (even if it seemed suitable for obtaining dentin) as a safety measure to remove any non-visible materials or products such as amalgam oxides, adhesives, etc.

The teeth were safely fractionated into pieces no larger than 4 or 5 mm using a diamond disc NTI 806 104 355 514, while holding the tooth with a Crile-Wood CT needle holder. These dental fractions were washed with saline solution and then dried using oil-free compressed air. The pieces were placed in the Tooth Transformer device in necessary amounts to prevent overloading the grinder. In several batches, the portion were processed for 5 minutes, resulting in a biomaterial ranging in size between 0.4 and 0.8 mm. Smaller particles were sieved and discarded from the receptacle containing the processed material, which has perforations at its base for this purpose.

Once it was observed that the tooth was sufficiently triturated and that no inappropriate-sized pieces remained in the container, the cartridge was perforated and inserted to allow the machine to proceed with a second cycle of demineralization, disinfection, washing, and hydration.

- During the graft material preparation, the alveoli were covered with gauzes moistened with saline solution (Vitalia 9%). When the second cycle of the Tooth-transforming device commenced, the surgical procedure recommenced, involving a thorough and comprehensive curettage of the alveolar area. Finally, the entire region to be regenerated underwent a gentle milling process using a round carbide Tungsten to ensure that only bone tissue remained in the alveolus and that it had sufficient bleeding.
- Once the alveolus was deemed suitable for regeneration, it was filled with the processed dentin. Subsequently, the coronal portion of the alveolus was sealed with a 0.2 mm thick type I highly purified equine atelocollagen membrane (Collygen), immobilized with suture points to the mucoperiosteal flap or allowed to be held in place by the weight of the flap. Additionally, this membrane was covered with an autologous CGF membrane (Concentrated Growth Factors).
- The flaps were repositioned, and in cases where necessary, prior surgical maneuvers were performed to ensure elongation coupled with basic nylon sutures for effective closure of the surgical site.
- At 10 days post-surgery, wound checks were performed, and sutures were removed.

Image Analysis:

- The image analysis was performed using the Blue Sky Bio 4 software, with images obtained from a Planmeca CBCT device, the ProMax 3D Mid.
- For the analysis, once the STL (Standard Triangle Language) files were loaded into the software, a quadrilateral was designed in the regenerated area to be implanted, excluding the buccal and palatal/lingual bone plates. This quadrilateral was divided into 6 zones: three vestibular zones and three buccal (palatal/lingual) zones. These zones were labeled Vc, Vm, and Va (coronal, medial and apical successively) for the vestibular areas, and Bc, Bm, and Ba for the buccal or palatal/lingual areas. At the center of each zone, using a dedicated tool in the program, the Hounsfield units were determined, and the average values were calculated (Fig 1). This procedure was carried out for images obtained in the regenerated area at 3, 6, 9, and 12 months, except for 11 cases where the analysis was performed at 3 and 6 months before subsequent implant surgery. In these implant cases, the Implant Stability Quotient (ISQ) was measured using the Ostell device.

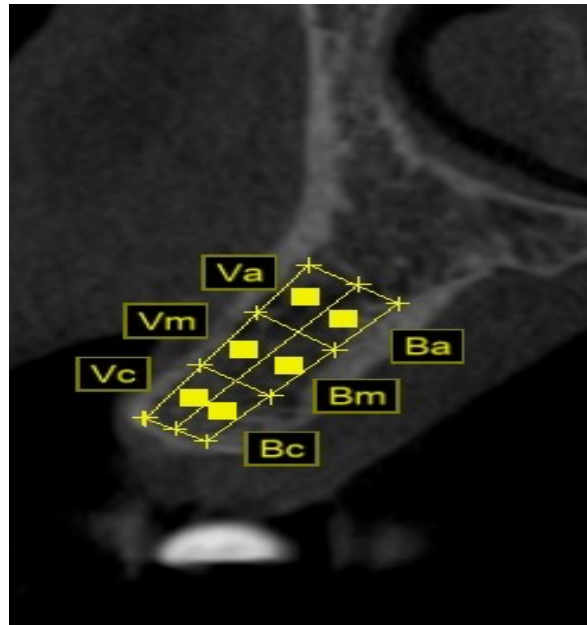


Fig. 1 Vc, Vm, and Va (coronal, medial and apical vestibular area) and Bc, Bm, and Ba (buccal or palatal/lingual areas).

Statistical Analysis:

To analyze the evolution of the Hounsfield units and compare them between groups, we used mixed-effects linear regression models with random intercepts and repeated measures, adjusted for tobacco use. Generalized Linear Mixed Models (GLMM) were run with robust covariance estimation to handle potential violations of model assumptions. Marginal means and 95% confidence intervals are reported for all analyses. Different levels of significance were employed in the analyses (1% ($\alpha=0.01$), 5% ($\alpha=0.05$), 10% ($\alpha=0.1$)). IBM SPSS Statistics 26 software was used for all statistical analyses.

III. Results:

A total of 56 patients were included in this study, comprising 30 women and 26 men, with ages ranging from 21 to 81 years and an average of 52.09 years of age (± 15.03) (Fig. 2). Among the participants, 25% were taking medications, 21% were smokers, and 11% had hypertension (Fig 3).

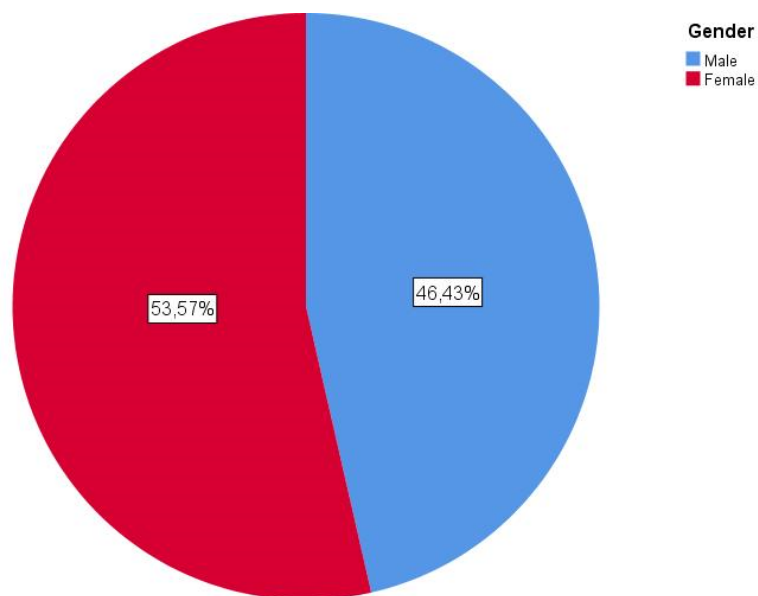


Fig 2

COMORBIDITIES

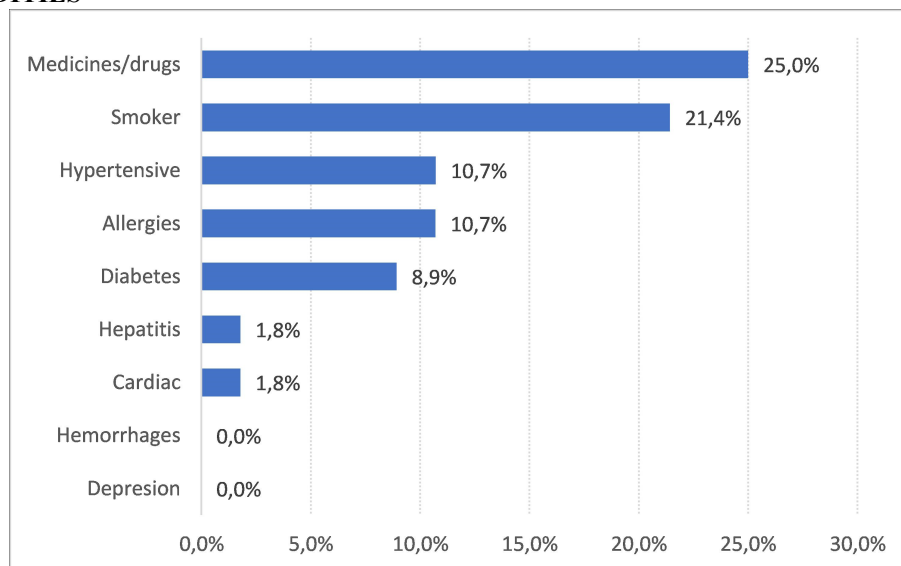


Fig.3

Based solely on the alveoli, 28.4% of the alveoli belong to patients who take medications, and 25.4% of the alveoli belong to patients who smoke.

To evaluate this study, we have established four distinct zones:

1. **UF** (Upper Front): Includes the upper canines and incisors.
2. **UB** (Upper Back): Includes the upper premolars and molars.
3. **LF** (Lower Front): Includes the lower canines and incisors.
4. **LB** (Lower Back): Includes the lower premolars and molars.

Evaluating all alveoli together without differentiating between regenerated and regenerated/implanted, there is an average increase of 137,307 Hounsfield units at 6 months, rising from 578,771 Hounsfield units at 3 months to 716,078 Hounsfield units at 6 months (+24%) (F(116.646,1,125), p 0.000).

However, there are no significant differences in the changes according to the mouth zone (F(0.190,3,128), p 0.903) (see Table 1):

- In the UF sector, the increase is 149,942 Hu.
- In the UB sector, the increase is 127,750 Hu.
- In the LF sector, the increase is 129,845 Hu.
- In the LB sector, the increase is 141,690 Hu.

For those who were only regenerated and not implanted, the mean value in Hounsfield units (Hu) at three months after the regeneration was 566,865 [518,623; 615,107], indicating a bone density compatible with type III bone. At six months, the density increased by approximately 25%, reaching an average of 707,574 Hu [666,399; 748,748] (t(9.707, 207) p 0.000), which brings it closer to type II bone (800-1200 Hu). At nine months, the density further increased to 812,457 Hu [761,651; 863,262] (+15% compared to six months and 43% over three months) (t(6.418, 207) p 0.000). Finally, at 12 months, there was a further increase, with an average of 910,527 Hu [851,169; 969,885] (t(4.595, 207) p 0.000), which is compatible with high-quality type II bone, and in some cases approaching type I bone (Table 1).

Overall, the evolutionary pattern of Hounsfield units differs significantly between mouth zones (F(3.982, 9,207), p 0.000). Between three and six months, the behavior is uniform in all mouth zones, with Hounsfield units increasing to the same extent. Between six and nine months, all zones show a similar increase in average Hounsfield units, except for the Lower Back zone (orange line), where there is no significant change (t(1.320,207) p 0.188). Between nine and twelve months, only the Upper Front and Upper Back zones show a significant increase (t(6.498,207) p<0.001 and t(2.369,207) p 0.019, respectively). (Fig 4)

Additionally, in general, the average Hounsfield units reached at each follow-up time differ significantly between zones (F(8.475,3,207) p 0.000). The average Hounsfield unit values are statistically higher in the Lower Front zone compared to the rest of the zones throughout the follow-up. At nine and twelve months, the average Hounsfield unit values in the Upper Front zone are also higher than in the Backs zones (UB and LB) (Table 2).

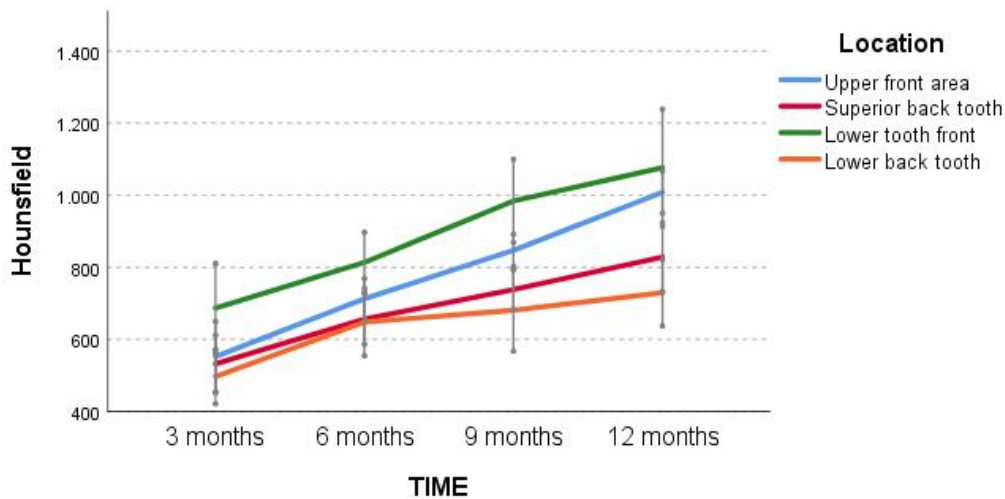


Fig 4

Among the participants patients, 11 of them underwent implant surgery six months after the regeneration process. High stability values, averaging around 70 in ISQ, were achieved correlating with average of 752.83 Hu (± 123.81). A noteworthy and affirmative correlation between ISQ and Hounsfield units was observed at 6 months (Spearman's Rho: 0.752, $p < 0.001$ with ISQ_BP_6 and Rho: 0.694, $p < 0.001$ with ISQ_MP_6). (Fig 5)

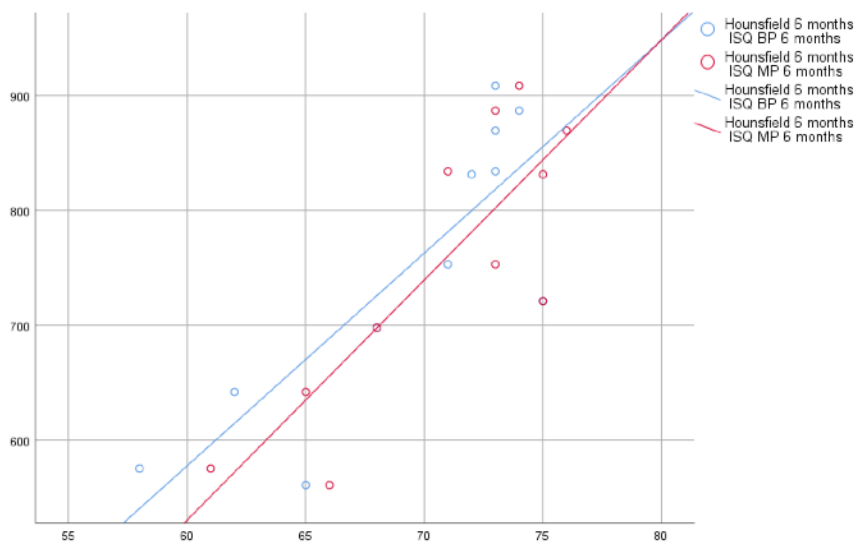


Fig 5

IV. Discussion:

The aim of this study was to evaluate the bone quality obtained over the course of one year following alveolar preservation with autologous dentin, as expressed by Hounsfield units.

While all biomaterials offer osteoconduction, not all of them are osteoinductive, like dentin, which directly stimulates bone formation through morphogenetic proteins.

Numerous studies, such as Lee's (11), provide excellent results supporting the existence of an effective response to dentin grafting, whether combined with xenograft or not, without finding any secondary complications in these works. Other studies, like Jeong's (12), attempted to demonstrate the effectiveness of demineralized dentin in the sinus lift technique. These had performed biopsies six months after the surgical technique in 27 patients and were able to observe adequate bone formation (46-87% of cases at six months) and implant survival of 78%.

One of the main characteristics of an ideal biomaterial is complete resorption: not occupying space that should be taken by new bone. In this regard, studies conducted by Kim et al. (13) have demonstrated significant resorption of dentin grafts at three months, leaving behind 39% to 79% of new bone based on biopsy findings. The research group of Kabir and Murata (14) evaluated dentin grafts through clinical and radiographic controls at 3 and 12 months, revealing the adequate replacement of a significant portion of demineralized dentin matrix with new bone tissue, preventing the distal bone resorption of the second molar that commonly occurs after third molar extraction.

The latest systematic reviews (15) highlight that there are no statistically significant differences between using dentin in granules or in block form, nor between using it alone or in combination with other biocompatible graft materials. Nonetheless, it is evident that a substantial variability exists within studies concerning this topic, characterized by diverse locations, anatomical considerations, evaluation methods and surgical techniques being employed. This lack of uniformity significantly impacts the resultant outcomes.

In a study published in 2019 by the team of Del Canto and Martínez González (16) two groups were established: a control group in which the alveolus remained unfilled after tooth extraction, and another group in which the alveolar defect was filled with freshly processed demineralized dentin. Subsequently, dimensional and densitometric analyses of the alveoli were conducted. The study concluded that the dentin grafting technique is a promising approach that requires standardized protocols.

One of the latest literature reviews was published in 2022 by the research team of Grawish (17). They analyzed all the searches in the Pubmed and Midline databases up until October 2021, which included relevant articles on the use of demineralized dentin grafts as a material for bone regeneration. The review did not reach any definitive conclusion and did not indicate a clear indication within the possible oral surgical techniques. However, it pointed out that by using the appropriate particle size and respecting its biological property, demineralized dentin can be efficiently used as a substitute for some of the commonly used biomaterials in guided bone regeneration techniques.

The latest systematic review we have been able to access was conducted by Luis Sanchez-Labrador from the Complutense University of Madrid. Following the PRISMA guidelines, this review included relevant clinical articles published before March 10, 2022 (18).

The review included studies in humans, with at least 4 patients whose treatment and subsequent regeneration involved at least one surgical technique. Its main conclusions are that, after tooth extraction, this technique is effective in maintaining bone volume, showing promising results in histological and histomorphometric analysis, while reflecting a low rate of complications.

Furthermore, this newly formed bone must have sufficient quality to receive an implant, as primary stability is essential for the success of implants. In a recent randomized and prospective clinical trial conducted by Pang's team (19), they compared the vertical dimension of the grafted bone in 24 patients, with 12 of them treated with demineralized dentin grafts and the other 12 with Bioss® grafts. The study demonstrated that both groups showed favorable surgical wound healing, similar coefficients of implant stability indicating comparable levels of osseointegration, and peri-implant bone maturation confirmed by biopsy and subsequent histological analysis.

V. Conclusions:

1. At 6 months after alveolar regeneration with autologous dentin, there is a 24% increase in bone density compared to 3 months.
2. There are no significant differences between the different areas of the mouth, as the magnitudes of the increases in each zone are statistically equal (Table 1).
3. In the alveoli that underwent regeneration without immediate implantation, there was a progressive increase in Hu values over the course of a year, resulting in a final 60% increase in bone density compared to 3 months, with some variations depending on the mouth area (Table 2 and Fig. 5).
4. In the alveoli regenerated using this technique and subsequently implanted at 6 months, we observed a highly positive and strong correlation between the immediately measured ISQ (Implant Stability Quotient) values after implant insertion and the bone density expressed in Hu (preoperative values) in that area.
5. This study highlights the efficacy of alveolar preservation using autologous dentin and its positive influence on bone quality expressed in Hounsfield units. These results suggest that this technique may be a viable option to enhance bone quality in edentulous areas before dental implant placement, which could have a significant impact on the predictability and long-term success of implant supported dental rehabilitations. However, further research is needed to confirm these findings and assess the clinical applicability in different patient populations.

Table 1		3 months		6 months		Difference 6 months -3 months		P-VALUE
		mean	e IC95%	mean	e IC95%	mean	e IC95%	
Hu	total	578.771 (537.298,620.244)	716.078 (682.393,749.763)	137.307 *** (112.146,162.468)			0.000***	
	Location	Upper Front (n=23)	562.562 (476.548,648.576)	712.504 (660.353,764.655)	149.940 *** (81.101,218.783)			0.903
		Upper Back (n=16)	534.763 (461.017,608.508)	662.513 (591.823,733.203)	127.75 *** (99.776,155.724)			
		Lower Front (n=14)	705.553 (601.692,809.414)	835.398 (765.496,905.301)	129.845 *** (74.501,185.19)			
		Lower Back (n=14)	512.207 (442.696,581.717)	653.897 (575.726,732.068)	141.690 *** (102.099,181.282)			

First p-value: Time effect (if there is, in general, a significant change at 6 months, without separating by groups)
 Second p-value: Time*Group effect (differences between changes per mouth area) Within each change between

moments, significance is indicated with asterisks:

- *p-value < 0.1 (significant result at 90%)
- ** p-value < 0.05 (significant result at 95%)
- *** p-value < 0.01 (significant result at 99%)

TABLE 2 Only regenerated		3 mont hs	6 mont hs	9 mont hs	12 mont hs	Difference 6 -3 months	Difference 9 -6 months	Difference 12- 9months	Difference 12 - 3months	P-VALUE	
		mean & IC95 %	mean & IC95 %	mean & IC95 %	mean & IC95 %	mean & IC95%	mean & IC95%	mean & IC95%	mean & IC95%		
Hu	total	566.8 65 (518.6 23, 615.1 07)	707.5 74 (666.3 99, 748.7 48)	812.4 57 (761.6 51, 863.2 662)	910.5 27 (851.1 69, 969.8 85)	140.709** * (112.132,1 69.286)	104.883** * (72.664,13 7.101)	98.070*** (55.995,14 0.145)	343.662** * (281.255,4 06.069)	0.000 ***	
	Location	Upper Front (n=20)	552.0 21 (454.4 15, 649.6 27)	712.7 04 (656.5 58, 768.8 5)	847.1 79 (802.7 6 ,891.5 98)	1008. 129 (949.8 21, 1066. 438)	160.683** * (84.987,23 6.38)	134.475** * (103.309,1 65.641)	160.95*** (112.119,2 09.781)	456.108** * (372.906,5 39.311)	0.000 ***
		Upper Back (n=13)	531.9 68 (452.1 84, 611.7 51)	656.1 73 (586.0 48, 726.2 98)	738.0 32 (683.1 14, 792.9 5)	828.2 63 (732.8 56, 923.6 69)	124.205** * (92.936,15 5.474)	81.859*** (39.039,12 4.679)	90.231** (15.14,165. 322)	296.295** * (189.521,4 03.069)	
		Lower Front (n=12)	686.7 23 (563.3 22, 810.1 23)	813.6 25 (730.2 54, 896.9 97)	983.9 59 (868.6 4, 1099. 278)	1076. 361 (914.1 73, 1238. 55)	126.903** * (62.424,19 1.381)	170.333** * (62.389,27 8.277)	92.403 (- 39.876,224 .681)	389.639** * (186.379,5 92.899)	
		Lower Back (n=11)	496.7 48 (421.0 49, 572.4 46)	647.7 93 (554.4 71, 741.1 15)	680.6 57 (567.4 48, 793.8 66)	729.3 54 (636.9 13, 821.7 94)	151.045** * (103.516,1 98.575)	32.864 (- 14.184,79. 911)	48.697* (- 3.988,101. 382)	232.606** * (179.995,2 85.217)	

First p-value: Time effect (if there is a significant overall change throughout the follow-up, without separating by groups)

Second p-value: Time*Group effect (differences in evolutionary patterns by mouth area)

Within each change between moments, it is indicated with asterisks if the change is significant or not.

- * p-value < 0.1 (significant result at 90%)
- ** p-value < 0.05 (significant result at 95%)
- *** p-value < 0.01 (significant result at 99%)

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