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Lucía Barallat Sendagorta

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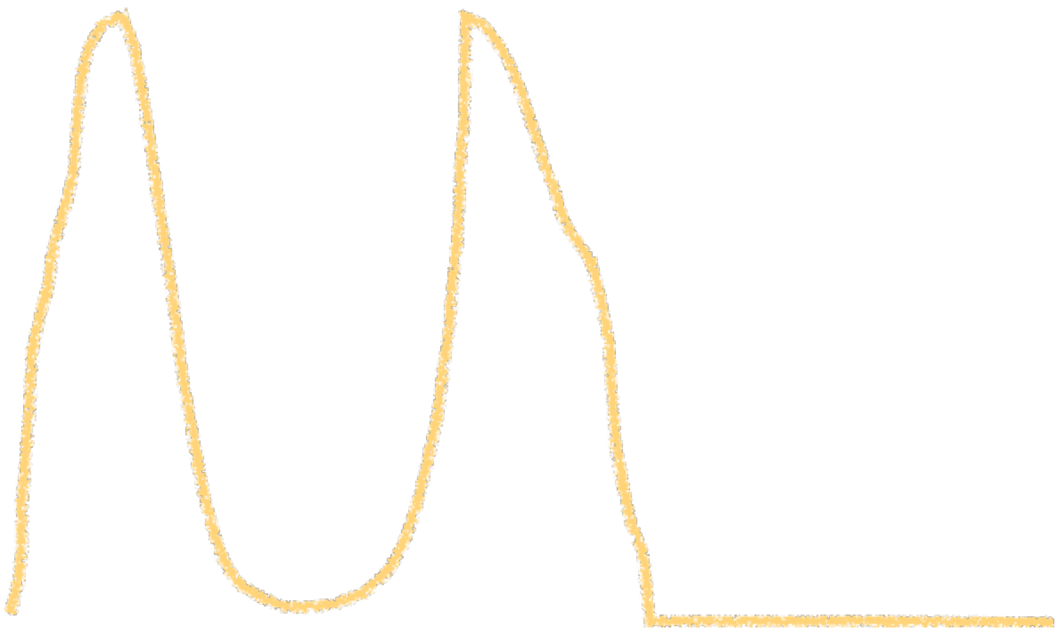

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- Barcelona 6 de junio 2016 -

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A Toni y a mi familia.

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Quiero agradecer a mis padres, hermanos y abuelos, que siempre han sido un ejemplo para mi, su apoyo incondicional y, a Toni, no sólo por ayudarme a ser mejor persona, sino también por lo feliz que me hace cada día.

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RESUMEN

El objetivo final de este proyecto de tesis doctoral era conocer mejor el comportamiento de distintos materiales de injerto en la técnica de preservación alveolar. Hay evidencia de que, después de la extracción dental, comienza un proceso de cicatrización durante el cual el coágulo sanguíneo es progresivamente reemplazado por hueso nuevo. Además, se produce una reducción en altura y anchura de la cresta alveolar, que puede a su vez dar lugar a una disponibilidad ósea limitada pudiendo comprometer la posterior colocación de implantes.

Por este motivo, se ha propuesto la introducción de distintos materiales de injerto en el alveolo postextracción. La literatura científica sugiere que los procedimientos de preservación alveolar minimizan estas alteraciones dimensionales de la cresta en sentido horizontal y vertical .

Desde un punto de vista histológico, múltiples estudios han evaluado la composición histológica de áreas donde previamente se había realizado una preservación alveolar para determinar la cantidad y calidad del hueso nuevo formado. Como el beneficio adicional a nivel histológico de la preservación alveolar con distintos materiales de injerto respecto a la cicatrización natural del alveolo postextracción no se conocía, realizamos una revisión sistemática para responder esta cuestión. El sulfato de calcio, la hidroxiapatita enriquecida con magnesio (MHA) y los xenoinjertos de origen porcino resultaron en un porcentaje de hueso nuevo formado significativamente mayor que las áreas control. Otros estudios que utilizaron autoinjertos, aloinjertos o biovidrios no

observaron diferencias significativas entre grupos. Sin embargo, debido a la gran variabilidad de los estudios incluídos, no se pudieron sacar conclusiones definitivas.

El injerto bovino desproteneizado (DBBM) y el injerto bovino desproteneizado en una matriz de colágeno (DBBM-C) han sido ampliamente utilizados en terapias regenerativas y, particularmente, en preservación alveolar aunque aún no se han analizado las posibles diferencias entre ambos materiales. Por eso se realizó un ensayo clínico randomizado a doble ciego comparando DBBM y DBBM-C en preservación alveolar. Cinco meses después de la extracción, se observó una reducción en anchura y altura de la cresta alveolar en ambos grupos de tratamiento, pero no se encontraron diferencias estadísticamente significativas entre ambos. Por otro lado, el análisis histomorfométrico demostró una composición histológica similar en áreas tratadas con DBBM y áreas tratadas con DBBM-C.

De los estudios mencionados previamente, se puede concluir que no hay un consenso sobre qué material de injerto ofrece los mejores resultados en cuanto a composición histológica. Particularmente, los resultados del ensayo clínico randomizado sugieren que no existen diferencias estadísticamente significativas entre DBBM y DBBM-C en cuanto a cambios dimensionales ni en cuanto a composición histológica 5 meses después de realizar la preservación alveolar.

SUMMARY

The main goal of this PhD project was to better understand how different types of bone grafts behave in ridge preservation procedures. There is clear evidence that, after tooth removal, a healing process takes place in which the blood clot that fills the socket is gradually substituted with new bone. This process is accompanied by a reduction in height and width of the alveolar ridge. These events may result in limited bone availability, which may compromise an adequate implant placement in order to replace the missing teeth.

For this reason, the insertion of different graft materials into the extraction socket has been reported. From the available evidence, it may be concluded that ridge preservation procedures do not completely prevent, but minimize loss of horizontal and vertical ridge alterations.

From an histological point of view, several studies have analyzed the histological composition of previously preserved areas in order to determine the amount of vital bone formed. Since the additional benefits of different graft materials in terms of newly formed bone compared to natural healing of the extraction socket was still unknown, we conducted a systematic review in order to answer this question. Calcium sulfate, magnesium enriched hydroxyapatite (MHA) and porcine-derived bone grafts resulted in a significant greater amount of newly formed bone than natural healing sites. Studies evaluating allografts, autologous bone and bioactive glass showed no statistical significant differences between treatment groups. Due to the great variability of the included studies, no firm conclusions could be drawn.

Demineralized bovine bone mineral (DBBM) and demineralized bone bovine mineral embedded in 10% collagen matrix (DBBM-C) have been widely used in regenerative therapies and particularly in ridge preservation procedures. However, the possible differences between both grafting materials had not previously been analysed. Therefore, a double blind randomized clinical trial comparing DBBM and DBBM-C in ridge preservation procedures was conducted. A reduction in height and width was observed 5 months after tooth extraction in sites preserved either with DBBM or DBBM-C, but no significant differences were encountered between treatment groups. On the other hand, the histomorphometric analysis resulted in a similar composition in terms of new bone formation, non-mineralized connective tissue and residual graft particles in both treatment groups.

From the above mentioned research projects it may be concluded that there is no consensus on which graft material offers the best outcomes from an histological point of view. More specifically, the results of the randomized clinical trial suggest that there are no statistically significant differences between DBBM and DBBM-C neither in height and width reduction of the alveolar ridge nor in their histological composition after a healing period of 5 months.

BACKGROUND

Causes for tooth removal

Different situations may require dental extractions such as advanced caries, traumatisms, endodontic lesions, developmental defects or advanced periodontitis (Lundgren et al. 2008). However, not only the extension of the carious lesion or the attachment loss determines the clinician´s decision on tooth extraction. This decision-making process is influenced by many other factors such as the clinician´s expertise, the treatment plan or the patient´s socioeconomic status (Holm-Pedersen et al. 2007). Additionally, the high survival rate of dental implants has completely changed the clinician´s mind towards tooth removal (Popelut et al. 2009; Lundgren et al. 2008).

Systematic reviews comparing the long-term survival rates of implant-supported single crowns (Jung et al. 2012), tooth supported single crowns (Pjetursson et al. 2007), endodontic treatments (Setzer & Kim, 2013; Torabinejad et al. 2015) or periodontal therapy (Huynh-Ba et al. 2009) observed similar survival rates for all treatment options. Even higher success rates, meaning less prevalence of biological, functional or esthetic complications were reported for treatment approaches aimed to maintain teeth. Thus, all these aspects should be taken into consideration before performing an extraction in order to make the best choice in each single case.

Moreover, a good understanding of the anatomy of the periodontal tissues as well as of the healing process that takes place after tooth removal is crucial especially if a future implant supported restoration is planned (Vignoletti et al. 2012).

Anatomy of the alveolar process

The periodontium is composed by the gingiva, the periodontal ligament, the root cementum and the alveolar process. Its main function is to attach the teeth to the bone tissue (Figure 1).

The alveolar process extends from the maxillary and mandibular basal bone and is composed by the external cortical walls and the bundle bone which lines the alveolar socket, both separated by trabecular bone. The periodontal ligament is a specialized connective tissue organized in fiber bundles that surrounds the teeth and connects the root cementum with the bundle bone. The portion of the periodontal ligament fibers that is inserted into the bundle bone and the root cementum is known as Sharpey´s fibers. This union allows for the transmission of masticatory forces and propioception (Nanci & Bosshardt, 2006; Lang & Lindhe, 2015).

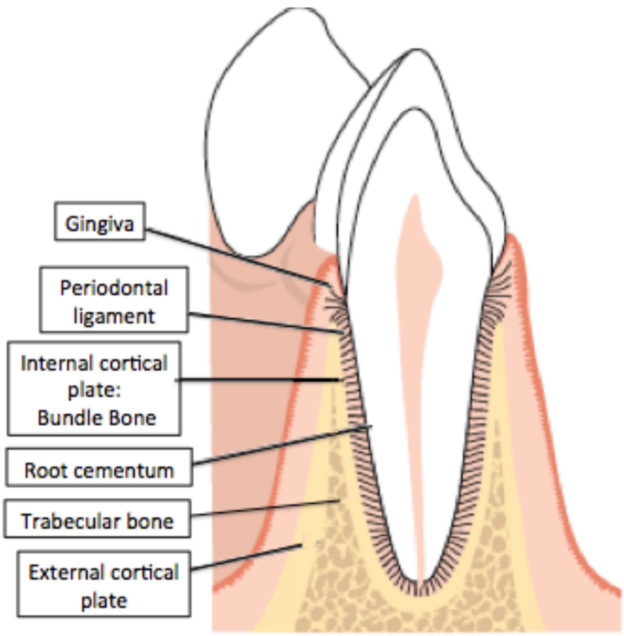

Figure 1. Components of the periodontium. Image obtained from Lang & Lindhe, 2015.

The mean thickness of the bundle bone has been estimated to vary between 0.1-0.4mm (Schroeder, 1986). Meanwhile, the thickness of the external buccal and lingual cortical plate varies considerably between sites (Figure 2). Thus, at the level of incisors and premolars the buccal plate is ussually thinner than at the lingual aspect whereas in the mandibular molar region the bone is usually thicker at the buccal aspect (Lang & Lindhe, 2015). In anterior teeth for example, the thickness of the buccal and lingual cortical plates have been reported to be 0.35± 0.31mm and 0.33±0.31mm respectively at the level of central incisors (Kim et al. 2012).

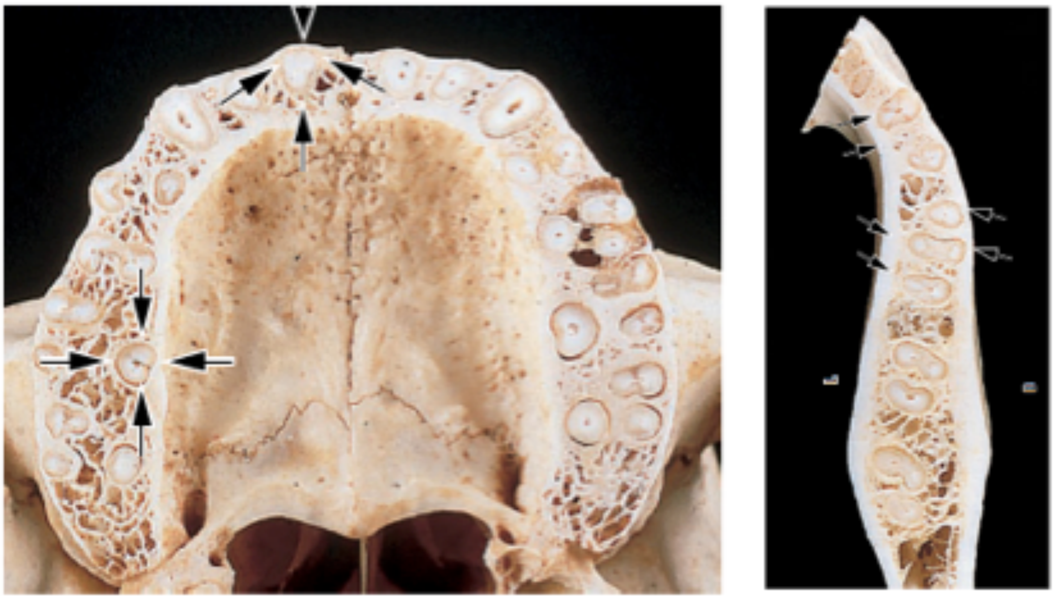

Figure 2. Section of the maxillary and mandibular alveolar process showing the different thicknesses of the external cortical plate at different areas. Image obtained from Lang & Lindhe, 2015.

The alveolar bone dimensions of maxillary anterior teeth were evaluated on cone beam computed tomoraphies (CBCTs) by Braut et al. (2011) who reported a mean buccal bone thickness of 0.5 to 0.7mm. These findings agree with those of another study on CBCTs in which in 50% of the cases, the buccal bone plate was reported to be less than 0.5mm thick (Januário et al. 2011). We may therefore assume that the buccal plate of maxillary anterior teeth is mainly composed by the external cortical bone and bundle bone, with no trabecular spaces in between (Al-Hezaimi et al. 2011).

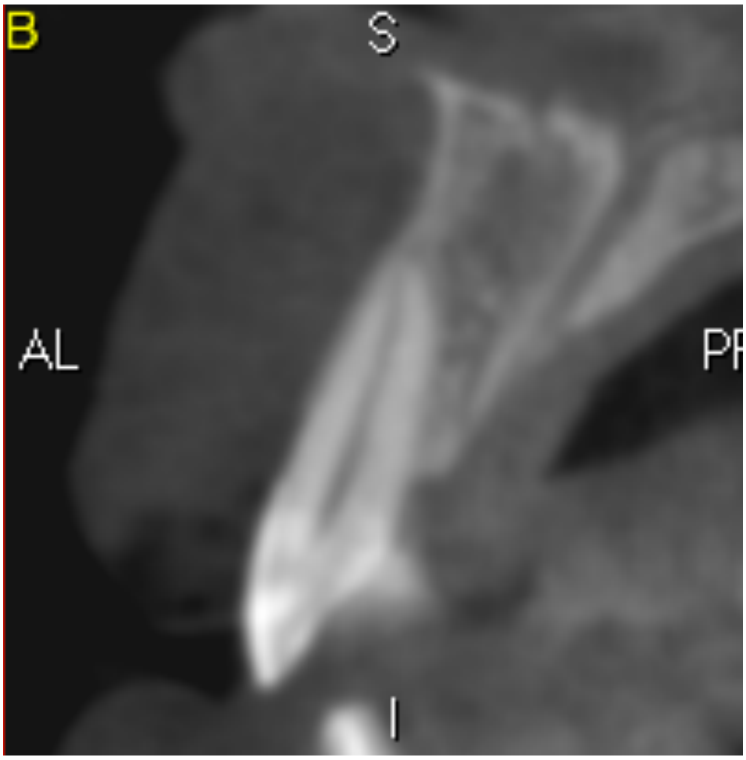

Figure 3. CBCT section of a maxillary central incisor showing a buccal cortical plate which is less than 1mm thick.

The vascular supply of the alveolar process comes from the periodontal ligament, the bone marrow spaces between the trabecular bone and the gingival tissues. The capillaries derived from the gingival tissues and the periodontal ligament anastomose forming a net-like structure in the alveolar process (Lang & Lindhe, 2015).

Healing of the extraction socket after tooth removal

Several animal and human studies have described the events involved in wound healing process of the alveolar socket following extraction (Amler 1969; Cardaropoli et al. 2003; Araújo et al. 2005; Trombelli et al. 2008). Shortly after removing a tooth, a blood clot composed by erythrocytes, platelets and leukocytes embedded in a fibrin matrix is formed. During the first week, it is replaced by granulation tissue, which is highly vascularized and contains inflammatory cells such as polymorphonuclears, macrophages and lymphocytes. At two to four weeks, the establishment of a provisional connective tissue matrix occurs. This matrix is mainly comprised by collagen-rich connective tissue. At this phase, the number of capillaries and inflammatory cells decrease. At 6 to 8 weeks, small osseous projections appear neighbouring vascular structures. At approximatelly 12 weeks of healing, the socket is filled with lamellar bone and bone marrow (Trombelli et al. 2008). Figure 4 shows an histological section of a human biopsy taken 6 months after tooth removal.

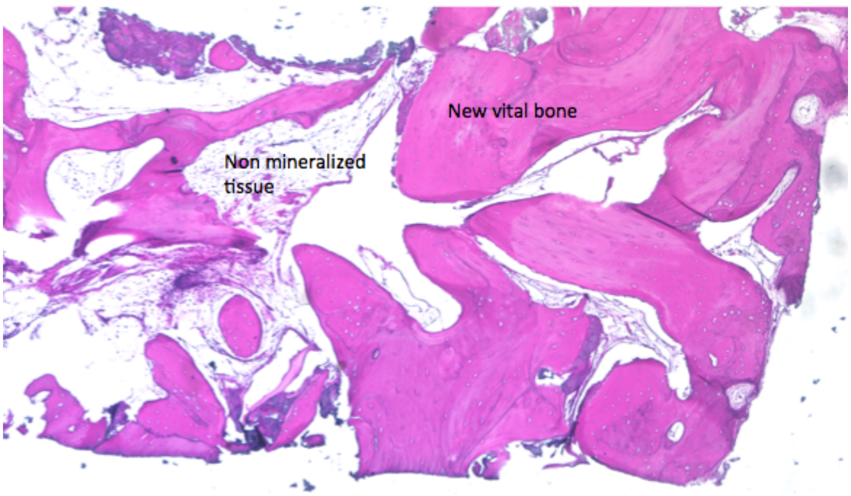

Figure 4. Histological section of a socket at 6 months of healing. Mature lamellar bone with connective tissue spaces can be observed.

Additionally, during this healing phase, dimensional changes take place. Araujo et al. (2005) performed an observational study on beagle dogs to describe the events involved in this process (Figure 5). The buccal bone wall was significantly thinner than the lingual wall, and therefore, a greater proportion of the buccal wall was solely composed by cortical and bundle bone. At two weeks of healing, the bundle bone and outer surfaces of the lingual and buccal bone walls were covered with a layer of osteoclasts. Bundle bone was completely resorbed at one month and some resorption of the external cortical bone was observed. At 8 weeks of healing the socket had been filled with osseous tissue and a reduction in height and width was observed. The buccal crest was located 2mm apically from the lingual crest (Araújo et al. 2005).

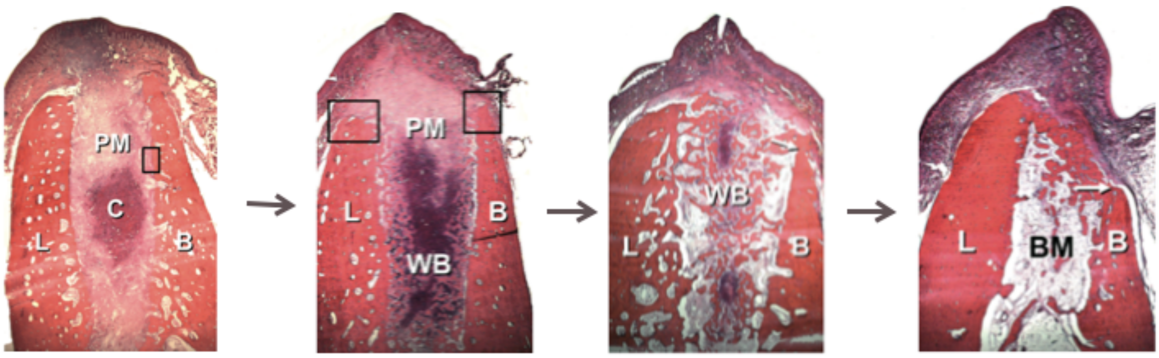

Figure 5. Histological images showing the healing process 1, 2, 4 and 8 weeks after removal of a premolar in a beagle dog model. At 8 weeks, a considerable reduction in height and width can be observed in the buccal and lingual walls. Images obtained from Araújo et al. 2005.

PM: provisional matrix; C: blood clot; B: buccal bone wall; L: lingual bone wall; WB: woven bone; BM: bone marrow.

Many studies have evaluated the dimensional hard tissue changes after tooth extraction in humans. A systematic review observed more horizontal bone loss (range: 29-63%; 3.79±0.23 mm), than vertical reduction (range: 11-22%; 1.24±0.11 mm on buccal sites) in human re-entry studies 6 months following tooth extraction. In general, major reductions occurred during the first 3-6 months, while a more gradual decrease in volume was observed after that period (Tan et al. 2012). Van der Weijden et al. (2009) confirmed these outcomes, and observed a mean vertical change of 1.67-2.03mm clinically and 1.53mm radiographically.

These changes may have negative clinical consequences particularly in the anterior maxilla, an aesthetically demanding area, where the vestibular cortical has been shown to be less than 1mm thick in 87% of the cases (Huynh-Ba et al. 2010). As mentioned before, considering that the bundle bone and the cortical plate together have a thickness of 0.5-0.7mm in maxillary anterior teeth, once a tooth is removed, the marked reduction of the buccal bone dimensions may be explained by two factors: 1) bundle bone looses its function 2) blood supply is hindered because of the lack of trabecular spaces and periodontal ligament. In this sense, Spinato et al. (2012) observed almost twice as much reduction in ridge width and buccal bone height in sockets with a buccal plate thickness <1mm than in sockets where the buccal plate thickness was >1mm 4 months after tooth extraction.

Not only cortical bone dimensions but also the number of teeth to be removed may be related to the amount of ridge width reduction. In this sense, Al-Askar et al. (2013) observed in a beagle dog model a significant greater buccolingual resorption at multiple extraction sites than at single tooth extraction sites at 4 months of healing. Furthermore, the amount of bone remodelling was related with the number of extracted teeth.

In conclusion, the natural healing process that takes place after tooth extraction, will irremediably lead to reduced ridge dimensions. For this reason, in the past decades, clinicians have developed different strategies to maintain the ridge contour.

Ridge Preservation

Hypothetically, there should be less alveolar ridge resorption with the use of socket grafting materials than by natural healing. Thus, in order to reduce alveolar ridge resorption, the placement of various graft materials into the extraction socket has been proposed. This technique was first described by Sheer & Boyne (1987) and has been extensively investigated since then. Graft materials such as allografts (Simon et al. 2000; Froum et al. 2002; Zubillaga et al. 2003; Iasella et al. 2003), autologous bone marrow (Pelegrine et al. 2010), polylactide and polyglycolide sponge (Serino et al. 2003, 2008), xenografts (Artzi et al. 2000; Carmagnola et al. 2003; Barone et al. 2008; Heberer et al. 2011; Cook & Mealey 2013) –Figure 6- or growth factors (Coomes et al. 2014) have been used.

Moreover, ridge preservation has been performed with different surgical techniques. For example, while some authors have coronally advanced the flaps in order to obtain primary closure (Smukler et al. 1999; Froum et al. 2002; Barone et al. 2008) others have preferred to replace the flaps in their previous position (Carmegnola et al. 2003; Iasella et al. 2003; Serino et al. 2003; Serino et al. 2007) or even a flapless approach (Aimetti et al. 2009; Cardaropoli et al. 2012; Crespi et al. 2009). In order to cover the graft several techniques have been proposed: reabsorbable membranes (Carmagnola et al. 2003; Vance et al. 2004; Cardaropoli et al. 2012), free gingival grafts (Jung et al. 2013; Tal et al.), acellular dermal matrix (Luczyszyn et al. 2005) and collagen sponges (Checchi et al. 2011; Canullo et al. 2013).

Recent systematic reviews have concluded that ridge preservation procedures do not completely prevent, but minimize loss of horizontal and vertical ridge alterations (Vignoletti et al. 2012; Orgeas et al. 2013; Ten Heggeler et al. 2011; Horvath et al. 2013; Ávila-Ortiz et al. 2014). Thus, when compared to natural healing, ridge preservation sites showed 1.47mm and 1.83mm less reduction in bone height and bone width respectively (Vignoletti et al. 2012). Factors related to the surgical procedure such as primary closure, flap elevation and the use of barrier membranes or the graft material seem to affect the outcomes, although there is no definitive evidence (Vignoletti et al. 2012; Ávila-Ortiz et al. 2014).

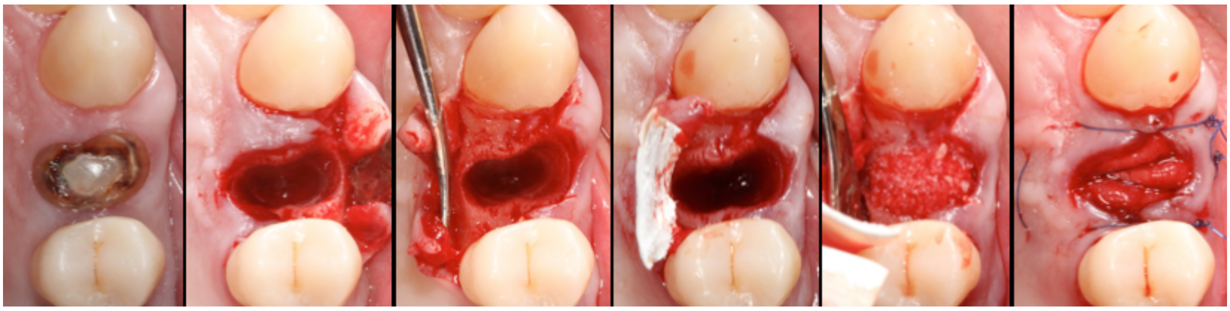

Figure 6. Ridge preservation using a xenograft and a collagen membrane.

On the other hand, many studies have analyzed biopsies taken several weeks following ridge preservation procedures to histologically evaluate the composition at the socket area in terms of newly formed bone, non-mineralized connective tissue and residual graft particles. Histological and histomorphometrical research allows the clinician to know the likelihood of the quality and quantity of the newly formed bone, to provide an adequate site for primary stability during implant placement as well as the healing period required to achieve a favourable outcome. However, no firm conclusions exist regarding the additional benefits of ridge preservation procedures in terms of histologic and/or histomorphometric outcomes when compared to healing of the extraction socket by blood clot formation .

One of the most widely used graft materials in this type of procedures has been deproteneized bovine bone mineral (DBBM). BioOss® (Geistlich Pharma; Wolhausen, Switzerland) is DBBM developed with a trabecular and porous structure similar to human bone (Haas et al. 1998; Wong et al. 2010). It is produced by the removal of all the organic components of bovine bone leading to a non-antigenic bone mineral matrix with osteoconductive properties (Baldini et al. 2010). DBBM has been used for guided bone regeneration (Hämmerle et al. 2008), guided tissue regeneration (Stavropoulos et al. 2010) and sinus floor elevation procedures (Schmitt et al. 2014) with clinically successful results.

BioOss Collagen® (Geistlich Pharma; Wolhausen, Switzerland), a composite bovine derived xenograft consisting of 90% deproteinized cancellous bone particles embedded in a 10% biodegradable collagen matrix of porcine origin (DBBM-C), has been introduced in regenerative therapy (Sculean et al. 2005; Alayan et al. 2015; Lindhe et al. 2014). The collagen facilitates graft handling allowing a good adaptation and stabilization of the graft to the defect (Wong et al. 2010).

A. 

B. 

Figure 7. A. BioOss®: commercially available (DBBM) B. BioOss® Collagen: commercially available DBBM in 10% collagen matrix (DBBM-C).

The standard of care in regenerative therapy is the combination of barrier membranes and bone grafts. This approach has also been evaluated in ridge preservation procedures (Iasella et al. 2003; Barone et al. 2008; Mardas et al. 2010). The membrane avoids epithelial downgrowth into the socket while the grafting material prevents membrane collapse, stabilizes the blood clot and enhances bone formation through osteoconduction and/or osteoinduction. Resorbable collagen membranes (BioGide®: Geistlich Pharma; Wolhausen, Switzerland) applied in conjunction with DBBM have shown to be effective in different regenerative procedures (Hämmerle et al. 2008; Schwartz et al. 2013).

Evaluation of ridge dimensional changes

Researchers have described different methods to determine dimensional alterations of the alveolar ridge. Intrasurgical direct measurements are considered to be the gold standard. Several authors have clinically evaluated hard and soft tissue dimensions using a calliper (Cardaropoli et al. 2014; Spinato et al. 2012). Study casts have been taken to determine alterations in the ridge contour (Schropp et al. 2003; Schneider et al. 2014).

On the other hand, radiographic osseous changes have been evaluated with periapical radiographs (Schropp et al. 2003; Crespi et al. 2009) and CBCTs (Jung et al. 2013; Araújo et al. 2015). Periapical radiographs only give information on the interproximal bone level changes and some degree of magnification is inevitable (Schropp et al. 2003). Meanwhile, radiological measurements on CBCTs have been compared with direct measurements on skulls and high degree of accuracy has been reported (Ludlow et al. 2007; Fu et al. 2011). Furthermore, Agbahe et al. (2007) observed that the volume of extraction sockets could be effectively measured on CBCTs and concluded that CBCTs were a reliable tool to determine the healing process of the extraction sockets. Jung et al. (2013) proposed a methodology to compare osseous dimensions of the same patient on CBCTs at different time points. Using anatomic structures as a reference, they were able to superpose the CBCTs by means of a software and calculate the differences in height and width between them (Figure 8).

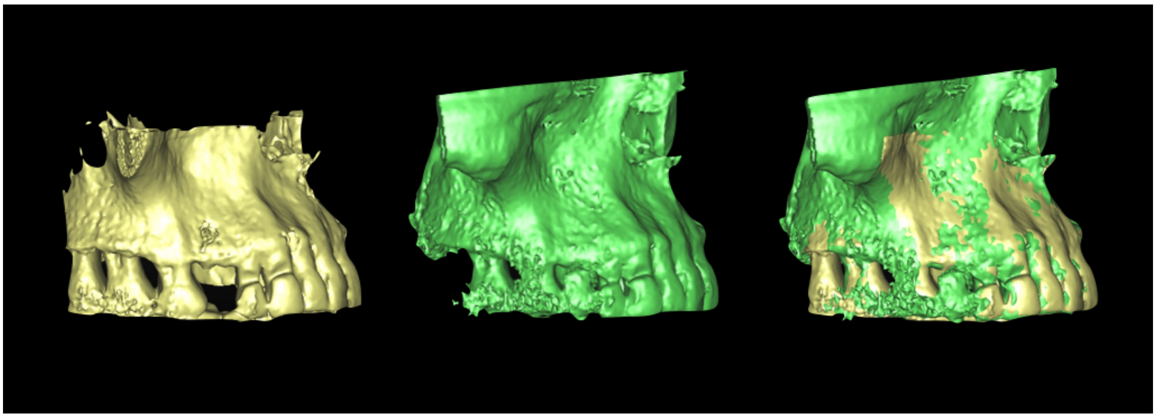

Figure 8. Using anatomic structures as reference, a CBCT taken after tooth extraction (yellow) and a CBCT taken several months after ridge preservation (green) can be superposed and compared.

JUSTIFICATION

The effectiveness of ridge preservation has been an extensively discussed topic in the last decades. Most systematic reviews (Vignoletti et al. 2012; Orgeas et al. 2013; Ten Heggeler et al. 2011; Horvath et al. 2013; Ávila-Ortiz et al. 2014) have been focused on dimensional alterations at grafted sites with respect to non-grafted sites. However, to our knowledge, it is still not known which graft material results in a greater amount of bone as well as the time required to complete the healing process after ridge preservation. Ideally, a graft material should be able to maintain the ridge dimensions and, at the same time, promote bone formation as fast as possible to shorten the treatment time.

Secondly, DBBM and DBBM-C have been extensively used in regenerative therapies but the possible additional benefit of the collagen matrix added to DBBM-C in maintaining the ridge contour and in promoting new bone formation has not been previously evaluated. Furthermore, our aim was to evaluate if buccal bone thickness is associated with the amount of bone resorption in ridge preservation procedures.

HYPOTHESES

Paper I:

Main hypothesis:

H_0: Ridge preservation sites will result in a greater percentage of newly formed bone than natural healing sites.

H_1: Ridge preservation sites will not result in a greater percentage of newly formed bone than natural healing sites.

Secondary hypothesis:

H_0: Ridge preservation sites will not result in a greater percentage of connective tissue than natural healing sites.

H_1: Ridge preservation sites will result in a greater percentage of connective tissue than natural healing sites.

Paper II:

Main hypothesis:

H_0: Areas treated with DBBM-C will present a greater reduction in height and width 5 months after tooth extraction than areas treated with DBBM.

H_1: Areas treated with DBBM-C will not result in a greater reduction in height and width 5 months after tooth extraction than areas treated with DBBM.

Secondary hypotheses:

H_0: Baseline buccal bone thickness will not influence the amount of ridge reduction in height and width 5 months after ridge preservation with DBBM and DBBM-C.

H_1: Baseline buccal bone thickness will have an influence on the amount of ridge reduction in height and width 5 months after ridge preservation with DBBM and DBBM-C.

H_0: Sites grafted with DBBM-C will not result in a greater percentage of newly formed bone and less percentage of residual graft particles and connective tissue than sites treated with DBBM after a healing period of 5 months.

H_1: Sites grafted with DBBM-C will present a greater percentage of newly formed bone and a less percentage of residual graft particles and connective tissue than sites treated with DBBM-C at 5 months of healing.

OBJECTIVES

Paper I:

Main objective:

To compare by histomorphometric analysis the percentage of newly formed bone of various graft materials in ridge preservation procedures versus healing of the extraction socket by blood clot formation.

Secondary objectives:

To compare the amount of residual graft particles and connective tissue at ridge preservation and natural healing sites.

Paper II:

Main objective:

To compare the dimensional changes on CBCTs following ridge preservation procedures with DBBM and a collagen membrane and DBBM-C and a collagen membrane 5 months after tooth extraction.

Secondary objectives:

To evaluate the histological composition of both treatment groups, DBBM and DBBM-C, in terms of new bone formation, residual graft particles and connective tissue after 5 months of healing.

To assess whether initial buccal bone width influences the amount of ridge width reduction.

PAPER I

Title:

Histomorphometric Results in Ridge Preservation Procedures Comparing Various Graft Materials in Extraction Sockets with Non-Grafted Sockets in Humans: A systematic review.

Authors: *Barallat, L., Ruíz-Magaz, V., Levi, P.A., Mareque-Bueno, S., Galindo-Moreno, P. & Nart, J.*

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Implant Dent 2014; 23:1-16.

Main findings

Sixteen studies compared ridge preservation with natural healing. Considerable heterogeneity was observed in the included papers with respect to study design, evaluation period, inclusion criteria (tooth type and defect morphology), graft material, methodology and surgical approach.

Table 1 summarizes the histomorphometric outcomes of the included studies. When comparing the percentage of newly formed bone between control and treatment groups, three studies using porcine xenografts and calcium sulfate, observed a statistically significant greater percentage in preserved sites (Barone et al. 2008; Crespi et al. 2009, 2011). More favourable outcomes were also obtained when using DFDBA –demineralized freeze-dried bone allograft- (Froum et al. 2002), polylactide and polyglycolic sponge (Serino et al. 2003, 2007) and bioactive glass (Froum et al. 2002) but it was not statistically significant. In four studies, control sites performed better than areas treated with DBBM, DBBM-C, FDBA –freeze-dried bone allograft- and hydroxyapatite (Carmagnola et al. 2003; Iasella et al. 2003; Lyczyszyn et al. 2005; Heberer et al. 2011). Last but not least, other four studies did not find significant differences between natural healing and sites treated with DFDBA, DBBM-C, autologous bone or FDBA (Smukler et al. 1999, Pelegrine et al. 2010; Cardaropoli et al. 2012; Spinato et al. 2012).

Controversial results were also found when evaluating the amount of connective tissue at test and control groups. With respect to the amount of residual graft particles at the time of re-entry, sites treated with porcine xenograft (Barone et al. 2008; Crespi et al. 2011), FDBA (Iasella et al. 2003) and resorbable hydroxyapatite (Luczyszyn et al. 2005) presented a much higher percentage of graft particles than sites treated with autologous bone (Pelegrine et al. 2010) or a polylactide and polyglicolic acid sponge (Serino et al. 2003, 2007) which were not detectable.

Author/year	Evaluation (months)	Group(s)	% Vital bone	% CT	R raft % Residual particles
Smukler et al. 1999	8-23	DFDBA + ePTFE	Max: 55,0±15,02% Mdb: 56,5±32,77%	-	Max: 8,7±7,5% Mdb: 2,45±1,0%
		NH	Max: 58,1±11,3% Mdb: 40,9±2,76%	-	Max: 0% Mdb: 0%
		P - value	?	-	?
Froum et al. 2002	6 - 8	Bioactive glass	59,5%	35,3%*	5,5%
		DFDBA	34,7%*	51,6%*	13,5%
		NH	32,4%*	67%*	0%
		P - value	P =0,074	P =0,06	P =0,01
Carmagnola et al. 2003	4-7	coll. membrane	40,1±15,9%	0±0%	0±0%
		BioOss®+ coll. membrane	26,0±23,7%	18,1±17%	18,1±17%
		NH	56,1±18,1%	0±0 %	0±0%
		P - value	?	?	?
Iasella et al. 2003	4 -6	FDBA+ coll. membrane	28±14%	-	37±18%
		NH	54±12%	-	-
		P - value	?	?	?
Serino et al. 2003	6	PL/PG	66,7%	-	0%
		NH	43,6%	-	0%
		P - value	?	?	?
Guarnieri et al. 2004	3	CaS	58,1±9,2 %*	-	-
		NH	47,2±7,7%*	-	-
		P - value	$P > 0,05$	-	-
Luczyszyn et al. 2005	6	RHA+ADMG	1%	57%	42%
		NH+ADMG	46%	54%	0%
		P - value	?	?	?
Serino et al. 2007	3	PL/PG	59,9±22,4%*	-	0%
		NH	48,8±14,4%*	-	0%
		P - value	P = 0,28		
Barone et al. 2008	7 -9	Xenogenic porcine graft+ coll. membrane	35,5±10,4%	36,6±12,6%	29,2±10,1%
		NH	25,7±9,5%	59,1±10,4%	0%
		P - value	$P < 0,05$	$P < 0,05$	-
Crespi et al. 2009	3	MHA	40±2,7%	41,3±13%	20,2±3,4%
		CaS	45±6,5%	41,5±6,7%	13,9±3,4%
		NH	32,8±5,8%	64,5±6,8%	-
		P – value	$P < 0,05$	$P < 0,05$	-

Author/year	Evaluation (months)	Group(s)	% Vital bone	% CT	% Residual graft particles
Aimetti et al. 2009	3	CaS	100%		0%
		NH	100%	-	-
		P - value	*P* < 0.0001		
Pelegrine et al. 2010	6	Autologous bone marrow	45,4±7,2%*	-	-
		NH	42,8±11,3%*	-	-
		P - value	*P* = 0,36	-	-
Heberer et al. 2011	3	BioOss Coll®	25%*	60%	
		NH	44%*	56%	15%
		P -value	*P* =0.03		
Crespi et al. 2011	4	Porcine xenograft	39,6±9,4%	26,0±9,9%	34,4±5,1%
		NH	29,5±5,0%	57,7±6,9	-
		P - value	*P* <0,05	*P* <0,05	
Cardaropoli et al. 2012	4	Bio-Oss Coll®+coll. membrane	44,8±11,4%*	55,2±11%*	18,4±11,1%
		NH	43,8±12,2%*	56,2±12,2*	-
		P - value	*P*>0,05	*P* > 0,05	
Spinato et al. 2012	4	FDBA+ coll. dressing	20,98%	56,35%	22,65%
		NH	22,57%	77,42%	-
		P - value	?	?	?

Table 1. Main results of studies comparing ridge preservation procedures with natural healing. Abbreviations: CT: connective tissue; NH: natural healing; Max: maxillar; Mdb: mandibular; DFDBA: demineralized freeze-dried bone allograft; FDBA: freeze-dried bone allograft; coll.: collagen; PL/PG: polylactide and polyglycolide acid sponge; CaS: calcium sulfate hemihydrate; MHA: magnesium enriched hydroxyapatite; RHA: reabsorbable hydroxyapatite; ADMG: acellular dermal matrix; BioOss Coll®: BioOss Collagen® *: not statistically significant; - : no available data; ?: not specified.

Barallat L, Ruiz-Magaz V, Levi PA,Jr, Mareque-Bueno S, Galindo-Moreno P, Nart J. Histomorphometric results in ridge preservation procedures comparing various graft materials in extraction sockets with nongrafted sockets in humans: a systematic review. Implant Dent 2014 Oct;23(5):539-554.

doi:10.1097/ID.0000000000000124

Paper II:

Title:

Radiographic and histologic evaluation of deproteinized bovine bone mineral vs. deproteinized bovine bone mineral with 10% collagen in ridge preservation. A randomized controlled clinical trial.

Authors: *Nart, J., Barallat, L., Jiménez, D., Mestres, J., Gómez, A., Carrasco, M.A., Violant, D., Ruíz-Magaz, V.*

Journal: Clinical Oral Implants Research

JCR Impact Factor (2016): 3.889

Reference:

Volume:

Number:

Letter of acceptance

Dear Mrs. Barallat:

It is a pleasure to accept your manuscript entitled "Radiographic and histologic evaluation of deproteinized bovine bone mineral vs. deproteinized bovine bone mineral with 10% collagen in ridge preservation. A randomized controlled clinical trial." in its current form for publication in Clinical Oral Implants Research. The comments of the reviewer(s) who reviewed your manuscript are included at the foot of this letter.

Main findings

Twenty-one patients (15 women/6 men; mean age: 56,76 years) completed this randomized clinical trial. Twenty-two teeth were included: 11 belonged to the DBBM group and 11 to the DBBM-C group. All surgeries healed uneventfully and no complications were reported during any of the surgical interventions.

No statistically significant differences between treatment groups were observed at baseline. In general, height and width decreased significantly at 5 months of healing in both groups. Baseline buccal plate thickness was 1,55±0,83mm, 1,72±1,18 mm and 1,48±1,10 at 1, 3 and 5mm respectively. No correlation was found between buccal plate thickness and ridge width reduction at 1, 3 and 5mm.

	Baseline				5 months			
	DBBM Mean (SD) mm N=11	DBBM-C Mean (SD) mm N=11	P value[1]		DBBM Mean (SD) mm N=11	P value[2]	DBBM-C Mean (SD) mm N=11	P value[3]
Vestibular height	8.78 (2.01)	8.82 (1.76)	0.89		8.21 (1.53)	0.045*	7.80 (1.42)	0.014*
Lingual height	8.58 (2.21)	8.57 (2.50)	0.95		7.90 (2.38)	0.006*	7.76 (2.15)	0.006*
Ridge width 1 mm	10.13 (0.74)	10.62 (2.15)	0.90		9.17 (1.41)	0.044*	9.33 (1.78)	0.018*
Ridge width 3 mm	11.12 (1.04)	12.15 (2.34)	0.19		10.76 (1.05)	0.005*	11.35 (2.53)	0.004*
Ridge width 5 mm	11.14 (1.26)	13.17 (2.36)	0.14		11.03 (1.25)	0.0038*	12.63 (2.33)	0.004*

[1] U Mann Whitney test
[2] Wilcoxon test (related analysis in DBBM group)
[3] Wilcoxon test (related analysis in DBBM-C group)
* Statistically significant

Table 2. Ridge dimensions at baseline and 5 months healing in the DBBM and DBBM-C groups.

Dimensional changes

When dimensional changes were compared in DBBM and DBBM-C groups, no significant differences in height and width were encountered at 5 months of healing. However, DBBM group showed less reduction in ridge width with respect to DBBM-C. Thus, while a ridge width reduction of 9.42%, 3.21% and 2.53% at 1, 3 and 5mm respectively occurred in the DBBM group, 13.83%, 6.43% and 4.16% reduction took place at the same levels in the DBBM-C group. Buccal height decreased 0.61mm and 0.98mm and lingual height 0.65mm and 0.85mm in the DBBM and DBBM-C sites respectively.

	GROUP	N	Mean	Standard deviation	Medians
Difference in buccal height (mm) P=0.92	DBBM	11	0.61	0.77	0.48
	DBBM-C	11	0.98	1.28	0.64
Difference in lingual height (mm) P=0.76	DBBM	11	0.65	0.65	0.63
	DBBM-C	11	0.82	0.61	0.55
Difference in ridge width 1mm (mm) P=0.29	DBBM	9	0.91	1.35	0.81
	DBBM-C	9	1.53	1.53	1.23
Difference in ridge width 3mm (mm) P=0.24	DBBM	10	0.358	0.31	0.24
	DBBM-C	11	0.788	0.76	0.8
Difference ridge width 5mm (mm) P=0.0011*	DBBM	11	0.065	0.172	0.11
	DBBM-C	11	0.16	0.76	0.53
Difference in reduction in buccal height (%) P=0.59	DBBM	11	9.69%	5.46%	9.48%
	DBBM-C	11	9.66%	11.14%	4.76%
Difference in reduction in lingual height (%) P=0.81	DBBM	11	13.79%	24.38%	6.24%
	DBBM-C	11	21.53%	31.67%	7.33&
Difference in reduction in ridge width 1mm (%) P=0.33	DBBM	9	9.42%	12.45%	7.77%
	DBBM-C	9	13.86%	12.66%	13.74%
Difference reduction in ridge width 3mm (%) P=0.30	DBBM	10	3.21%	2.71%	2.25%
	DBBM-C	11	6.43%	5.86%	7.11%
Difference in reduction in ridge width 5mm (%) P=0.065	DBBM	11	2.53%	3.69%	1.27%
	DBBM-C	11	4.16%	2.73%	4.06%

SD: standard deviation *statistically significant

Table 3. Mean dimensional changes between baseline and 5 months in both treatment groups.

Histological evaluation

In general, DBBM particles were found to be more frequently surrounded by new vital bone than by connective tissue. One sample showed fibrosis and chronic inflammatory infiltrate around the residual graft particles. In those cases where vital bone was in direct contact with the DBBM particles, no signs of particle resorption were observed.

Eighteen samples were included for histomorphometric analysis: in one case it was not possible to obtain a biopsy at re-entry at 5 months and in 3 cases the samples were rather comprised by native cortical bone. In the DBBM group, the mean percentage of vital bone, residual graft particles and connective tissue was 33.44±17.82%, 13.14±8.32% and 53.88±17.43% respectively. On the other hand, in the DBBM-C group 37.68±13.38% of vital bone, 16.00±11.60% of residual graft particles and 50.31±19.20% of non-mineralized connective tissue were detected. No statistically significant differences in the percentage of vital bone (p= 0.89), residual graft particles (p=0.75) and connective tissue (p=0.69) were observed between groups.

Nart J, Barallat L, Jimenez D, Mestres J, Gomez A, Carrasco MA, et al. Radiographic and histological evaluation of deproteinized bovine bone mineral vs. deproteinized bovine bone mineral with 10% collagen in ridge preservation. A randomized controlled clinical trial. Clin Oral Implants Res 2016 Jun 22.

doi:10.1111/clr.12889

GENERAL DISCUSSION

Maintenance of the original ridge contour will frequently facilitate the following steps of our treatment plan. In the last *Osteology Consensus Report*, it was concluded that ridge preservation procedures are indicated to maintain the soft and hard tissue contour, maintain a stable ridge volume for optimizing functional and aesthetic outcomes and simplify subsequent treatment procedures (Hämmerle et al. 2012). It has been observed that placing a graft into the extraction socket completely or partially avoids the need further regeneration at the time of implant placement when compared to natural healing (Horvath et al. 2013).

Graft selection for ridge preservation procedures

As mentioned before, the ideal graft material should be able to: 1) minimize ridge shrinkage and 2) promote bone formation as fast as possible to shorten the treatment time.

With respect to the first topic, Ávila-Ortiz et al. (2014) observed that allografts and xenografts were significantly more effective than alloplastic materials in preserving buccal bone height. No statistically significant differences between biomaterials were found for changes in ridge width or lingual height.

The outcomes of our systematic review have shown different histological profiles not only between natural healing and grafted sites, but also between different graft materials.

Taking into account our findings and the observations of a recent meta-analysis (De Risi et al. 2015) we may conclude that a greater percentage of vital bone was observed when using alloplastic materials and that xenografts present a greater percentage of residual graft particles. In accordance to other investigations (Horvath et al. 2013; De Risi et al. 2015) ridge preservation procedures not always led to more bone formation than untreated sites. However, in our systematic review, 12 studies showed a similar or greater percentage of newly formed bone in ridge preserved and naturally healed sites. For this reason, it may be suggested that there is no need to extend the healing time over 3-4 months after ridge preservation to allow for implant placement (De Risi et al. 2015).

The question of how implants placed in ridge preservation sites perform in the long term has been recently addressed (Barone et al. 2012; Rocuzzo et al, 2014; Cardaropoli et al. 2015). Cardaropoli et al. (2015) observed similar survival rates and marginal bone levels at implants placed in native bone and implants placed at sites grafted with DBBM-C and a collagen membrane during a 1-year follow-up. Furthermore, Barone et al. (2012) made similar observations 3 years after placing implants in areas that had been previously grafted with porcine xenograft.

Factors influencing the outcomes of ridge preservation procedures

Anatomic aspects

Some evidence suggests that, the greater the number of contiguous teeth to be removed, the more reduction in height and width may be expected if healing is left undisturbed (Al-Askar et al. 2013). However, when ridge preservation is performed, no significant differences seem to exist between single and multiple extraction sites (Al-Hamoudi et al. 2015).

Socket anatomy may also have an influence on dimensional changes. Thus, as it has been mentioned before, the presence of a thin buccal plate for example, may lead to a greater reduction in height and width of the alveolar socket (Spinato et al. 2012). When we analysed the influence of baseline buccal plate thickness on ridge width reduction, no correlation was found between baseline buccal plate thickness and ridge width at 5 months healing. This is in accordance with a recent study in which initial buccal bone thickness was negatively correlated with ridge width reduction in natural healing sockets while no association was found when ridge preservation was performed with DBBM-C plus a collagen membrane (Cardaropoli et al. 2014).

Thus, although the number of teeth to be removed as well as the buccal bone thickness seem to influence the amount of ridge reduction after tooth removal, these factors do not appear to be associated with greater dimensional changes after ridge preservation procedures.

Surgical approach

Several investigations have aimed to determine which surgical approach leads to less dimensional changes of the alveolar ridge. When it comes to flap management, raising a flap has been associated with significantly less horizontal (Vignoletti et al. 2012) and vertical bone reduction (Ávila-Ortiz et al. 2014). Furthermore, Vignoletti et al. (2012) observed a slight trend towards less ridge width changes when primary closure was achieved, while Engler-Hamm et al. (2011) observed no differences between primary and secondary intention healing. Last but not least, evidence suggests that placing a membrane in combination with a graft favours the maintenance of the ridge dimensions (Vignoletti et al. 2012; Ávila-Ortiz et al. 2014; Orgeas et al. 2013).

Ridge preservation with DBBM and DBBM-C versus natural healing

Dimensional changes

Our randomized clinical trial did not include a negative control group in order to evaluate the additional benefits of ridge preservation procedures using either DBBM or DBBM-C. Taking into account the meta-analysis by Tan et al. (2012), if a socket is left undisturbed a mean reduction of 29-63% horizontally and a mean vertical reduction of 11-22% on buccal sites may be expected at 6 months. In our investigation, sites grafted with DBBM and DBBM-C showed 9.66-9.69% decrease in buccal plate height and 2.53-13.86% in ridge width. Although sites treated with DBBM resulted in slightly less ridge shrinkage, no statisically significant differences were encountered between this two biomaterials. Thus, we may conclude that DBBM and DBBM-C are effective in minimizing volumetric bone alterations after tooth removal.

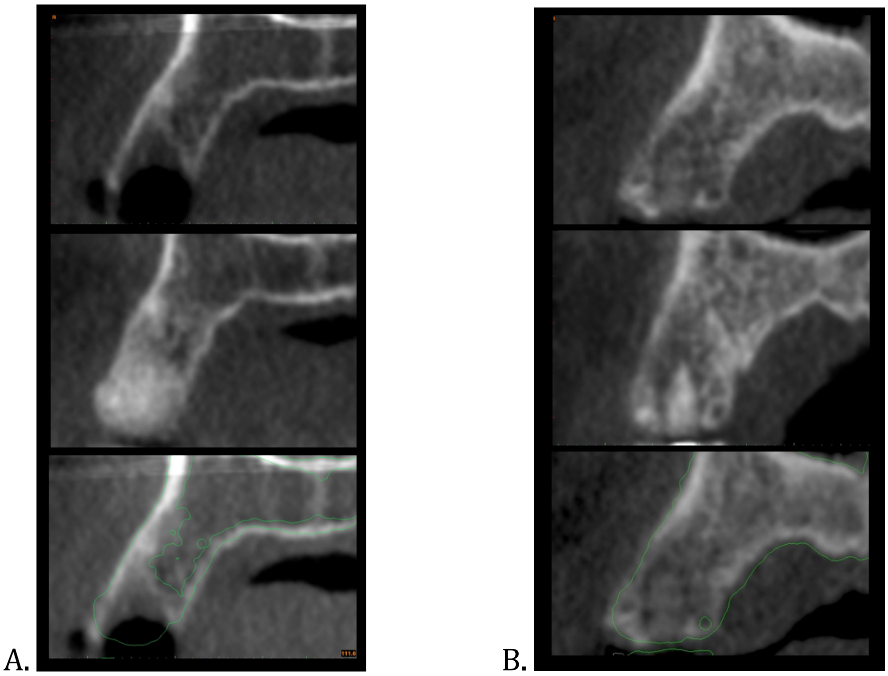
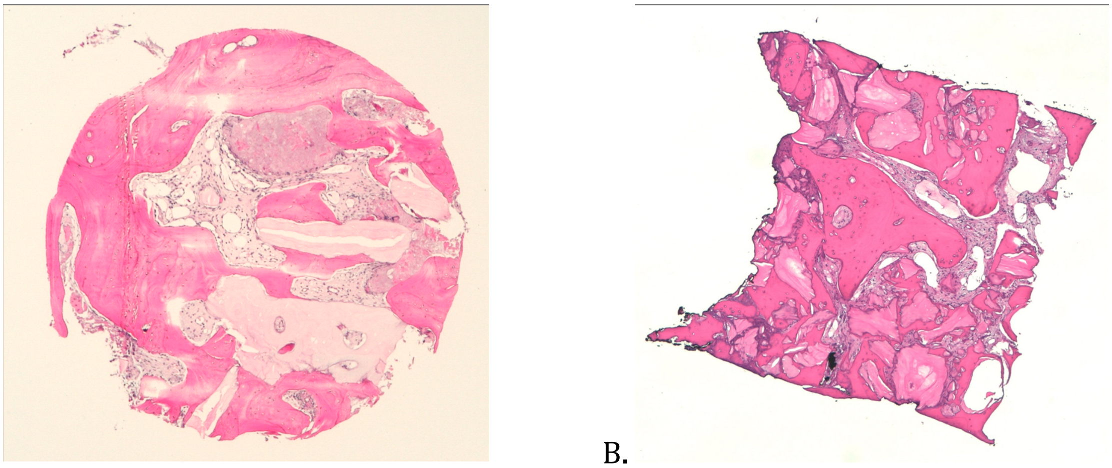


Figure 9. A. Site treated with DBBM at baseline and at 5 months healing. The lower image shows the CBCT superposition and the dimensional changes. B. Baseline and 5-month situation at a site treated with DBBM-C. Dimensional changes can be observed at on the CBCT superposition.

Our randomized clinical trial focused on osseous dimensional changes but information regarding soft tissues was lacking. In this sense, Schneider et al. (2014) analysed soft tissue changes on digitalized study casts in ridge preservation with DBBM-C plus a collagen membrane and natural healing sockets and observed a more pronounced ridge width reduction in the control group, but the differences were not statistically significant. Regarding the position of the mucosal margin, Rocuzzo et al. (2014) observed no differences in the marginal soft tissue levels 10 years after placing implants in areas treated with DBBM-C and control sites.

Histologic outcomes

From a histomorphometric point of view, we may compare our outcomes with the data collected in the presented systematic review. Thus, in non preserved sockets, the percentage of newly formed bone and connective tissue at 4 to 7 months ranged between 45.8-56.1% and 0-57.7% respectively. DBBM and DBBM-C sites showed a slightly lower percentage of newly formed bone (33.44±17.82% and 37.68±13.38). However, if we take into account that most residual particles (13.14 ± 8.32% 16±11.60%) were surrounded by vital bone, we could consider these graft remnants as part of the osseous structure (Carmagnola et al. 2003; Araújo et al. 2008, 2009, 2010).



A. B.

Figure 10. A. Histological section of a socket treated with DBBM. B. Histological section of a socket treated with DBBM-C.

The histomorphometric outcomes of the presented randomized clinical trial are in agreement with previous data. The use of DBBM and a collagen membrane resulted in 33.44% of newly formed bone at 5 months of healing, which is slightly superior to previous investigations. Norton et al. (2003) found 26.9% newly formed bone, Lee et al. (2009) 23.6% and Vance et al. (2004) 26% at 4 to 6 months of healing. Moreover, we observed a mean percentage of 13.14% of residual graft particles while other investigations report around 25% at 4-6 months of healing (Norton et al. 2003; Lee et al. 2009). When it comes to DBBM-C, samples showed 37.68% of newly formed bone. This is in agreement with previous findings were 32.83% of newly formed bone was found after

5 months of healing after grafting the extraction sockets with DBBM-C (Cook & Mealey, 2013). However, other reports have shown around 25% of newly formed bone at 3 and 4 months of healing (Cardaropoli et al. 2013; Alkan et al. 2013; Heberer et al. 2011). It may be assumed that, the longer the healing period, the more vital bone will be formed and therefore, a greater amount was encountered in the specimens of the present study at 5 months.

CONCLUSIONS

According to the results of the presented publications, we may conclude that:

- Due to the high heterogeneity of the included studies with respect to study design, healing time, sample size, inclusion criteria or surgical approach it was very difficult to assess which type of graft material is ideal in ridge preservation procedures from an histological point of view.

- In terms of newly formed bone, magnesium enriched hydroxyapatite, calcium sulfate and porcine xenografts seem to offer the most promising results. However, autografts, allografts ans alloplastic materials resulted in a similar bone quantity as natural healing sites suggesting that they might also be suitable for ridge preservation.

- DBBM and DBBM-C minimize alveolar ridge alterations in a similar manner. Histologically, there are no significant differences between them at 5 months of healing. Thus, both biomaterials may be suitable for ridge preservation.

- Buccal bone thickness does not seem to have an influence on bone volume changes at sites grafted with DBBM and DBBM-C.

FUTURE PERSPECTIVES

A huge effort towards keeping the alveolar ridge intact has been made in the last years in order to achieve an aesthetic outcome. Ridge preservation seems to be an efficient procedure but there are still some questions to be answered. *Which surgical approach is more effective in avoiding ridge reduction? What graft material should be used? How long should we wait to place an implant? What happens to the soft tissues during the healing process? How stable are soft and hard tissues in the long term?* Due to the little available evidence, further well-designed randomized clinical trials with a negative control group should try to elucidate these questions.

Most of the investigations on ridge preservation have included sockets with intact walls. Nowadays, there is clear evidence that placing implants in fresh extraction sockets is a predictable treatment alternative if there is an adequate quantity of basal bone and all the socket walls are present. Immediate implants not only shorten the treatment time, but also reduce the number of surgical interventions. Even in sockets with previous chronic periapical infection immediate implants have succesfully been placed. However, there is limited information comparing the effectivennes of implants placed in ridge preserved areas and immediate implants with simultaneous bone grafting in terms of implant survival, esthetic outcomes, complication rates as well as maintenance of hard and soft tissue dimensions. If both interventions were equally effective, the indication for ridge preservation would probably be limited to pontic areas, 3-wall sockets and/or insufficent basal bone to ensure primary stability of the implant.

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ANNEXES

Annex I: Letter of aproval of the PhD project

Universitat Internacional de Catalunya

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uic barcelona

En Barcelona, a 27 de noviembre de 2015

LUCÍA BARALLAT SENDAGORTA

Apreciada Lucía:

Por la presente te comunico que después de la reunión de la Comisión Académica del Doctorado en Salud, la Escuela de Doctorado ha recibido la aprobación de cambio del proyecto de tesis aprobado inicialmente.

Aprovecho para recordarte que según lo estipulado en el Real Decreto 99/2011, tu plazo máximo de defensa es el 30 de septiembre de 2017.

Recibe un saludo muy cordial

Universitat Internacional de Catalunya
uic barcelona

Dra. Consuela Dobrescu
Secretaria de la Escuela de Doctorado
Universitat Internacional de Catalunya

Annex II: Approval of the Ethical Commitee

Universitat Internacional de Catalunya

La Comisión Científica de la Facultad de Odontología de la Universitat Internacional de Catalunya, CERTIFICA, que

El presente protocolo de investigación titulado: "**Preservación del reborde alveolar con Bio-Oss y una membrana colágena comparado con Bio-Oss Collagen y una membrana colágena en áreas para la colocación de implantes: un estudio clínico e histológico en humanos.**", cuyo investigador principal es el Dr. José Nart y cuyo investigador secundario son los alumnos **Lucia Barallat y Daniel Jiménez,** y cuyos tutores son Vanessa Ruiz Magaz y Santiago Mareque.

ha sido evaluado satisfactoriamente y es apto para ser presentado e iniciar su investigación.

Firmado en Sant Cugat del Vallès, a 13 de mayo del 2011.

Universitat Internacional de Catalunya
Facultat d'Odontologia

Dr Lluis Giner Tarrida
Director de la Comisión Científica de Odontología

Titulo:	**Preservación del reborde alveolar con Bio-Oss y una membrana colágena comparado con Bio-Oss Collagen y una membrana colágena en áreas para la colocación de implantes: un estudio clínico e histológico en humanos.**
Investigador secundario:	**Lucia Barallat y Daniel Jiménez**
Director de la investigación:	**Dr. José Nart**
Tutor:	**Vanessa Ruiz Magaz y Santiago Mareque**
Número de estudio:	**PER-ECL-2011-05-CM.**

Annex III: SEPA/Inibsa/Osteology Research Academy Scholarship (July 2014)

SEPA

FUNDACIÓN
ESPAÑOLA
DE PERIODONCIA
E IMPLANTES
DENTALES

Estimada Dra. Barallat:

Desde SEPA, y como participante de la convocatoria de becas organizada por INIBSA y SEPA con su trabajo de título "Preservación del alveolo utilizando Bio-Oss® y una menbrana de colágeno comparado con Bio-oss Collagen® y una menbrana de colágeno en áreas para la colocación de implantes. Un estudio histológico en humanos", le doy la más sincera enhorabuena por ser el ganador de una de ellas.

Nuevamente le felicitamos y le agradecemos que nos ayude a crecer como Sociedad científica.

Reciba un cordial saludo,

Antonio Bujaldón Daza
Secretario

Annex IV: SEPA-Osteology Foundation Award (SEPA Valencia, May 2016)

Evaluación radiográfica e histológica comparando injerto bovino desproteneizado versus injerto bovino desproteneizado en una matriz de colágeno en técnicas de preservación alveolar. Un ensayo clínico randomizado a doble ciego.

L. Barallat, D. Jiménez, J. Mestres, A. Gómez, J. Nart, V. Ruíz-Magaz

SEPA Osteology Foundation

INTRODUCCIÓN

Estudios en modelos animales y humanos han observado que, después de la extracción dental, la cresta alveolar sufre una reducción en anchura y altura.[1,2] Estas alteraciones pueden comprometer el resultado estético de nuestros tratamientos, sobretodo cuando se planifica una rehabilitación implantosoportada.
Con el objetivo de minimizar dichos cambios, se ha propuesto la introducción de injertos óseos en el alveolo.[3,4]
El injerto bovino desproteneizado (DBBM) y el injerto bovino desproteneizado en una matriz de colágeno (DBBM-C) han sido ampliamente utilizados en terapias regenerativas.[5,6] Sin embargo, no se han publicado estudios comparando ambos materiales.

OBJETIVOS

1. Comparar los cambios dimensionales entre alveolos preservados con DBBM y DBBM-C 5 meses después de la extracción dental.
2. Evaluar si existe asociación entre el grosor inicial de la tabla vestibular y los cambios dimensionales de la cresta alveolar.
3. Comparar DBBM y DBBM-C a nivel histológico en cuanto a porcentaje de nuevo hueso formado, tejido conectivo y partículas residuales.

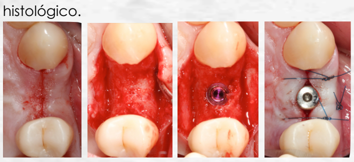
MATERIAL Y MÉTODOS

Pacientes sanos con dientes no molares deshauciados que fuesen a ser extraídos y rehabilitados posteriormente con un implante.
Criterios de inclusión: dientes unitarios con dientes vecinos sin patología periapical aguda ni periodontitis avanzada, alveolos de 4 paredes.

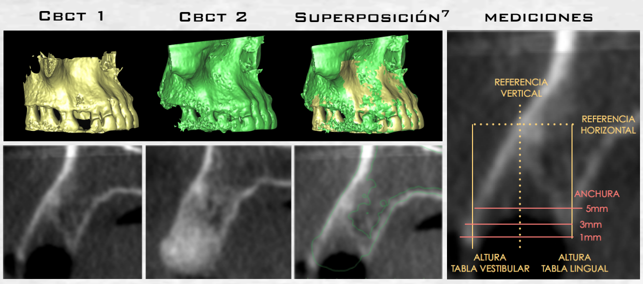
SECUENCIA

Justo después de la extracción se tomó un CBCT (CBCT1).
Dos grupos de tratamiento asignados de forma randomizada:

A los 5 meses, previamente a la colocación del implante, se tomó un segundo CBCT (CBCT2) y se obtuvo una biopsia del área previamente preservada para su análisis histológico.

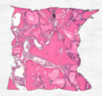


EVALUACIÓN RADIOGRÁFICA



EVALUACIÓN HISTOLÓGICA

Decalcificación, seccionamiento y tinción con hematoxilina-eosina.
Fotografías estandarizadas a 40x para su análisis histomorfométrico.



% hueso nuevo
% tejido conectivo
%partículas residuales

RESULTADOS

22 Localizaciones / 21 pacientes (edad media: 56.76 años). No había diferencias estadísticamente significativas entre grupos al inicio del estudio

RESULTADOS RADIOGRÁFICOS

No se observó correlación entre la anchura inicial de la tabla vestibular y reducción en anchura y altura de la cresta alveolar (P>0.05)

Ambos grupos de mostraron una reducción significativa en anchura y altura (P>0.05)

No se observaron diferencias significativas entre grupos en altura ni anchura a 1 y 3mm (Tabla).

	Grupo	Media±SD
Diferencia en altura tabla vestibular (P=0.92)	DBBM DBBM-C	0.61±0.77mm 0.98±1.28mm
Diferencia altura tabla lingual (P=0.76)	DBBM DBBM-C	0.65±0.65mm 0.82±0.61mm
Diferencia en anchura a 1mm (P=0.29)	DBBM DBBM-C	0.91±1.35mm 1.53±1.53mm
Diferencia en anchura a 3mm (P=0.24)	DBBM DBBM-C	0.35±0.31mm 0.78±0.76mm
Diferencia en anchura a 5mm **(P=0.0011*)**	DBBM DBBM-C	0.06±0.17mm 0.16±0.76mm

RESULTADOS HISTOLÓGICOS

Se incluyeron 18 muestras.
No se observaron diferencias estadísticamente significativas entre grupos en cuanto a porcentaje de hueso nuevo formado, partículas residuales y tejido conectivo.

	DBBM	DBBM-C
Nuevo hueso formado (%) P=0.89	33.44±17.82%	37.68±13,38%
Partículas residuales (%) P=0.75	13.14±8,32%	16.00±11.60%
Tejido conectivo (%) P=0.69	53.88±17.43%	50.31±19.20%

CONCLUSIONES

1. No parece que haya diferencias entre DBBM y DBBM-C en cuanto a su capacidad para minimizar los cambios dimensionales de la cresta alveolar.
2. El grosor inicial de la tabla vestibular no parece estar asociado con la reducción en anchura y altura de la cresta.
3. Ambos grupos de tratamiento mostraron una composición histológica similar.

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La Dra. **LUCÍA BARALLAT** ha recibido **PREMIO AL MEJOR PÓSTER DE COMUNICACIÓN SEPA-OSTEOLOGY FOUNDATION,** por el trabajo *"Evaluación radiográfica e histológica comparando injerto bovino desproteneizado vs injerto bovino desproteneizado en una matriz de colágeno en técnicas de preservación alveolar. Un ensayo clínico randomizado a doble ciego"* firmado por Lucía Barallat ,Daniel Jiménez, Jaume Mestres, Alberto Gómez, Vanessa Ruiz Magaz y José Nart en la **50ª Reunión Anual de SEPA** celebrada en Valencia los días 12 al 14 de Mayo de 2016.

Y para que así conste a los efectos oportunos, firma el presente Certificado en Valencia, a 14 de Mayo 2016.

Dr. Antonio Bujaldón
Secretario de SEPA

Dr. Kay Horsch
Director Ejecutivo Osteology Foundation